# HANDBOOK OF CHILDREN'S PALLIATIVE CARE MALAYSIA

Chief Editor | Dr. Lee Chee Chan | Dr. Tan Chai Eng

Kementerian Kesihatan Malaysia

# HANDBOOK OF

# CHILDREN'S PALIATIVE CARE

# MALAYSIA

Chief Editors

Dr Lee Chee Chan & Dr Tan Chai Eng

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## Contents

## FOREWORD FROM YB. MINISTER OF HEALTH, MALAYSIA

Assalammualaikum warahmatullah wabarakatuh and salam sejahtera,

I would like to first congratulate the editors and all who have contributed to the development of this Handbook of Children's Palliative Care Malaysia. This is the first handbook of its kind in Malaysia and we should be proud of this achievement.

The core of the National Palliative Care Strategy 2019-2030 is the provision of holistic and comprehensive care for patients with life-limiting illnesses. The Ministry of Health sees the importance of such care especially for our pediatric population. In line with this, there is a need to expand our pediatric palliative care services. Besides optimizing quality of life in these children, it will also provide much needed support for their families. More importantly, it is the patients' right to receive good palliative care, and this is seen in-line with the World Health Organization (WHO) recommendation.

This handbook provides a concise and practical guide for healthcare workers on the core concepts of pediatric palliative care, symptom management, multidisciplinary management, care transition as well as end of life care. In recognition of the different settings and resources available in Malaysia, this handbook has been adapted to local healthcare settings.

I believe this handbook will be useful to guide our local healthcare professionals in providing palliative care to children.

Thank you and keep pressing forward for our children's benefit.

**Dato' Seri Dr Adham Baba**
Minister of Health, Malaysia

## FOREWORD FROM THE DIRECTOR GENERAL OF HEALTH

Assalamualaikum and may everyone be in good health,

The National Palliative Care Policy and Strategic Plan (2019-2030) was first launched on 6th November 2019 at Selayang Hospital. This policy helps to ensure comfort and dignity is part of the standard care for children facing life-limiting illnesses.

However, as we know, palliative care needs for children are unique and to a certain extent, different from adults. Many of the rare conditions that require palliative intervention may not be familiar to all clinicians and caregivers. The needs of each child may also differ depending on their developmental milestone. Hence, we must have the right knowledge, supervision and training for healthcare professionals and better collaboration between public and private hospitals, community health clinics, and non-governmental organisations to manage children requiring paediatric palliative care better, together.

This Handbook of Children's Palliative Care Malaysia offers practical guidance to various levels of healthcare professionals irrespective of their clinical background. The modules address essential aspects and provide common grounds for clinical management of paediatric palliative care. The contributors of this handbook have covered a wide breadth of topics including symptom control, support to the living family, respecting choice and allowing dignified care at the end-of-life. They have also emphasised the importance of understanding the unique needs of each child and family.

I wish to commend the efforts of the committee and all those involved in making this handbook a reality. The Handbook of Children's Palliative Care Malaysia is a testament of the continuous commitment by the Ministry of Health and the Government of Malaysia in our effort to achieve the Sustainable Development Goals and 'Leaving No One Behind'.

**Datuk Dr Noor Hisham bin Abdullah**
Director General of Health, Malaysia

# PREFACE

Palliative care for children is an approach to improve the quality of life of children with life-limiting illnesses and their family, by preventing and relieving suffering. Healthcare services for children would be incomplete without provision of paediatric palliative care (PPC) services. Unfortunately, there is still a great unmet need for PPC in Malaysia.

PPC is relevant to various life-limiting diseases in children including perinatal conditions, chromosomal abnormalities, congenital malformations and deformations, malignancies and neurological disorders. An estimated 80,000 Malaysian children will require PPC at some point of their life, based on a prevalence analysis of conditions which warrant PPC support. Of these, nearly a third will require specialist PPC support. However, PPC services in Malaysia are still far from adequate to meet these needs.

While palliative care services for adults have been developing steadily in Malaysia since the 1990s, PPC is still lagging far behind. Many regions, especially rural areas, still do not have access to PPC services. PPC services in Malaysia was championed by individual paediatricians in hospitals since 2008. To date, most PPC services are provided by individual paediatricians in public hospitals and by non-governmental organisations (NGOs) in the community. Sadly, after a decade, PPC provision has yet to achieve nationwide coverage, even in urban areas.

Different levels of PPC can be provided by different healthcare professionals, including general paediatricians, family physicians, general practitioners, and paediatric nurses. All healthcare professionals who work with children should receive basic training to provide level I PPC. Meanwhile, specialist doctors who frequently care for children with serious life-threatening conditions, such as oncologists, cardiologists, intensivists and neonatologists, should receive intermediate-level training for level II PPC. PPC training for these healthcare professionals would benefit from a practical and concise manual for PPC to guide them in their day-to-day practice.

This handbook was written with the combined experience and expertise of more than thirty contributors, consisting of paediatric palliative paediatricians, senior paediatricians, family medicine specialists, nurses, and allied health workers. These contributors were involved in providing palliative care for their patients and family in their respective settings, utilising available but limited resources. Work on this handbook, which began since April 2019, have been carefully reviewed and adapted to our local culture and healthcare settings.

This handbook is an essential tool for the implementation of the National Palliative Care Policy and Strategic Plan 2019-2030. We hope that this handbook will aid Malaysia to achieve the three main goals for PPC in the National Policy which are:

1. To expand PPC services in all major hospitals by incorporating PPC into comprehensive paediatric care.
2. To achieve seamless and holistic transition of PPC from hospital to community and home.
3. To systematically establish community-based PPC services.

We would like to take this opportunity to thank all the people involved in this handbook writing, as well as Dr Hishamshah bin Mohd Ibrahim (ex-National Advisor for Paediatrics) and the Medical Development Division, Ministry of Health, Malaysia, for their invaluable support.

We look forward to seeing Paediatric Palliative Care develop further to meet the needs of Malaysian children.

**From the Editors of the Handbook**

## EDITORS

**Dr Lee Chee Chan**
*Paediatric Palliative Paediatrician,*
Dept of Paediatrics, Hospital Tunku Azizah (previously Kuala Lumpur Women and Children's Hospital)

*President,*
Malaysian Association of Paediatric Palliative Care (MAPPAC)

**Dr Tan Chai Eng**
*Family Medicine Specialist and Lecturer,*
Department of Family Medicine, Universiti Kebangsaan Malaysia.

## CO-EDITORS

**Dr Sharifah Najwa Binti Syed Mohamad**
*Family Medicine Specialist and Lecturer,*
Family Medicine Unit, Primary Care Department, Faculty of Medicine and Health Sciences, Universiti Sains Islam Malaysia.

**Dr Lim Shu Xian**
*Palliative Medicine Subspecialty Trainee,*
Internal Medicine Specialist, Ministry of Health, Malaysia.

**Dr Halimah Abdul Halim**
*Paediatrician, Department of Paediatrics,*
Faculty of Medicine and Health Sciences, Universiti Sains Islam Malaysia.

# LIST OF CONTRIBUTORS

**Dato Dr Kuan Geok Lan**
*Clinical Associate Professor,*
Dept of Paediatric,
International Medical University

**Dr Ch'ng Gaik Siew**
*Consultant Clinical Geneticist,*
Dept of Genetics, Hospital Pulau Pinang.

**Dr Fahisham Taib**
*Paediatric Palliative Paediatrician and Lecturer,*
Dept of Paediatrics, Universiti Sains Malaysia.

**Dr Janet Liew Huey Jing**
*Paediatrician*
Dept of Paediatrics, Hospital Umum Melaka.

**Dr Kamal Abu-Shamsieh**
Ziyara Spiritual Care.

**Dr Lee Chee Chan**
*Paediatric Palliative Paediatrician,*
Dept of Paediatrics, Women and Children's Hospital Kuala Lumpur.

**Dr Lim Voon Lee**
*Paediatrician,*
Dept of Paediatrics, Hospital Pulau Pinang.

**Dr Ng Su Fang**
*Paediatrician,*
Dept of Paediatrics, Sabah Women and Children's Hospital.

**Dr Rozita bt Zakaria**
*Consultant Family Medicine Specialist,*
Klinik Kesihatan Presint 18, Putrajaya.

**Dr Susan Pee**
*Consultant Paediatric Nephrologist,*
Dept of Paediatrics, Hospital Sultan Ismail.

**Dr Tan Chai Eng**
*Family Medicine Specialist and Senior Lecturer,*
Dept of Family Medicine, Universiti Kebangsaan Malaysia.

**Dr Tan Mei See**
*Paediatrician,*
Dept of Paediatrics, Hospital Seberang Jaya.

**Dr Tan Ru Wei**
*Paediatrician,*
Columbia Asia Hospital, Klang.

**Dr Teoh Yen Lin**
*Paediatrician,*
Dept of Paediatrics, Hospital Seberang Jaya.

**Dr Zainah Sheikh Hedra / Hidrah**
*Consultant Paediatrician,*
Dept of Paediatrics, Hospital Batu Pahat.

**Ee Su Im**
*Occupational Therapist,*
Dept of Occupational Therapy, Women and Children's Hospital Kuala Lumpur.

**Hidayah Rosli**
*Pharmacist,*
Dept of Pharmacy, Women and Children's Hospital Kuala Lumpur.

**June Thow Mei Jiun**
*Palliative Care Nurse,*
ASSISS Palliative Service, Hospital Assunta.

**Karen Sim Kai Loon**
*Clinical Psychologist,*
Dept of Psychiatry, Women and Children's Hospital Kuala Lumpur.

**Maggie @ Umairah Balqis Liong bt Abdullah**
*Registered Nurse*
Dept of Paediatrics, Women and Children's Hospital Kuala Lumpur.

**Nisha a/p Gunasakaran**
*Palliative Care Nurse,*
Hospis Malaysia.

**Nor Azura Abd Majid**
*Medical Social Worker,*
Dept of Medical Social Welfare, Women and Children's Hospital Kuala Lumpur.

**Sakinah Alhabshi**
Ziyara Spiritual Care

**Sornaletchumi a/p Koran**
*Physiotherapist,*
Dept of Physiotherapy, Women and Children's Hospital Kuala Lumpur

# REVIEWERS

## *INTERNATIONAL REVIEWERS*

**Dr Chong Poh Heng**
*Medical Director,*
HCA Hospice Care, Singapore

**Dr Rever Chak-Ho Li**
*Consultant Paediatrician,*
Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital, Hong Kong

**Serene Wong Su Ling**
*Palliative Care Nurse,*
HCA Hospice Care, Singapore

## *MALAYSIAN REVIEWERS*

**Dr Aaron Hiew Wi Han**
*Palliative Medicine Physician,*
Hospital Kuala Lumpur.

**Dr Aina Mariana bt Abdul Manaf**
*Consultant Paediatrician and Head of Paediatric Department,*
Hospital Port Dickson.

**Dr Khoo Teik Beng**
*Consultant Paediatric Neurologist,*
Dept of Paediatrics, Hospital Tunku Azizah, Kuala Lumpur.

**Dr Lam Chee Loong**
*Palliative Medicine Physician,*
Faculty of Medicine, Universiti Malaya.

**Dr Chong Lee Ai**
*Consultant Paediatrician, Pain and Palliative Care Unit,*
Dept of Paediatrics, Faculty of Medicine, Universiti Malaya.

**Dr Intan Nor Chahaya bt Abdul Shukor**
*Consultant Paediatrician,*
Dept of Paediatrics, Hospital Segamat.

**Dr Teoh See Wie**
*Family Medicine Specialist,*
Klinik Kesihatan Segamat.

**Dr Yang Wai Wai**
*Clinical Psychologist and Lecturer,*
Dept of Paediatrics, Faculty of Medicine, Universiti Kebangsaan Malaysia.

**Dr Richard Lim Boon Leong**
*Consultant and National Advisor of Palliative Medicine,*
Palliative Care Unit, Hospital Selayang.

**Dr Salmiah Mohd Shariff**
*Consultant Family Medicine Specialist,*
Klinik Kesihatan Seremban.

**Dr Sri Wahyu Taher**
*Consultant Family Medicine Specialist,*
Klinik Kesihatan Simpang Kuala.

**Dr Teh Siao Hean**
*Consultant Paediatrician,*
Dept of Paediatrics, Sarawak General Hospital.

**Prof Col (R) Dr Wan Pauzi bin Wan Ibrahim**
*Consultant Paediatric Cardiologist,*
Faculty of Medicine, Universiti Sultan Zainal Abidin (UNISZA)

**Prof Dr Tong Seng Fah**
*Assistant Dean & Professor of Family Medicine,*
Faculty of Medicine, Universiti Kebangsaan Malaysia.

**Lee Voon Yee**
*Visiting Clinical Pyschologist,*
Klinik Yeoh and Hazli.

**Muslimah Yusof**
*Chief Matron,*
Tunku Azizah Women and Children's Hospital, Kuala Lumpur.

## LIST OF ABBREVIATIONS

| | |
|---|---|
| AADC | Aromatic l-amino acid decarboxylase |
| ACP | Advanced care plan |
| ACT | Association of Children's Palliative Care |
| ADLs | Activity of Daily Living |
| AED | Anti- epileptic Drug |
| AML | Acute Myeloid Leukemia |
| CAUTI | Catheter-associated urinary tract infection |
| CF | Compassion fatigue |
| CFU | Colony-forming unit |
| CN | Cranial nerve |
| CSCI | Continuous Subcutaneous Infusion |
| CTZ | Chemoreceptor Trigger Zone |
| DIVC | Disseminated Intravascular Coagulation |
| FFP | Fresh frozen plasma |
| FMS | Family medicine specialist |
| GABA | Gamma aminobutyric acid |
| GERD | Gastro-oesophageal reflux disease |
| GI | Gastrointestinal |
| GLUT 1 | Glucose Transporter Type 1 |
| GMFCS | Gross Motor Function Classification System |
| ICP | Intra-cranial pressure |
| ID | Intellectual Disability |
| JKM | Jabatan Kebajikan Masyarakat |
| JPA | Jabatan Perkhidmatan Awam |
| LTOT | Long-term oxygen therapy |
| MACAS | Malaysian Children Aid Society |
| MAKNA | Majlis Kanser Nasional |
| MAPPAC | Malaysian Association of Paediatric Palliative Care |
| MAS | Modified Ashworth Scale |

| | |
|---|---|
| MDT | Multidisciplinary team |
| MSAS | Memorial System Assessment Scale |
| NGO | Non -government organization |
| NICU | Neonatal Intensive Care Unit |
| NIV | Non-invasive ventilation |
| NMDA receptor | N-Methyl-D Aspartate receptor |
| NRD | National Registration Department |
| OKU | Orang kurang upaya / persons with disabilities |
| OT | Occupational therapist |
| OT | Operating theatre |
| PaPaS | Paediatric Palliative Screening |
| PCC | Percutaneous cervical cordotomy |
| PICU | Paediatric Intensive Care Unit |
| PLAN | Paediatric Longitudinal Assessment of Needs |
| PPC | Paediatric Palliative Care |
| ProQOL | Professional Quality of Life (c) |
| PT | Physiotherapy |
| RCPCH | Royal College of Paediatrics and Child Health |
| ROM | Range of movement |
| SCP | Symptom Care Plan |
| SLT | Speech and language therapy |
| SOP | Standard operating procedure |
| SPUB | Sistem Pendispensan Ubat Bersepadu / Integrated Drug Dispensing System |
| STS | Secondary traumatic stress |
| TBP | Tabung Bantuan Perubatan / Medical Aid Fund |
| TCE | Trans-catheter chemo-embolisation |
| UTI | Urinary tract infection |
| WHO | World Health Organisation |

# Module 1

## Introduction to Paediatric Palliative Care

- Introduction to palliative care for children
- Referral to paediatric palliative care
- Patient assessment during follow up

# Module 1:
# Introduction to Paediatric Palliative Care

## *World Health Organisation (WHO) definition of palliative care for children*[1]

Palliative care for children represents a special, albeit closely related field to adult palliative care. The World Health Organization (WHO) defines palliative care appropriate for children as:

"The active total care of child's body, mind and spirit in the prevention and relief of suffering associated with life-threatening illness and involves giving support to the family."

The principles of palliation apply to all chronic paediatric disorders. It begins when the illness is diagnosed and continues regardless of whether the child receives treatment directed at the disease. Health providers must evaluate and alleviate the child's physical, psychological, social and spiritual distress.

Effective palliative care requires a broad multidisciplinary approach that includes the family and utilizes available community resources; it can be successfully implemented even if resources are limited.

It can be provided in tertiary care facilities, in community health centres and at home.

## *Why is palliative care in children different from adult palliative care?*[2]

Palliative care needs for children is unique and very different from adult palliative care:

- Types of health conditions: While some conditions overlap with those in adult palliative care, many chronic non-communicable diseases are congenital in nature and may have genetic causes. The natural history of these conditions is different. The prognosis and life expectancy may be unclear especially for the rarer conditions.

- **Developmental milestones:** Palliative care needs will change as the child grows older, depending on the child's developmental milestones. These needs involve age-appropriate information, recreation/play, education and coping mechanisms.
- **Dilemmas in decision-making:** Children's status as minors from a legal viewpoint puts decision-making in the hands of their parents or legal guardians. The level of maturity required for making decisions will evolve as the child grows older, with issues involving the child's wishes and rights. In most cases, decisions are made based on parents, family members and healthcare professionals' discussion on what would be the best interests for the child and the whole family.

### *Palliative care needs of children in Malaysia*

To date, Malaysia does not have a registry of children who suffer from 'life-limiting conditions'. The World Health Organization estimates that 63 out of every 100,000 children aged less than 15 years will require palliative care annually.[1]

From a global cross-sectional analysis of prevalence, it is estimated that about 80,000 (0.29%) Malaysian children would need some form of palliative care and 28.5 per 10 000 population aged 0 to 18 years require specialised palliative care.[3] Specialised palliative care provides full time palliative services which includes complex symptom management, communication regarding goals of care, coordinating multidisciplinary team meetings, terminal and end-of-life care, transition care, parental support for grief and bereavement.

Paediatric palliative care is relevant for children from the perinatal period until the age of 18 years. In 2016, the two commonest causes of death for the under five age group are conditions originating in the perinatal period and congenital malformations, namely deformations (35.0%) and chromosomal abnormalities (27.2%).[4] This highlights the need for perinatal palliative care services in our country.

Beyond the neonatal period, the commonest categories of children that have palliative care needs are those with neurological disorders and neoplasms.[5]

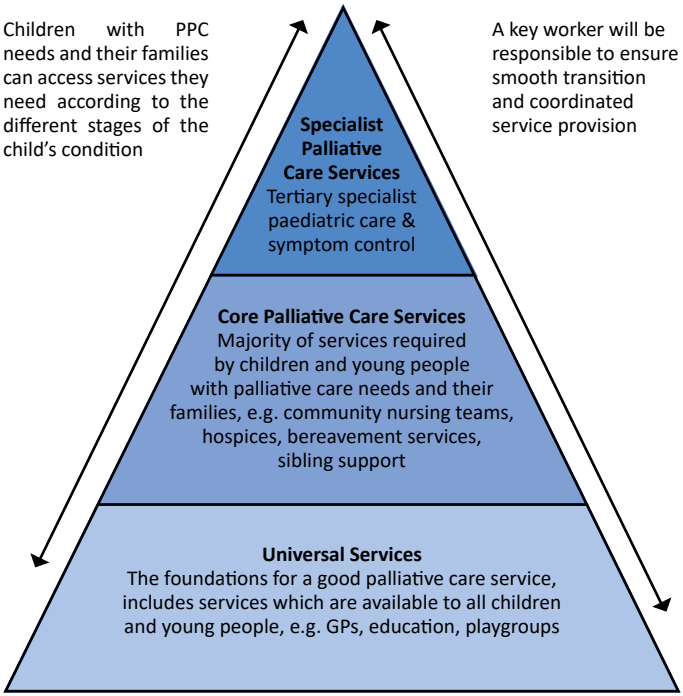
All these children need a holistic approach to meet their needs in all aspects (physical, psychosocial, spiritual and emotional). Bereaved parents of children with life-limiting illnesses in Malaysia perceived inadequate symptom control for their children but there was also poor communication and lack of anticipatory guidance in care.[6]

Many Malaysian healthcare providers lack knowledge and understanding of palliative care, with 79% citing the lack of accessible palliative care services as biggest barrier for referral.[7] Thus, health care providers need to be trained to manage this special group of children.

### *Who can provide paediatric palliative care (PPC)?*

Palliative care should be part of comprehensive paediatric care.

| Level | Provision of PPC |
|---|---|
| **I** | Basic PPC services can be provided by paediatricians, general practitioners, family medicine specialists and paediatric nurses with basic training in PPC principles. |
| **II** | Specialist doctors who frequently care for children with serious or life-threatening conditions, such as oncologists, cardiologists, intensivists and neonatologists, general paediatricians should be required to receive intermediate-level training in PPC. |
| **III** | Specialist PPC consultants and teams should be involved if a child or young person has unresolved distressing symptoms especially when they approach the end of life. |




**Levels of paediatric palliative care[8]**

### *Who are the children who need palliative care?[9]*

Children who need palliative care are children with the following conditions:

- **Life-threatening conditions:** Illnesses or conditions with a high risk of dying for children or young adults, and for which medical treatment may cure but may also fail, resulting in death.
- **Life-limiting conditions:** Illnesses or conditions for which there is no cure, and which are extremely likely to result in death at some point in time during childhood or young adulthood.

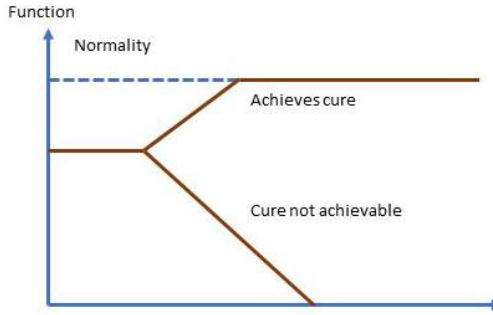
Categories and disease trajectory of life-threatening and life-limiting condition (ACT/RCPCH categories)[10]

| Category | Definition | Palliative care needs |
|---|---|---|
| **1** | Life-threatening conditions for which curative treatment may be feasible but can fail. Access to palliative care services may be necessary when treatment fails or during an acute crisis, irrespective of the duration of threat to life. On reaching long-term remission or following successful curative treatment there is no longer a need for palliative care services. | Intensive symptom management and psychosocial support beginning from diagnosis |
| | Example: Cancer, irreversible organ failures of heart, liver, kidney. | |
| **2** | Conditions when premature death is inevitable. There may be long periods of intensive treatment aimed at prolonging life and allowing participation in normal activities. | Requires longer term palliative care support, beginning with rehabilitation and caregiver support, and leading to symptom management and end-of-life care as the disease progresses. |
| | Example: Cystic fibrosis, Duchenne muscular dystrophy. | |
| **3** | Progressive conditions without curative treatment options. Treatment is exclusively palliative and may commonly extend over many years. | Symptoms will change over time. Goals of care is more focused on symptom management rather than rehabilitation. |
| | Example: Batten disease, mucopolysaccharidoses. | |

| Category | Definition | Palliative care needs |
|---|---|---|
| **4** | Irreversible but non-progressive conditions causing severe disability, leading to susceptibility to health complications and likelihood of premature death. | Caregiver training especially home care is essential in the beginning phase. Provision of caregiver support, nursing care and respite care is the main need for this category. |
| | Example: Severe cerebral palsy (GMFCS level VI or level V), multiple disabilities such as following brain or spinal cord injury, complex health care needs, high risk of an unpredictable life-threatening event or episode. | |

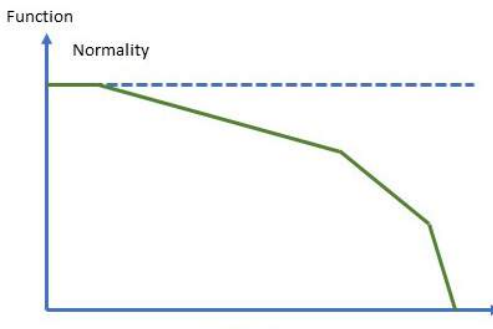
*GMFCS = Gross motor function classification system

Disease trajectories based
on ACT/RCPCH categories



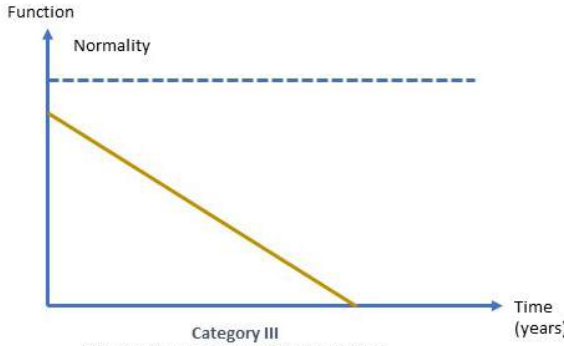

**Category I**

Life-threatening conditions for which curative treatment may be feasible but can fail. Access to palliative care services may be necessary when treatment fails or during an acute crisis, irrespective of the duration of threat to life. On reaching long-term remission or following successful curative treatment there is no longer a need for palliative care services.

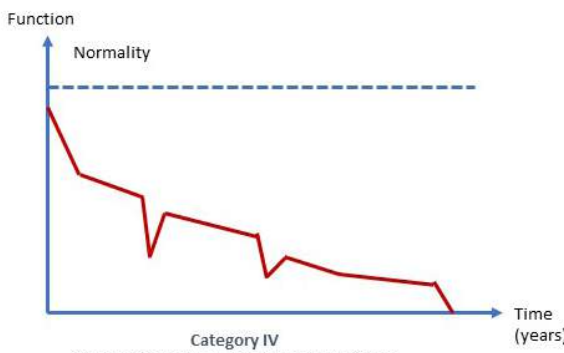



**Category II**

Conditions when premature death is inevitable. There may be long periods of intensive treatment aimed at prolonging life and allowing participation in normal activities.




**Category III**
Progressive conditions without curative treatment options. Treatment is exclusively palliative and may commonly extend over many years.




**Category IV**
Irreversible but non-progressive conditions causing severe disability, leading to susceptibility to health complications and likelihood of premature death..

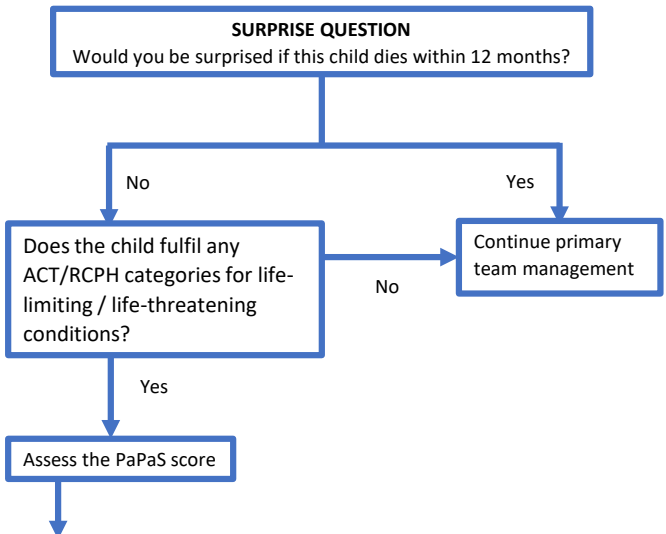
## *The scope of paediatric palliative care*

Paediatric palliative care encompasses:

- Supportive care and symptom management during curative treatment or life-prolonging treatment
- Symptom management and optimisation of quality of life when curative treatment is unavailable or is not an option
- End-of-life care
- Grief and bereavement support

Paediatric palliative care may go hand-in-hand alongside curative treatment, with varying levels of involvement at different stages of illnesses.

## *Referral to paediatric palliative care*




| PaPas Score | Action | Provider | Priority of care |
|---|---|---|---|
| **0-9** | Evaluation | Primary team | Curative treatment |
| **10-14** | Explain goals of PPC | Primary team | Life-prolonging treatment with supportive symptom management |
| **15-24** | Prepare start of PPC | Primary team with PPC consultation | |
| **25 and above** | Start PPC | Primary team with PPC consultation | Symptom management, psychosocial care and possible end-of-life care |

### *Introducing Paediatric Palliative Care (PPC) to family*

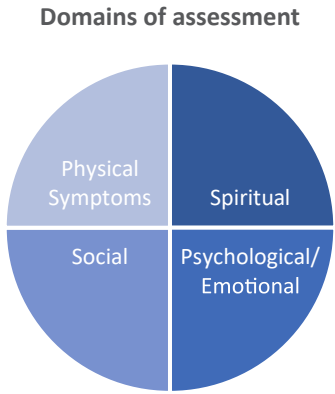
The following are useful phrases when communicating with family members to introduce the role of paediatric palliative care:

- As an extra layer of support, besides the primary team.
- To lessen child's symptom that is bothering him/her.
- To provide family support (physical, psychosocial and spiritual).

It is also useful to integrate paediatric palliative care into current services, such as clinics, inpatient management, home visits and policies.

Seamless provision of PPC services will reduce family apprehension towards the perception of PPC as loss of hope. Instead it should promote hope for better quality of life and prevent the perception of abandonment.

### *Patient assessment during follow up*

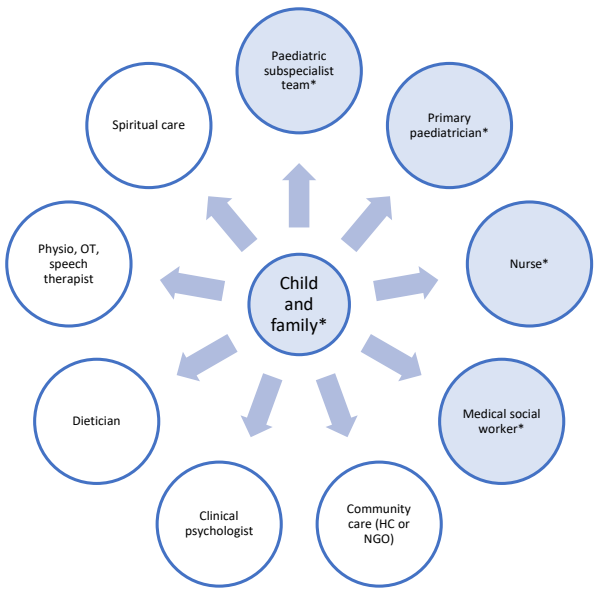



It is important to ensure that holistic assessment (bio-psychosocial-spiritual) of the child's care needs are done as care planning and reviewed regularly as the child's condition progresses.

a) General holistic assessment
b) Comprehensive assessment using validated tools e.g. Memorial Symptom Assessment Scale (MSAS) – there are versions for children of different ages.
c) Specific symptom assessment tools, e.g. pain scale, dyspnoea scale, functional disability inventory.

## *Multidisciplinary team (MDT)*

Children with life-limiting conditions have simple to complex needs that changes across the disease trajectory. The multidisciplinary team (MDT) approach is tailored to individual needs and optimising the use of available resources. This requires coordinating care across different disciplines and care settings.




***Core members of the multi-disciplinary team (MDT) HC=home care***

The extended multidisciplinary team (MDT)

Members of the MDT meet not just the child and caregivers regularly to assess needs but also with the rest of the team members to formulate a care plan to address those needs. This enhances collaborative decision-making and sets out agreed goals of care. After the plan is executed, the outcomes should be monitored, and the care plan revised or updated as necessary.

An example of a structured MDT assessment is shown below in the form of the Paediatric Longitudinal Assessment of Needs (P.L.A.N.) Guidelines.

### *Paediatric Longitudinal Assessment of Needs (PLAN) Guidelines*

| No | Domain | Issues |
|---|---|---|
| 1 | Physical / nursing care | Pain<br>Fever<br>Diarrhoea or Constipation<br>Nausea or vomiting<br>Bladder/urinary problems<br>Wounds or pressure sores<br>Cough<br>Itch<br>Swelling of arms, legs or abdomen (oedema)<br>Breathing-related problems<br>Insomnia / Sleeping problems<br>Gastro-intestinal problems<br>Diet and nutrition |
| 2 | Psycho-emotional | Acceptance, coming to terms with the disease<br>Stress<br>Depression, negative emotions<br>Anticipatory grief<br>Guilt and shame<br>Anxiety and anger<br>Fears of physical suffering/pain, death, treatment, abandonment, uncertainties of the future<br>Loss of emotional control<br>Changed body image and its associated emotions<br>Overwhelmed by decision-making family/patient)<br>Fulfilling patient's last wishes<br>Bereavement support (family) |

| No | Domain | Issues |
|---|---|---|
| 3 | Practical / Financial | Equipment related: BIPAP, CPAP, suctioning, ventilator, O2 concentrator/cylinder<br>Daily needs- Nutrition, Diapers<br>Special beds (e.g hospital bed), ripple mattress<br>Respite care<br>Transportation (clinic, hospital, school)<br>Extra family expenditure due to the illness<br>Reduced family income due to the illness |
| 4 | Social / Family | Spouse<br>Parent-child<br>Extended family relationships (grandparents, etc)<br>Healthcare team in the hospital<br>Healthcare team in community<br>School<br>Friendship |
| 5 | Spirituality/ Existential | Sense of playing a useful role<br>Ability to be present for others' needs<br>Loss of faith - God or religion<br>The meaning of life and death<br>Loss connection with the self (i.e. self-acceptance, self-esteem) |
| 6 | Legal / Ethical | Legal matters (last will and testament, insurance etc.)<br>Ethical decision making / dilemmas |

Adapted from STAR PALS ( Singapore HCA Hospice Care)

## *Appendix*

**Revised PaPaS scale[11,12]**

| | | | |
|---|---|---|---|
| **Domain 1: Trajectory of disease and impact on daily activities of the child** | | | |
| 1.1.1 | With reference to the past 3 months, the disease trajectory of the child, in comparison with the child's own baseline, is… | …Stable | 0 ☐ |
| | | …Stable, but slowly deteriorating | 1 ☐ |
| | | …Unstable with slow deterioration | 2 ☐ |
| | | …Unstable with significant deterioration (Please skip 1.1.2) | 4 ☐ |
| 1.1.2 | With reference to the past 3 months, the impact of condition on daily activities of the child, in comparison with the child's own baseline. | No impact | 0 ☐ |
| | | Daily activities are impacted/ restricted | 1 ☐ |
| | | Daily activities are severely impacted/restricted | 2 ☐ |
| 1.2 | In the past 6 months, there was a more than 50% increase in unplanned hospital admissions *(compared to previous periods)* | No | 0 ☐ |
| | | Yes | 3 ☐ |
| **Domain 2: Expected outcome of treatment directed at the disease and burden of treatment** | | | |
| 2.1 | Treatment directed at the disease, even if not administered…<br><br>(does not include treatment of disease-related complications, such as pain, dyspnea or fatigue) | …is curative. | 0 ☐ |
| | | …controls disease and prolongs life with good quality of life. | 1 ☐ |
| | | …does not cure or control but has a positive effect on quality of life. | 2 ☐ |
| | | …does not control and has no effect on quality of life. | 4 ☐ |
| 2.2 | Burden of treatment, including both disease-directed and symptom-directed treatments.<br><br>(consider frequency and skills involved; e.g. side effects, hospital stay, additional tasks for patients/caregivers) | No/minimal burden OR no treatment is planned | 0 ☐ |
| | | Low level of burden (e.g. simple oral medication or diet modification) | 1 ☐ |
| | | Medium level of burden (e.g. feeding tubes, catheters, medications with adverse effects) | 2 ☐ |
| | | High level of burden (e.g. hospitalization, tracheostomy, BiPAP/C-PAP, PICC line, frequent suctioning) | 4 ☐ |

| Domain 3: Symptom and problem burden | | | |
|---|---|---|---|
| 3.1.1 | Symptom intensity over the past 3 months (consider unplanned hospitalization or outpatient visits, symptom crises) | Patient is asymptomatic (Please skip 3.1.2) | 0 ☐ |
| | | Symptom(s) are mild | 1 ☐ |
| | | Symptom(s) are moderate | 2 ☐ |
| | | Symptom(s) are severe (Please skip 3.1.2) | 4 ☐ |
| 3.1.2 | Difficulty of symptom control over the past 3 months (consider unplanned hospitalization or outpatient visits, symptom crises) | Symptom(s) are easy to control | 0 ☐ |
| | | Symptom(s) are controllable | 1 ☐ |
| | | Symptom(s) are difficult to control | 2 ☐ |
| 3.2 | Psychological distress of patient related to symptoms | Absent | 0 ☐ |
| | | Mild | 1 ☐ |
| | | Moderate | 2 ☐ |
| | | Significant | 4 ☐ |
| 3.3 | Psychological distress of parents or family related to symptoms and suffering of the child | Absent | 0 ☐ |
| | | Mild | 1 ☐ |
| | | Moderate | 2 ☐ |
| | | Significant | 4 ☐ |
| **Domain 4: Preferences of Health Professional** | | | |
| 4.1 | Patient/parents wish to receive palliative care or formulate needs that are best met by palliative care. | No | 0 ☐ |
| | | Yes (Please skip 4.2) | 4 ☐ |
| 3.1.2 | You or your team feel that the patient would benefit from palliative care. | No | 0 ☐ |
| | | Yes (Please skip 4.2) | 4 ☐ |
| **Domain 5: Estimated Life Expectancy** | | | |
| 5.1 | Estimated life expectancy/Prognosis | Several years | 0 ☐ |
| | | 1 – 2 years | 1 ☐ |
| | | 3 months to a year (Please skip 5.2) | 3 ☐ |
| | | Less than 3 months (Please skip 5.2) | 4 ☐ |
| 5.2 | Would you be surprised if this child died in 6 months' time? | Yes | 0 ☐ |
| | | No | 2 ☐ |
| | | Total | |
| Decision | | | |

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# Module 2

## Symptom Management

- Pain
- Cardiorespiratory symptoms: Breathlessness, chest pain, cough, hiccups
- Neurological symptoms: Dystonia, Seizures, Sleep disturbance
- Renal failure: Uraemia
- Haematological problems: Anaemia, bleeding
- Gastrointestinal symptoms: Nausea and vomiting, constipation, diarrhoea, anorexia-cachexia
- Perinatal palliative care pathway
- Nursing care: Oral care, tube feeding, gastrostomy tube care, tracheostomy care, urinary care, bedbound patients
- Multidisciplinary paediatric palliative care
- Caregiver and healthcare provider self-care
- Spiritual Care

# Module 2: Symptom Management

## Pain

### *Definition*

Pain is any unpleasant sensory or emotional experience associated with tissue damage or described by the patient in those terms, e.g. burning, stabbing pain. [1]

### *Concept of total pain*

Pain interacts with other forms of distress and contributes to overall suffering in patients.

Pain is multi-dimensional; it is helpful to think in terms of total pain, encompassing physical, psychological, social and spiritual aspects of suffering. [2]

| Physical Pain | Psychological Pain |
|---|---|
| • Nociceptive pain<br>• Neuropathic pain<br>• Aggravated by other symptoms (e.g. nausea, fatigue)<br>• Adverse effects of treatment (e.g. chemotherapy)<br>• Concurrent multiple causes of pain | • Anger<br>• Anxiety<br>• Sad<br>• Loneliness<br>• Fear<br>• Previous experience of pain |
| **Spiritual Pain** | **Social Pain** |
| • Hopelessness<br>• Loss of faith<br>• Fear of unknown<br>• Anger at fate / higher power<br>• Personal image | • Dependency on family members<br>• Discontinuation of learning in school<br>• Family conflict<br>• Isolation from peers |

## *Pathophysiology of pain*

There are multiple pathways involved in pain perception:

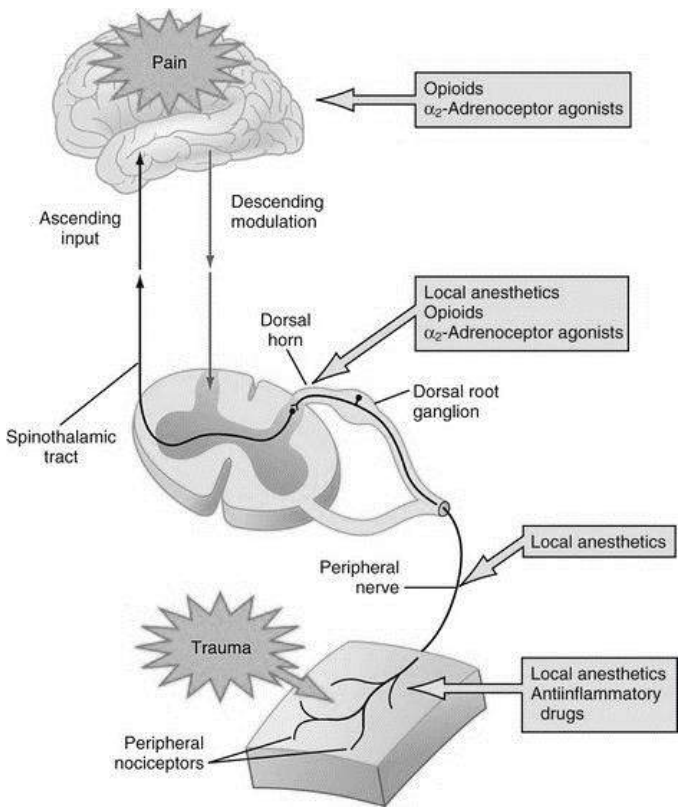
a) Ascending myelinated and unmyelinated fibres

The pathway where pain stimulus is carried from the peripheral nociceptors to the brain

b) Descending inhibitory pathways for pain modulation

The pathway which controls the quality and perceived severity of the pain

Ascending and descending pain pathway and its analgesic[3]



### *Classification of pain*

There are various classifications of pain.

- **Pathophysiological mechanism of pain** (nociceptive or neuropathic)
- **Duration of pain** (chronic or acute, breakthrough pain)
- **Aetiology** (cancer or non-cancer)
- **Anatomic location of pain** (myofascial, rheumatic, skeletal, neurological and vascular)

| **Nociceptive pain** | |
|---|---|
| • Originates from mechanical, chemical or thermal damage to body tissue<br>• Subdivided into somatic / visceral pain<br>• Involve activation of nociceptors | |
| **Somatic pain** | Nociceptors in either surface tissues (skin, mucosa of mouth, nose, urethra, anus)<br>Superficial somatic pain - sharp and localised<br>Deep somatic pain - dull and aching |
| **Visceral pain** | Nociceptors located in the visceral organs (e.g. gut, ureters)<br>Diffuse, difficult to localise<br>May have referred pain e.g. diaphragm irritation referred to right shoulder tip |

| **Neuropathic pain** |
|---|
| • Results from abnormal nerve function e.g. nerve damage by drugs, impingement by tumours, or physical damage to the nerve itself.<br>• **Allodynia** – pain caused by stimulus which usually does not cause pain e.g. light touch.<br>• **Hyperalgesia** – increased or excessive pain from a stimulus which can cause pain<br>• Examples of neuropathic pain: spinal cord metastases causing pain over related somatosensory area, phantom pain after limb amputation |

### *Causes of pain*

In palliative care, pain can generally be divided into cancer or non-cancer pain.

| Cancer pain | Non-cancer pain |
|---|---|
| • Pain directly associated with tumour (tumour infiltration, bone metastasis)<br>• Pain associated with cancer therapy (chemotherapy, surgery or radiation)<br>• Pain due to cancer debility (decubitus) | • Arthritis<br>• Metabolic neuropathies<br>• Chest pain<br>• Post-traumatic injury<br>• Post-stroke pain<br>• Immobility<br>• Abdominal pain<br>• Peripheral vascular disease<br>• Decubitus ulcers and other skin disorders |

### *Principles of pain assessment (Q.U.E.S.T.T.)*

The following are principles to guide pain assessment in a child[4]

**Q**uestion the parent/ child
**U**se appropriate pain rating scale
**E**valuate behaviour / physiologic change
**S**ecure family involvement
**T**ake holistic cause of pain into account
**T**ake action and evaluate results

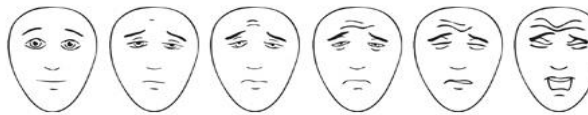
### *Pain Assessment Tools*

There are various tools that can be used to assess severity of pain. Tools are chosen based on child's developmental age and verbal ability.

### *Faces Pain Scale*

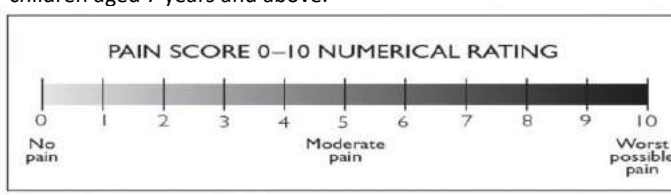
• Can be used in children less than 7 years of age.[5]

• Say to the child, “Point to the face that shows how much you hurt (right now)”




### *Numeric Scale*

• Use zero (no pain) to 10 (worst pain you can imagine) scale for children aged 7 years and above.[6]




### *FLACC Scale*

This is a nonverbal pain scale which can be used in children aged 1 month to 3 years.[7]

| Category | Scoring | | |
|---|---|---|---|
| | 0 | 1 | 2 |
| Face | No particular expression or smile | Occasional grimace or frown, withdrawn, disinterested | Frequent to constant quivering chin, clenched jaw |
| Legs | Normal position or relaxed | Uneasy, restless, tense | Kicking or legs drawn up |
| Activity | Lying quietly, normal position, moves easily | Squirming, shifting back and forth, tense | Arched, rigid or jerking |
| Cry | No cry (awake or asleep) | Moans or whimpers, occasional complaint | Crying steadily, screams or sobs, frequent complaints |
| Consolability | Content, relaxed | Reassured by occasional touching, hugging or being talked to, distracted | Difficult to console or comfort |
| Each of the five categories (F) Face, (L) Legs, (A) Activity, (C) Cry, (C) Consolability, is scored from zero to two, which results in a total score between zero and 10. | | | |

## *Non-pharmacological pain management*

| Method | Examples |
|---|---|
| **Physical methods** | Cuddles/hugs, massage, comfort positioning, heat, cold, TENS (Transcutaneous Electrical Nerve Stimulation) |
| **Cognitive behavioural techniques** | Guided imagery, Hypnosis, Abdominal breathing, Distraction, Biofeedback |
| **Multi-sensory** | Acupuncture, Acupressure, Aromatherapy |
| **Infants** | Nesting / Swaddling, Kangaroo care, Dimming light and noise, and Administration of breast milk or sucrose for painful procedures |
| **Parental involvement** | Soothing environment, favourite toys, distraction, books, bubbles, interactive story-telling, asking the child what helps |

## *Principles for cancer pain management*

| Principles[8] | Description |
|---|---|
| **BY THE CLOCK**<br>***Dosing at regular intervals*** | Regular scheduling ensures steady blood level, reducing peaks and troughs of PRN-dosing |
| **BY THE INDIVIDUAL**<br>***Adapting treatment to the individual child*** | Treatment should be tailored to individual child<br>Opioid analgesics should be titrated on individual basis |
| **BY THE MOUTH**<br>***Using the appropriate route of administration*** | Use oral/enteral route<br>Alternative routes: sublingual, buccal, transdermal, rectal |
| **BY THE LADDER**<br>***Using a 2-step strategy*** | **WHO step 1:**<br>Mild pain, use paracetamol and/or ibuprofen<br><br>**WHO step 2:**<br>Moderate to severe pain, use Morphine, Fentanyl, Oxycodone, Methadone |

### *Pharmacological management (based on WHO ladder)*

| Step 1: Mild to moderate pain[8] | | |
|---|---|---|
| **Medication** | **Mode of action** | **Caution** |
| **Paracetamol** | Simple analgesic and antipyretic. Weak inhibitor of the synthesis of prostaglandins (PGs) and interacts on serotonergic, opioid, nitric oxide and cannabinoid pathways in CNS. | Side effects are rare in recommended doses, hepatotoxicity if overdose |
| **Ibuprofen** | Non-steroidal anti-inflammatory drugs (NSAIDs). Inhibit cyclo-oxygenase (COX) mediated prostaglandin production. Side effects are related to COX-1 inhibition. | Peptic ulcer, GI bleed, platelet dysfunction, nephrotoxicity, cardiac events |

| Step 2: Moderate to severe pain[8] | | |
|---|---|---|
| **Medication** | **Mode of action** | **Caution** |
| **Morphine** | Strong opioid that binds to mu, kappa, gamma opioid receptors to block the release of substance P in CNS and dorsal horn of spinal cord.<br>Duration of action: 3-4 hours<br><br>Active metabolites morphine-6-glucuronide and morphine-3-glucuronide can lead to neurotoxicity, especially in renal impairment. | Common side effects:<br>Nausea, vomiting, constipation, drowsiness<br><br>Uncommon side effects:<br>Sweating, euphoria, pruritus, myoclonus, delirium |

| Step 2: Moderate to severe pain[8] | | |
|---|---|---|
| **Medication** | **Mode of action** | **Caution** |
| **Transdermal fentanyl** | Suitable for stabilised background pain.<br>100 times more potent than morphine.<br>Duration of action: 48-72 hours.<br>Preferred for patients with renal impairment – accumulation of inactive metabolites | Not for initial titration or breakthrough pain.<br>Sedative<br>Caution must be used in handling/ disposal of patches.<br>Absorption affected by changes in body temperature. |
| **Oxycodone** | Short-acting and long-acting preparations available<br>Oral oxycodone is 1.5 more potent than oral morphine<br>IV oxycodone is equipotent to IV morphine<br>Duration of action: 3-4 hours | Side effects comparable to morphine<br>Reserved for those who are unable to tolerate morphine due to cost considerations |
| **Methadone** | Useful for both neuropathic and nociceptive pain.<br>Preferable for patients with renal impairment.<br>Only indicated if patient is unable to tolerate other opioids or poor response to morphine. | Needs experience in titration. Consult paediatric palliative care specialist. |

## *Case example for opioid titration*

Aiman is a 10-year-old boy with relapsed Acute Lymphoblastic Leukemia with bone metastasis. He complains of generalised pain with pain score of 6/10. He is opioid naïve with normal renal and liver function. His weight is 20kg and he is currently at home.

1. Please give the choice of opioid, route of administration and write the opioid prescription.

   Immediate release oral Morphine 0.2mg/kg/dose x 20kg = 4mg q4h (maximum initial dose is 5mg/dose for children) = 24mg/day

   Breakthrough dose: 1/10 to 1/6 of daily dose (2.5mg-4mg), can be served 1-2 hours after previous dose of morphine.

2. Aiman requires 4 breakthrough doses of 4mg Morphine in a day, please titrate his morphine dose.

   Total morphine 24mg + 16mg = 40mg/day
   Dose adjusted to 6mg every 4 hour, breakthrough dose 6mg prn

3. Aiman's pain is well-controlled with oral morphine 40mg/day with no breakthrough dose required, what next?

   As pain is well-controlled with oral morphine 40 mg/day, morphine can be converted to extended-release morphine with 20mg every 12h and breakthrough dose of oral morphine of 5mg prn

## *Opioid switching*

Different opioids have different side effect profiles and pharmacological properties. Individuals will have different responses to different types of opioids. Switching or rotating opioids may be indicated if:

- pain is not well controlled despite optimal titration
- intolerable side effects occur with morphine
- development of renal impairment
- patient cannot swallow oral medications

*Opioid conversion table*

| To / From | Oral codeine mg/d | Oral morphine mg/d | SC/IV morphine mg/d | Oral Oxycodone mg/d | Fentanyl patch mcg/h |
|---|---|---|---|---|---|
| **Oral codeine mg/d** | | ÷8 | ÷20 | ÷12 | ÷24 |
| **Oral morphine mg/d** | x8 | | ÷2.5 | ÷1.5 | ÷3 |
| **SC/IV morphine mg/d** | x20 | x2.5 | | ÷0.6 | ÷1.2 |
| **Oral Oxycodone mg/d** | x12 | x1.5 | x0.6 | | ÷2 |
| **Fentanyl patch mcg/h** | x24 | x3 | x1.2 | x2 | |

Adapted from Malaysian Clinical Practice Guidelines for Cancer Pain Management 2010[6]

*Examples of opioid conversion*

**1. Oral morphine to IV/SC morphine**
Divide dose of oral morphine by 2.5 to convert to IV/SC morphine.
10mg of oral morphine is equivalent to 4mg of IV or SC morphine.

**2. Fentanyl patch**
When converting total daily oral morphine dose to fentanyl patch (divide by 3), round up to the lower adjustable dose. The lowest dose is 6.25mcg/h (half of the 12.5mcg/h patch).

| Oral morphine | Fentanyl patch |
|---|---|
| 45 mg /24h | 12.5 mcg/h |
| 90 mg/24h | 25 mcg/h |
| 180 mg/24h | 50 mcg/h |

**2. Oxycodone**
When converting from oral morphine to oral oxycodone, use an initial dose conversion ratio of 1.5:1
e.g. 15 mg Morphine = 10mg Oxycodone, then titrate to optimize the analgesia.

## *Medications for neuropathic pain*

In children, neuropathic pain can be treated with NSAIDs, opioids or other agents such as gabapentinoids, anticonvulsants and tricyclic antidepressants.[10]

Medications used for neuropathic pain

| Medication | Mechanism of action | Undesirable effects |
|---|---|---|
| Amitriptyline | Prevent re-uptake of serotonin and norepinephrine | Anti-muscarinic effects, drowsiness, postural hypotension |
| Gabapentin | Inhibition of glutamate excitatory system. Selective calcium-channel blockage | Drowsiness, dizziness, ataxia, headache, and myoclonus |
| Pregabalin | Selective calcium-channel blockage | Drowsiness, dizziness, ataxia, headache, and myoclonus |
| Sodium Valproate | Block influx of sodium ions, preventing depolarization and generation of an action potential. | Drowsiness, tremor, hair thinning, hair loss, menstrual irregularities, weight gain, and thrombocytopenia. |
| Methadone* | NMDA receptor antagonist | Nausea, vomiting, constipation, dry mouth, biliary spasm, respiratory depression, drowsiness, muscle rigidity, hypotension, bradycardia. |
| Ketamine* | NMDA receptor antagonist | Dissociated hallucination, agitation, anxiety, dysphoria, sleep disturbance, urinary tract symptoms (dysuria, hematuria) |

*(required specialist advice)

*Interventional strategies for pain control*

| Procedures | Indications | Benefits |
|---|---|---|
| Regional anaesthesia[10] (Epidural or intrathecal neurolytic blocks) | Post-operative pain<br>Neuropathic pain<br>Terminal pain | Modifies the neuroendocrine stress response, provides profound post-operative pain relief, ensure a more rapid recovery, shorten hospital stay, fewer opioid-induced side effects. |
| Percutaneous cervical cordotomy (PCC)[11] | Unilateral pain below the clavicle | Ablates the sensory pathways of the lateral spinothalamic tract |

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# Cardiorespiratory Symptoms

## *Breathlessness*

### *Definition*

Breathlessness is the **unpleasant subjective sensation of being unable to breathe adequately[1].**

### *Pathophysiology*

It arises from **mismatch** between the need of breathing and the perceived work of breathing, related to activity of **mechanoreceptors** (stretch receptors in airways, lung parenchyma, intercostal muscles and diaphragm), **chemoreceptors** (hypoxia and hypercarbia) and **direct ascending stimulation** from respiratory centre (anxiety, claustrophobia).[2]

### *Possible Causes*

Dyspnoea or breathlessness is a complex symptom involving physiological, psychological, environmental and functional factors.

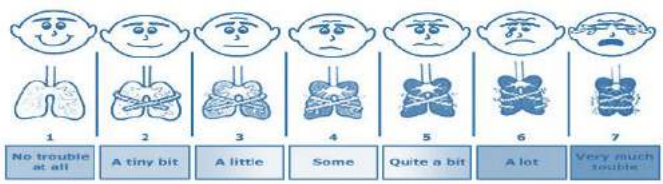
| Pathophysiology | Causes |
|---|---|
| Airway obstruction | Congenital airway anomaly<br>Bronchial asthma<br>External compression or invasion by tumour |
| Intrathoracic extra-parenchyma abnormalities | Pneumothorax<br>Pleural effusion<br>Lung empyema |
| Lung parenchyma abnormalities | Pneumonia<br>Pulmonary haemorrhagic tumour<br>Pulmonary oedema |
| Psychological | Anxiety |
| Ventilation: perfusion (VQ) mismatch | Anaemia |
| External compression of the diaphragm | Ascites<br>Massive intra-abdominal tumour |

### *Assessment*

Assessing dyspnoea in children can be challenging. Children may describe dyspnoea as “chest pain”, “tummy pain”, or “tiredness”. Usually the degree of breathlessness is interpreted clinically based on their level of activities.

Formal scoring may be done at baseline and after intervention for children who are able to understand the scale. Care should be taken in interpreting the scale as it is highly dependent on the child’s understanding and perception of the symptom.

### *Paediatric Dyspnoea Scale*[3]




### *Numerical rating scale (1- 10)*

### *Non-pharmacological management*

- Use a hand-held fan towards the face
- Cooling and open space (open windows, air conditioner)
- Loose and comfortable clothing
- Positioning (usually the child will choose their most comfortable position)
- Breathing techniques (deep breathing, pursed-lip breathing, abdominal breathing)
- Relaxation and distraction (music visualisation, art, play, massage) for anxiety management
- Chest physiotherapy (percussion, vibration and postural drainage).
- Encourage cough (staggered breathing technique) for patients with neuromuscular disorders.
- Calm approach to patient and family
- Consider additional non-invasive breathing support. Carefully weigh the benefits and risks of NIV for each patient because they may cause more symptoms or worsening breathlessness in certain cases. NIV may cause secretion retention, airway dryness, claustrophobia, and barotrauma.
- Plan and schedule the activities to avoid over-exertion

### *Pharmacological and Procedural Management*

| Causes | Treatment of underlying causes |
|---|---|
| Upper airway obstruction | Steroids, tracheostomy, radiotherapy |
| Bronchospasm | Bronchodilators, steroids |
| Pneumonia | Antibiotics |
| Heart Failure | Diuretics |
| Pleural Effusion | Pleural drainage, pleurodesis |
| Anaemia | Blood transfusion, erythropoietin |
| Superior vena cava obstruction | Steroid, radiotherapy, chemotherapy |

| Treatment | Symptom management for dyspnoea |
|---|---|
| Oxygen | • Use if $SpO_2$ < 90% or patient finds oxygen supplement helpful |
| Non-Invasive Ventilation (NIV) | • Consider early use for children with neuromuscular disorder who are admitted for pneumonia.<br>• Increase ventilator setting or check for machine dysfunction if child is already on 24-hour home ventilation NIV. |
| Opioids | • Reduces the sensation of breathlessness<br>• Do not cause respiratory depression at recommended doses<br>• Give 1/3 of the pain dosage (starting dose of Sy morphine 0.05 to 0.1 mg/kg/dose 4 hourly and prn).<br>• Consider concurrent laxative to avoid constipation |
| Anxiolytics | For episodic anxiety:<br>• Short acting e.g. midazolam<br>• Intermediate acting e.g. alprazolam lorazepam<br>For sustained anxiety:<br>• Long-acting e.g. oral clonazepam, diazepam |

# Chest pain

## *Introduction*

Chest pain in children can be very alarming for parents, but very few have a cardiac cause.[4]

## *Causes and pathophysiology*

| Common Causes | Pathophysiology of pain |
|---|---|
| Costochondritis (most common) | Inflammatory process of costochondral cartilages that causes localized tenderness and pain of the anterior chest wall due to direct trauma, aggressive exercise, repeated cough or idiopathic. |
| Pneumonia | Pleurisy. Worsening sharp pain after cough. |
| Upper gastrointestinal causes (e.g. oesophagitis, gastritis, reflux | Raised intra-abdominal or intra-gastric pressure (e.g. from dystonia, tube feeding, scoliosis), gastro-oesophageal sphincter dysfunction (e.g. NG tubes, hiatus hernia)<br>Drugs (anticholinergics, steroids and non-steroidal anti-inflammatory agents). |
| Anxiety | Children respond less well to change, uncertainty, blocked communication, stressful home and school life. |
| Cardiac causes: e.g. pericarditis, myocarditis | Referred pain from the heart |

### *Assessment*

Look for:

- signs of cardiorespiratory distress (poor perfusion, hypotension, hypoxia, muffled heart sound, distended neck veins).
- risk factors of underlying serious disorders.

| Important causes | Associated features |
|---|---|
| Cardiac causes | Pain radiating to arm or back<br>Associated dizziness or collapse<br>Underlying congenital cardiac disease and connective tissue disease |
| Pulmonary embolism | Pleuritic pain<br>Sudden onset dyspnoea<br>Haemoptysis<br>Hypoxia<br>Possible causes: malignancy, blocked or infected central venous catheter, deep vein thrombosis. |
| Respiratory causes | Tachypnoea<br>Abnormal lung examination findings e.g. pneumonia, foreign body, pneumothorax, asthma exacerbation and lung collapse. |
| Gastroesophageal reflux | Symptoms related to food intake and positioning |

### *Non-pharmacological management*

| **Costochondritis** |
|---|
| Local analgesia (methylsalicylate or NSAID cream)<br>Stretching exercises<br>Application of ice for 20-minute intervals<br>Advise to minimize activity of the patient's upper limbs |
| **Anxiety** |
| Listen to the child's ideas, concerns, thoughts, feelings and fears especially about death and illness |
| Explain to the child that anxiety is normal and acceptable when they are facing illness |
| Maximize normalization – keep family routine, boundaries, school activities unchanged |
| Advise on non-pharmacological methods for anxiety – listening or playing music, cuddling, breathing techniques, progressive muscle relaxation, guided visualization and relaxation. |
| Avoid false reassurance. Be honest when answering their questions and promote positive coping mechanism. |
| Manage the family as a whole |
| Consider referral for formal psychotherapy |
| **Gastroesophageal Reflux** |
| Diet modification: frequent small meal, food thickener (commercial or rice/corn flour) |
| If on tube feeding, adjust the volume, rate or frequency of feeding |
| Positioning: Left lateral position when not feeding. Prop up during and immediately after feeding for at least 30 minutes |
| Drugs: Withhold or reduce causative drugs |

### *Pharmacological management*

| **General** |
| --- |
| Treat the underlying causes (such as the underlying causes of persistent cough) |
| **Costochondritis** |
| Paracetamol and Non-steroidal Anti-inflammatory Drugs (NSAIDS) |
| **Anxiety** |
| Refer to section for breathlessness |
| **Gastroesophageal Reflux** |
| Antacids and raft forming agents such as alginates<br>H2-antagonists (e.g. ranitidine) or proton-pump inhibitors (e.g. omeprazole or lansoprazole)<br>Prokinetic (Domperidone / metoclopramide / erythromycin to improve gastric emptying)<br>Consider surgery if failed medical treatment (e.g. fundoplication) |

# Cough

## *Introduction*

Coughing is a physiological defence mechanism that helps to prevents pulmonary aspiration, promotes ciliary activity and clears airway debris.[5]

## *Pathophysiology*

Cough becomes pathological and needs further assessment and management when:

- It becomes ineffective e.g. in neuromuscular diseases or poor cognitive function
- It adversely affects sleep, rest, eating and social activities
- It causes complications such as muscle strain, rib fracture, vomiting, syncope, headache or urinary incontinence
  Cough efficiency depends on physical/ mechanical aspects (respiratory muscles, mucus, airway calibre and larynx) and integrity of the neurophysiological pathway of cough.

## *Possible causes*

- Infection
- Gastro-oesophageal reflux
- Post-nasal drip
- Asthma
- Impaired swallowing in neurological conditions
- Foreign bodies in the airway
- Psychogenic cough
- Congenital lung conditions e.g. cystic fibrosis

## *Assessment*

History and physical examination to look for underlying causes and complication of cough

Distinguish between

- Episodic and recurrent cough
- Productive/wet cough and dry cough

### *Management*

*Productive/ Wet cough*

| Non-pharmacological management |
| --- |
| For patients who still can cough effectively, encourage them to cough with steam inhalation or nebulized sodium chloride 0.9% PRN to loosen tenacious mucous, together with position, breathing technique and chest percussion/vibration |
| **Pharmacological management** |
| • N-acetylcysteine - reduce sputum viscosity<br>• Antibiotic may be appropriate as symptomatic treatment to reduce secretion<br>• Nebulised salbutamol for bronchospasm<br>• Consider steroid and radiotherapy for lung tumours |

*Dry Cough*

| Non-pharmacological management |
| --- |
| • Encourage fluid intake<br>• Lozenges to sooth the throat<br>• Avoid cigarette smoke |
| **Pharmacological management** |
| Cough suppression with<br>• Non-opioid linctus<br>• Codeine*/pholcodine* linctus<br>• Oral morphine syrup<br>• Promethazine |

* Use with caution in children <12 years old

# Hiccups

## *Introduction*

Hiccup is an abnormal respiratory reflex characterised by spasm of one or both sides of the diaphragm, causing sudden inspiration with associated closure of the vocal cords.[6]

## *Pathophysiology*

This reflex involves phrenic nerve, vagus nerve, thoracic sympathetic fibres brainstem and hypothalamus. This reflex arc is usually inhibited by pharyngeal and glossopharyngeal nerves. Any disturbance to this reflex arc may cause hiccup.

## *Possible causes*

- Liver metastasis with diaphragmatic irritation
- Uraemia
- Gastro-oesophageal reflux
- Pneumonia
- Gastric distension
- Medications (e.g. benzodiazepines, ondansetron)
- Air swallowing (eating too fast, smoking)
- Anxiety
- Brain tumour
- Noxious fumes

## *Assessment*

Identify the underlying cause. This will be helpful to guide your treatment.

### *Management*

| Non-pharmacological management |
| --- |
| • Stimulation of pharynx e.g. holding iced water in the oropharynx<br>• Hold the breath or re-breathe into a bag<br>• Small frequent meals<br>• Nasogastric tube aspiration to decompress the stomach |
| **Pharmacological management** |
| • Reduce gastric distension:<br>- Prokinetic drugs (e.g. domperidone/ metoclopramide) to reduce gastric distension<br>- Anti-flatulent antacids e.g. Simethicone before and after meals<br>- Proton-pump inhibitors (e.g. Omeprazole)<br>• Smooth muscle relaxant (e.g. baclofen, midazolam, nifedipine)<br>• Suppress central irritation from CNS tumour as indicated - dexamethasone<br>• Suppress central hiccup reflex e.g. metoclopramide / levomepromazine/ haloperidol / gabapentin/ chlorpromazine/ sodium valproate<br>• Phrenic nerve stimulation/ablation (for intractable hiccup) |

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# Neurological Problems

## Dystonia and Spasticity

### *Introduction*

Dystonia is defined as an involuntary movement disorder where sustained or intermittent muscle contractions (spasm) that cause twisting and repetitive movements or abnormal postures.[1] Spasticity is hypertonia with resistance to externally imposed movement.[1] Dystonia and spasticity often co-exist.

### *Pathophysiology*

Dystonia is due to damage to deep structures of the brain (such as basal ganglia, thalamus and cerebellum) which alters the activity of dopamine and acetylcholine.

Spasticity can be caused by damage to the brain that reduces the activity of GABA (a relaxing neurotransmitter).

### *Impact of spasticity and dystonia*

- Reduced or absent mobility (or even control over movements)
- Profound fatigue
- Muscle contractures leading to bone and joint deformity
- Reduced/asymmetrical bone growth leading to small and/or deformed stature
- Excessive secretions, drooling and feeding problems from impaired motility of the gastrointestinal tract.

### *Causes of dystonia*

| | | |
|---|---|---|
| **Inherited** | Neurometabolic disorders | Disorders of biogenic synthesis (Dopa-responsive dystonia<br>AADC deficiency<br>GLUT1 deficiency |
| | Organic acidemia | Glutaric aciduria type 1<br>Methylmalonic academia<br>Propionic acidemia |
| | Heavy-metal related disorder | Wilson disease<br>Neurodegeneration with brain iron accummulation (NBIAs) |
| **Acquired/ sporadic** | Medications | Anti-epileptic drugs (carbamazepine, phenytoin)<br>Cinnarizine<br>Levodopa<br>Dopamine antagonists / agonists e.g. prochlorperazine<br>metoclopramide<br>Haloperidol, Risperidone, all D-2 receptor blockers |
| | Toxins | Bilirubin (kernicterus) |
| | Vascular | Stroke (haemorrhagic or ischaemic)<br>Vascular malformation<br>Vasculitis |
| | Infection | Toxoplasmosis |
| | Autoimmune | Anti-NMDA receptor encephalitis<br>Anti-phospholipid syndrome<br>Reye's syndrome<br>Sjogren's syndrome<br>Systemic lupus erythematosus<br>Subacute sclerosis panencephalitis |
| | Structural | Abscess<br>Arnold-Chiari malformation<br>Atlanto-axial subluxation |
| | Tumours | Brain, spine tumour |
| | Others | Trauma<br>Cerebral palsy<br>Hypoparathyroidism |

### *Assessment*

Dystonia is a clinical diagnosis.

Getting the family to video episodes is very useful as children may not show dystonia when you meet them.

| Assessment | Questions to ask |
|---|---|
| Confirm that dystonia is present | • How was the child's tone prior to treatment?<br>• What is the child's level of spasticity?<br>• Does the child have episodes of arching, posturing, "toning," or stiffening?<br>• Does the child appear to be in pain before or during muscle spasms?<br>• Do comfort measures such as repositioning, cuddling, or massage help lessen spasms? |
| Assess for co-morbidities or underlying causes | • Spasticity, joint problems, signs of gastrointestinal dysmotility, and seizures. |
| Assess the severity of symptoms: Frequency and the level of functional impairment. | • How often does the child experience muscle spasms in a typical day?<br>• Ask the child or family to describe, in detail, their 'typical day' for a full 24 hours.<br>• Barthel Index of Activities of Daily Living (ADLs) |
| Identify potential triggers | • Anything that would make the child feel tense or stressed.<br>• Pain, urinary retention, constipation, inter-current illness, loud noises, bright lights, unfamiliar contact or positions, seizures |
| Assess for complications of dystonia | • Pain, gastro-oesophageal reflux, constipation, joint problems, dental decay, recurrent chest infections, anxiety and agitation.<br>• Severe status dystonicus may result in rhabdomyolysis, with a risk of acute renal failure. |

| Assessment | Questions to ask |
|---|---|
| Define the goals of treatment | • Decide at the outset on interventions, when to stop treatment, and when to consider another intervention.<br>• This baseline information can then be used to "measure" and follow the degree of benefit from any treatment. |
| Assessment of treatment outcome | • What degree of benefit do you see in your child since treatment started?<br>• Is it easier to provide care such as clothing, bathing and transferring?<br>• Do you consider your child to be a little or a lot better— 25%, 50%, or more than 50% better?<br>• Has there been a decrease in the frequency and severity of muscle spasms and associated features such as arching or stiffening?<br>• Is your child more comfortable?<br>• How does the clinical examination since treatment started compare with the initial exam? |

### *Modified Ashworth Scale for spasticity*

The Modified Ashworth Scale (MAS) measures resistance during passive soft tissue stretching and is used as a simple measure of spasticity.[2] We use this as an objective assessment.

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The Modified Ashworth Scale (MAS) measures resistance during passive soft tissue stretching and is used as a simple measure of spasticity.[2] We use this as an objective assessment.

Modified Ashworth Scale

| | |
|---|---|
| 0 | No increase in muscle tone |
| 1 | Slight increase in muscle tone, manifested by a catch and release, or by minimal resistance at the end of the range of motion when the affected part is moved in flexion or extension |
| 1+ | Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the range of movement (ROM) |
| 2 | More marked increase in muscle tone through most of ROM, but affected parts easily moved |
| 3 | Considerable increase in muscle tone, passive movement difficult |
| 4 | Affected part rigid in flexion and extension |

The goals of therapy are to ameliorate involuntary movements, correct abnormal postures, reduce pain, prevent contractures, and improve overall function and quality of life.

### *Non-pharmacological management*

- Treat any cause of anxiety or pain.
- Help the child to relax through positioning, correct seating, massage, physiotherapy, warm bathing or distraction.
- Physical and occupational therapy help to mobilize frozen joints, limit mounting contractures, establish appropriate exercise programs, and provide assistive devices.
- Sensory motor retuning, also known as constraint-induced movement therapy, may be useful in hand dystonia.

### *Pharmacological Management*

- Stop any medication that may cause dystonia
- Diphenhydramine can be used to treat medication-induced dystonic reactions

## Oral medications (ABCD)

| Intervention | Medication | Side effects |
|---|---|---|
| Anti-cholinergics | Trihexyphenidyl, atropine, hyoscine hydrobromide, hyoscine butylbromide | Sedation, blurry vision, dry mouth, constipation, urinary retention |
| Baclofen | Baclofen (presynaptic GABA receptor agonist) - Exact mechanism of action is unknown | Sedation, dizziness, urinary urgency or hesitancy |
| Clonazepam (Benzodiazepines) | Clonazepam | Sedation, confusion, impaired coordination |
| Dopaminergics | Levodopa and carbidopa<br>(Dopa-responsive dystonia represent up to 5% of childhood dystonia)<br>Bromocriptine | Carbidopa/levodopa: Nausea, orthostasis, constipation |
| Others | Gabapentin | Sedation, prolonged QT syndrome, nausea and vomiting |

| Other interventions for dystonia (refer to paediatric palliative consultant) | | |
|---|---|---|
| | **Mechanism of action** | **Adverse effects** |
| Botulinum toxin | Blocks the release of acetylcholine into the neuromuscular junction, thereby weakening the dystonic muscles and ameliorating dystonic symptoms.<br>Effects generally take effect in the first 2 weeks and last for 3 – 4 months.<br>To avoid developing resistance, injections are best performed at intervals of ≥3 months and the lowest possible doses that are effective should be used. | Weakness of the injected muscles or weakness of nearby muscles due to local diffusion of the toxin.<br>Systemic symptoms are uncommon. |
| Surgical treatment | Selective denervation<br>Intrathecal baclofen<br>DBS (deep brain stimulation) of the globus pallidus | |

# Seizures

## *Introduction*

Seizures in palliative care patients may be either:

**Acute**

Recent in onset
Can be frightening to patients and families

**Causes:**
- cerebral metastases
- infection
- metabolic disorder
- hypoxia

**Treatment:**
- antiepileptic drug (AED)
- treat underlying cause

**Chronic**

Part of a long-standing underlying seizure disorder
Worsening seizure control may indicate:
- disease progression
- factors related to AED dose, class, or administration

Children with severe neurological impairment (SNI), may have pseudo-seizures (episodes of arching and posturing, repeated muscle spasms and exaggerated startle reactions.)

In PPC setting, a 'good enough' outcome may be when a child is not necessarily seizure-free, but with seizures having minimum distressing impact on the child.

### *Causes of poor seizure control*

| | |
|---|---|
| **Factors that can lower the seizure threshold** | • Missed dose of an AED<br>• Abrupt discontinuation of a benzodiazepine or AED<br>• Starting or stopping a medication that can alter the metabolism of an AED. |
| **Medications that can lower the seizure threshold** | Baclofen, carbapenem antibiotics, metoclopramide, neuroleptics, tramadol |
| **Neurological disorders** | Brain tumours, neurological diseases, hypoxia, raised intracranial pressure |
| **Other triggers** | Illness and fever, sleep deprivation, obstructive sleep apnoea, pain and discomfort |

### *Assessment and practical approach to the management of seizures*

Seizure episodes may settle spontaneously

- **DON'T PANIC:** take a long, deep breath; breathe it out slowly and check your watch
- Ensure the child is not in immediate danger (e.g. from falls, burns, drowning)
- Do not place anything in the mouth (e.g. spoons, tongue depressors)
- Ensure airway is secure and give oxygen if available
- Place child in side-lying position during the seizure to prevent aspiration
- If seizure does not stop within 5 minutes or if the child is turning blue, give either:
- Subcutaneous, buccal or IV midazolam 0.1–0.5mg/kg (the injectable form can be given buccally if the buccal preparation is not available)
- Rectal diazepam 5-10mg (slower onset of action)

If seizures continue despite above measures for a further 5 – 10 minutes

- Repeat measures above
- Arrange for immediate transfer to hospital

Please refer to module 4 for management of terminal seizures.

# Insomnia

## *Introduction*

Insomnia is a common and distressing sleep disturbance in children with life-threatening illness. Insomnia can include difficulty in initiating or maintaining sleep. It may result in fatigue, mood disorders, daytime somnolence and demoralisation. The aetiologies are multi-factorial and is often a combination of physical, psychological, drugs and environmental factors.

## *Causes of insomnia*

| | |
|---|---|
| **Uncontrolled physical symptoms** | Pain<br>Dyspnoea<br>Cough<br>Nausea & vomiting<br>Delirium<br>Bowel & bladder symptoms |
| **Unmet psychological issues** | Depression<br>Anxiety<br>Anger<br>Fear of dying in sleep<br>Negative thought or rumination |
| **Environmental changes** | Admission to hospital<br>Noise from beeping machines<br>Noise from healthcare providers<br>Night-time medication dispensing, vital signs checking |
| **Drugs** | Corticosteroids<br>Bronchodilators<br>Psychostimulants (Methylphenidate)<br>Beta-blockers e.g. propranolol (nightmares)<br>Diuretics<br>Substance withdrawal from:<br>Benzodiazepines<br>Tobacco<br>Alcohol<br>Caffeine |

### *Non-pharmacological management*

| *Non-pharmacological* | |
|---|---|
| Improve symptoms control | Pain, dyspnoea, cough |
| Lifestyle changes | Improve sleep hygiene, exercise |
| Establish good sleep hygiene | Regular bedtimes<br>Minimize daytime napping<br>Reduce evening stimulants e.g. caffeine<br>Comfortable bedding<br>Comfortable temperature<br>Avoid staying in bed awake for more than 5-10minutes; return to bed only when sleepy<br>Avoid watching TV, reading or playing with smartphone |
| Relaxation techniques | Music, meditation, massage, progressive muscle relaxation, hypnosis, aromatherapy |
| Cognitive behavioural therapy | Address thoughts that keep child from sleeping well, have a detailed sleep diary to help identify thoughts and behaviours that cause sleep problems and replace it with habits that promote sleep. |

### *Pharmacological management*

| Drugs[3] | Indication | Side effects |
|---|---|---|
| Antihistamines e.g. diphenhydramine | Transient insomnia | Anticholinergic side effects |
| Sleep hormones e.g melatonin | Delayed sleep onset | Possible exacerbation of autoimmune disease |
| Benzodiazepine (GABA agonists) e.g. clonazepam, lorazepam | Interrupted sleep, insomnia associated with parasomnia, frequent arousal | Avoid in patients with OSAS – respiratory depression |
| Alpha-2 receptor agonist e.g. clonidine | Delayed sleep onset, interrupted sleep, REM suppression | Anticholinergic side effects, hypotension, bradycardia, rebound insomnia upon abrupt discontinuation |
| Selective benzodiazepine receptor agonists e.g. zolpidem | Delayed sleep onset, interrupted sleep | Rebound insomnia upon abrupt discontinuation, off-label use for children |

# Drooling

## *Introduction*

Drooling is the uncontrolled leakage of saliva outside the mouth, generally as a result of difficulty in swallowing the saliva produced.[4]

It is normal until 18-24 months of age, though in some cases the condition can persist up to four years of age.[4] A good diagnosis of the problem must be established, with identification of the implicated factors in each case.

Complications of drooling include skin irritation or abrasions, unpleasant smell and in the more severe presentation, the need to wear bibs or frequently change clothing. Posterior drooling may also increase the risk of recurrent micro-aspirations.

## *Pathophysiology*

An intact swallowing process comprises of 3 steps:
a) Ability to close the mouth (oral)
b) Ability to retain the food or fluid in the mouth (oral)
c) Coordinated swallowing reflex (pharyngeal and oesophageal)
This motor sequence is coordinated by a swallowing centre located in the brain stem.

## *Causes*

| **Neurological conditions** | |
|---|---|
| • Brain paralysis or mental retardation | 58% of children with brain paralysis suffer drooling, 33% have severe drooling |
| • Neuromuscular and neurogenetic disorders | Congenital supra-bulbar paralysis, encephalitis, hypoxic encephalopathy, severe intellectual disability (ID), hydrocephalus, certain rare syndromes (e.g. Moebius syndrome, Angelman syndrome, Freeman Sheldon syndrome, Landau-Kleffner syndrome) |

| Local causes | |
|---|---|
| • Problems leading to an open mouth position | Lack of lip sealing, certain malocclusions (eg anterior open bite), oropharyngeal tumour |
| • Tongue deformities | |
| • Anaesthesia or hypoesthesia of the anterior sectors of the mouth | |
| • Body posture | Unable to maintain erect head position |
| • Lack of sensitivity in the oral phase of swallowing | CN VII facial nerve and CN XII hypoglossal nerve lesions |
| • Alterations precluding mandibular stabilization | Required for correct swallowing. |

| Associated factors |
|---|
| Allergic rhinitis,<br>Upper airway disorders,<br>Gastroesophageal reflux. |

### *Assessment*

**Drooling Score**

= [Drooling severity score] + [drooling frequency score]

**Drooling Severity Score (Thomas-Storell & Greenberg) for measuring the intensity or grade of drooling**

| Score | Grade | Description |
|---|---|---|
| 1 | Dry | Never drools |
| 2 | Mild | Only wet lips |
| 3 | Moderate | Wet on lips and chin |
| 4 | Severe | Drools to extent that clothing becomes damp |
| 5 | Profuse | Clothing, hands, tray, and objects become wet |

**Drooling frequency**

| Score | Description |
|---|---|
| 1 | Never drools |
| 2 | Occasionally drools |
| 3 | Frequently drools |
| 4 | Constantly drools |

### *Management*

| Non-pharmacological management for drooling | |
|---|---|
| Myofunctional therapy | Physiotherapy to rehabilitate orofacial neuromuscular function from a young age.<br>To improve nasal breathing, lip seal and oral closure.<br>To ensure adequate control of neuromuscular groups in order to improve chewing and swallowing, facilitate correct feeding via the oral route, and secure adequate control of the position of the head |
| Behavioural change programmes | Behavioural reinforcement using acoustic feedback technique to reduce drooling by conditioning the patient to swallow each time a signal is heard from the electronic system equipped with a timer device.<br>A chin humidity sensor that triggers a signal when humidity increases – thereby inducing the patient to swallow. |
| Nursing care | Lateral positioning to allow secretions to flow out.<br>Use towel to absorb secretions<br>Protect the face / skin with barrier cream<br>Oral suctioning only if necessary<br>May need to cut down fluids temporarily |

| Pharmacological Management | |
|---|---|
| **Anticholinergic drugs** | The salivary glands are controlled by autonomic nervous system. Muscarinic cholinergic receptor blockade reduces salivary flow e.g. atropine sulphate, glycopyrrolate, scopolamine.<br>Side effects: vomiting, diarrhoea, irritability, urinary retention, mood changes and insomnia<br>Transdermal scopolamine patch offers longer action and less side effects but precautions required in patients with cardiac and gastrointestinal disorders. |
| **Botulinum injection to salivary gland** | Exerts a local and temporary effect, without the risk of side effects.<br>Can be used in selective cases of drooling characterized by a predominant spasticity component |
| **Surgery** | Used as a last resort after carefully evaluating other possible treatment alternatives for the patient.<br>e.g.: salivary gland resection, salivary duct ligation, salivary duct trans-positioning (most widely used option and involves fewer adverse effects)<br><br>**Submandibular gland duct trans-positioning** towards the tonsillar pillars may facilitate the swallowing of saliva;<br>**Post-operative complication:** appearance of ranulas or loss of smooth muscle function of the terminal sphincters, extreme dry mouth, loss of taste sensation, tongue mobility problems in the anterior sector, swelling and a tendency towards sialoadenitis. |

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# Renal failure

## Uraemia

### *Introduction*

Children with end-stage renal disease may suffer uremic symptoms such as:

- Nausea and vomiting
- Hiccups
- Fatigue
- Itchiness
- Insomnia
- Peripheral neuropathy
- Agitation / confusion
- Seizures

### *Assessment*

Children with uraemia can present with nonspecific symptoms especially in infancy, such as feeding intolerance, persistent crying and restlessness.

Blood investigations are helpful to rule out reversible causes (other than uraemia) such as metabolite derangements (calcium, phosphate, sodium, potassium, bicarbonate) and anaemia.

| Management of symptoms of uraemia | | |
|---|---|---|
| **Symptoms** | **Non-pharmacological management** | **Pharmacological management** |
| Nausea and vomiting | Avoid strong odours<br>Small but frequent meals according to the child's appetite | Omeprazole<br>Domperidone<br>Promethazine (second line)<br>Haloperidol (third line) |
| Hiccup | Pharyngeal stimulation | Metoclopramide<br>Gabapentin<br>Haloperidol |
| Fatigue | Consider treating anaemia<br>Small but frequent meals<br>Enough rest and sleep | Low-dose dexamethasone<br>Methylphenidate |
| Itchiness | Avoid strong sunlight and maintain cool environment<br>Wear soft cotton clothing<br>Wear gloves / mittens to prevent scratching<br>Advise patient to rub the skin instead of scratching<br>Apply moisturizers and emollients | Trial of oral anti-histamine<br>Gabapentin (second line) |
| Insomnia | Aromatherapy<br>Massage | Treat the causes (e.g. pain, anxiety, depression)<br>Sedating anti-histamines<br>Chloral hydrate |
| Neuropathic pain | Lignocaine gel/patch | Gabapentin<br>Amitriptyline |

| Symptoms | Non-pharmacological management | Pharmacological management |
|---|---|---|
| Agitation/ Confusion | Reassure the patient and family<br>Promote a calm and restful environment e.g. limit loud voices<br>Promote patient's orientation to his / her environment e.g. wall clock, night & day, calendar, avoid sudden changes in environment<br>Introduce each visitor or team member to the patient each time | Haloperidol<br>Benzodiazepine (midazolam) |
| Seizure | Maintain airway<br>No fluids or food directly after a seizure<br>Anticipate symptom and parent / carer education supported with written guidelines for anti-seizure medication | Use short-acting benzodiazepine e.g. buccal Midazolam / Diazepam PR / Lorazepam IV for stop seizures<br>Consider regular anticonvulsant medication after first seizure e.g. Levetiracetam (Keppra) / Phenytoin<br>Consider midazolam /phenobarbitone infusion for severe terminal seizure |

# Haematological problems

## Anaemia

### *Introduction*

Anaemia is the most frequent hematologic manifestation in patients with cancer.[1,2]

Symptoms of anaemia such as fatigue, dyspnoea, reduced effort tolerance and decreased appetite, may be debilitating and can significantly affect patients' quality of life.[2]

### *Causes of anaemia in palliative care patients*

- Blood loss
- Impaired red cell formation by the marrow
- Excessive red cell destruction

### *Why do patients with cancer get anaemia?*[3]

- Direct effects of cancer (bone marrow replacement, blood loss)
- Results of cancer treatment itself
- Chemical factors produced by the cancer (overproduction of cytokines inhibiting erythropoiesis)

### *Assessment*

- It is important to identify, document and treat the cause of anaemia if possible
- Symptoms should be recorded before and after the transfusion to determine whether there has been any benefit.
- This will facilitate decision-making regarding future transfusions.
- The patient should give informed consent for the procedure and this should be documented in the patient notes.

### *Management*

Indications for blood transfusion:

1. Patients with symptomatic anaemia, presented with respiratory and cardiac symptoms.
2. Patients with terminal illness when there is acute blood loss and symptomatic
3. Chemotherapy-related anaemia

Special considerations

- If prognosis is estimated to be short weeks, blood transfusion may not be appropriate.
- Studies have shown that pre-transfusion haemoglobin levels do not correlate with response to transfusion.[4]

Discontinuation of blood transfusion

- Some patients do not respond symptomatically to blood transfusion or may only respond for a short period of time.
- Decisions to continue blood transfusions should consider: symptoms, prognosis, response to previous transfusions and patient wishes.[4]

# Bleeding

## *Introduction*

Massive external bleeding as a mode of death in childhood is uncommon. Clinically significant bleeding occurs in 6 – 10% of patients with advanced cancer.[5] There are some specific sites, which when they bleed, are more likely to result in a major haemorrhage.[6] However, massive bleeding is extremely distressing to the patient, family and healthcare providers.

Advanced planning is necessary in all bleeding circumstances especially in patients with a poor prognosis and in those with the potential for massive bleeding. Interventions are based on prognosis, performance status, patient preferences and previous therapies.

## *Assessment*

Patients who suffer from a malignancy should be assessed for their bleeding risk.

| **Risk factors for major haemorrhage[7,8]** | |
|---|---|
| Anatomical | Fungating wounds<br>Large head and neck carcinomas<br>Large centrally-located lung cancers<br>Site of lesion close to a major vessel |
| Systemic disease | Bone marrow failure<br>Refractory acute and chronic leukaemias (M3 AML)<br>Myelodysplasia/Myeloproliferative disorders<br>Coagulation disorders<br>DIVC<br>Infection at the site of the lesion<br>Malabsorption/reduced vitamin K<br>Severe liver disease<br>Uraemia<br>Platelet count < 20,000/$mm^3$<br>Radiotherapy to a post-operative site |
| Medication | Chemotherapy (causing mucositis)<br>Heparin<br>NSAIDs<br>Warfarin |

## *Management*

Before bleeding occurs

- Decisions regarding the future management of bleeding should be documented in the patient's case notes.[9,10] This information should be communicated to the relevant health care professionals who are involved in that patient's care.[10]
- Review all medications, including risk of bleeding. The decision and reason to continue to use anticoagulation and NSAIDs should be documented in the notes.[10]
- Midazolam can be prescribed prophylactically as an anxiolytic.
- Advise family to prepare dark towels to disguise bleeding if it should occur.[9,10]

## *Management of bleeding*

| **Local measures** | |
|---|---|
| **Techniques** | **Indications** |
| Packing | Bleeding from hollow organs e.g. nose, rectum<br>Vasoconstrictors (cocaine/ epinephrine and silver nitrate) for epistaxis |
| Compression dressings<br>• Alginates, foams, hydrocolloid dressings | |
| Topical haemostatics<br>• Fibrin sealants (FS) | Bleeding from malignant wounds. |
| Astringents<br>• Silver nitrate<br>• Alum (\|$AlH_4NO_8S_2$ or AlK(SO4)2) | |
| Postural modifications<br>• Place patient in lateral decubitus position toward the site of bleeding | Refractory bleeding when patient is near death |

| Techniques | Indications |
|---|---|
| Radiation therapy | Gynaecologic malignancies<br>lung cancer<br>superficial skin tumours |
| Palliative transcatheter chemoembolization (TCE) | Controlling bleeding from many cancer e.g. head and neck, bladder, prostate, cervix, lung, hepatocellular, renal cell, neuroendocrine tumours, metastatic disease to lung, bone, liver and vagina (choriocarcinoma) |

| Systemic measures | |
|---|---|
| **Examples** | **Indications** |
| Plasma products<br>• Fresh frozen plasma (FFP)<br>• Cryoprecipitate. | DIVC<br>End-stage liver disease<br>Bleeding secondary to warfarin use |
| Platelet transfusions | Continuous bleeding of mouth and gums<br>Overt haemorrhage (GI tract, gynaecologic, urinary)<br>Extensive and painful hematoma<br>In the setting of thrombocytopenia:<br>• recent disturbed vision<br>• severe and recent headache<br>• severe anaemia |
| Vitamin K | Vitamin K deficiency<br>Bleeding secondary to warfarin use<br>Liver disease<br>DIVC |
| DDAVP | Von Willebrand's disease<br>Haemophilia A |
| Antifibrinolytic agents e.g. tranexamic acid<br>aminocaproic acid | Haematuria<br>bleeding from fungating tumours<br>haemoptysis<br>bleeding per rectum |

Please refer to module 4 for management of terminal bleeding.

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# Gastrointestinal Symptoms

## Nausea and Vomiting

### *Introduction*

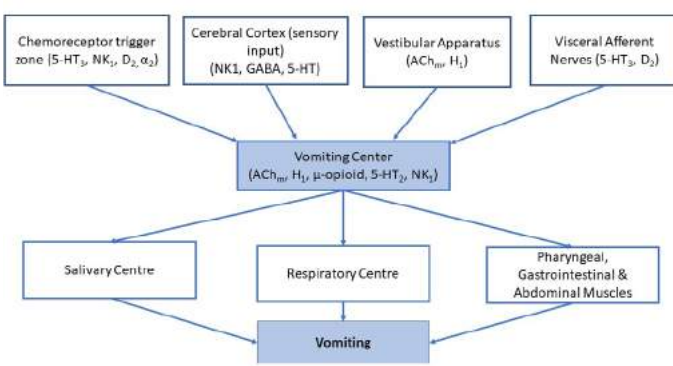
Nausea is an unpleasant sensation experienced over the pharynx and stomach with an urge to vomit.

Vomiting is the forceful expulsion of gastric or gut contents through the mouth or nasal cavity.

### *Pathophysiology*

The vomiting centres receive afferent signals from at least four major sources:

- The chemoreceptor trigger zone (CTZ)
- Visceral afferents from the gastrointestinal tract (vagus or sympathetic nerves) - these signals inform the brain of conditions such as gastrointestinal distention (a very potent stimulus for vomiting) and mucosal irritation.
- Visceral afferents from outside the gastrointestinal tract - this includes signals from bile ducts, peritoneum, heart and a variety of other organs. For example, a stone in the common bile duct can result in vomiting.
- Afferents from extramedullary centres in the brain - certain psychic stimuli (odours, fear), vestibular disturbances (motion sickness) and cerebral trauma can result in vomiting.




Pathophysiology of Nausea & Vomiting

### *Assessment*

- Frequency of vomiting
- Amount of vomitus
- Hydration status
- Complications (e.g. haematemesis, electrolyte imbalance)

### *Symptoms and causes*

| | |
|---|---|
| Vertigo and symptom association with movement | Vestibular dysfunction |
| Morning headache and neurological symptoms | Elevated intracranial pressure |
| Polyuria and polydipsia | Hyperglycaemia or hypercalcaemia |
| Altered mental status | Uraemia, hyponatremia, elevated ICP |
| Neck stiffness | Meningeal disease |
| Syncopal episodes, early satiety | Autonomic insufficiency |
| Infrequent, hard stool, abdominal fullness, straining with defecation | Constipation |
| Constipation, crampy abdominal pain, green colour | Bowel obstruction |
| Bloating, early satiety, residual gastric content | Gastric stasis |
| Esophageal burning, sour taste, worse lying down | GERD |
| Right upper-quadrant pain | Gallbladder or liver disease |
| Epigastric pain radiating to back | Pancreatitis |
| Fever, diarrhoea | Gastroenteritis |
| Worry, emotional responses | Anxiety |
| Others | Ileus, drug adverse effects, seizure |

### *Nonpharmacological management*

- Assess trigger factors
- Hot / cold packs for abdominal pain
- Encourage small amount of diet/ fluid as tolerated, chosen by child
- Provision of favourite drinks
- Hypnosis and breathing techniques
- Good oral care
- Avoid discomfort smells
- Aromatherapy
- Acupressure (P6 point)
- Nausea arising from anxiety may be reduced with behavioural therapies

### *Pharmacological management*

- Reduce or change causative treatment or medication
- Laxative for constipation
- Regular anti-emetics depending on the cause and review symptoms by 24 – 48 hours
- Consider intravenous / subcutaneous fluid if dehydrated
- Consider anti-reflux medication
- Consider dexamethasone (post-chemo/tumour control)

| Receptor activity | Medication |
|---|---|
| 5-$HT_3$-receptor antagonists | Ondansetron, granisetron |
| Dopamine ($D_2$)-receptor antagonists | Metoclopramide, haloperidol, domperidone |
| Histamine (H1) / muscarinic acetylcholine ($ACh_m$) receptor antagonists | Diphenhydramine, promethazine, hyoscine butylbromide |
| Dopamine ($D_2$)- and histamine (H1) / muscarinic acetylcholine ($ACh_m$) receptor antagonists | Chlorpromazine, prochlorperazine |
| Neurokinin-1 (NK1) receptor antagonists | Aprepitant |

## *Opioid induced nausea and vomiting*

**Mechanism:**
1. Opioid-induced activation of the chemoreceptor trigger zone
2. Sensitization of the labyrinth and activation of the vestibular system
3. Gut dysmotility

**Treatment:**
Step 1: D2 receptor antagonist, Serotonin receptor antagonist and/or Antihistamine/ Anticholinergic
Step 2: Opioid switch

# Constipation

## *Introduction*

- Constipation is a symptom, not a disease. It is subjective and defined differently by patients or carers.
- Characterized by difficult or painful defecation.
- Associated with infrequent bowel opening, hard and small faeces.
- Including faecal incontinence (encopresis).
- Aim to prevent constipation by the early introduction of laxatives.
- The cause of the constipation should be identified and treated. Bowel obstruction should be managed appropriately.

## *Causes*

- In paediatrics, most patients have functional constipation (95%) with no evidence of primary or biochemical cause
- Organic causes are much more common in children with life-threatening illness e.g. anatomic, metabolic, gastrointestinal conditions, neuropathic conditions, intestinal muscle/nerve disorders, abnormal abdominal musculature, drugs, miscellaneous

## *Possible underlying causes*

- Immobility (e.g. bedbound)
- Dehydration (review fluid intake and diuretics)
- Neurological compromise: lower extremity motor weakness, paraesthesia, urinary retention, faecal incontinence
- Fear of opening bowel, rectal tears or pain
- Hypercalcaemia, hypokalaemia
- Medications adverse effects: opioids, 5-HT3-receptor antagonists, anticholinergics, tricyclic antidepressants, phenothiazines, anticonvulsants
- Environmental – lack of privacy
- Hypothyroidism

### *Assessment*

- History, normal bowel habit, medication and other causative factors
- Abdominal: palpation, percussion and auscultation
- Consider using Bristol Stool Chart to monitor stool

### *Non-pharmacological management*

- Regular bowel routine
- Increase of activity
- Increase oral fluid intake
- Abdominal massage

### *Pharmacological management*

| Class | Medications |
|---|---|
| Osmotic laxatives | Lactulose, polyethylene glycol |
| Stool softeners | Docusate |
| Stimulants | Bisacodyl, senna |
| Lubricant | Glycerin, liquid paraffin |

| Condition | Medications |
|---|---|
| Faecal impaction | Fleet enema, docusate, lubricant suppositories |
| Opioid-induced constipation | Consider osmotic or stimulant laxatives, consider opioid switch |
| Complete bowel obstruction | Octreotide (indicated if severe abdominal pain and vomiting) |

# Diarrhoea

### *Definition*
- Passage of loose or watery stools
- Acute (< 7 days) or Chronic (> 14 days)

### *Causes*
- Gastroenteritis
- Malabsorption (e.g. Short gut syndrome)
- Laxatives overuse
- Overflow diarrhoea (spurious diarrhoea) due to faecal impaction
- Adverse effects of medication e.g. antibiotics, chemotherapy, radiotherapy
- Concurrent illness e.g. colitis
- Anal leakage following surgical or pathological injury to anal sphincter

### *Management*
Treat the underlying causes e.g. medication side effect, acute causes and chronic causes

### *Non-pharmacological management*
- Oral rehydration with glucose/electrolyte (WHO) solution
- Consider decrease of milk intake
- Consider decrease of enteral intake
- Prevention of skin breakdown

### *Pharmacological management*
- Dose reduction or discontinuation of medication with adverse side effects
- Specific directed therapy if diarrhoea is life-threatening, e.g. Antibiotic for Shigella, Campylobacter, C. difficile

### *Treatment options for chronic diarrhoea*

| | |
|---|---|
| **Loperamide** | Anti-motility agents |
| **Cholestyramine** | Short gut syndrome |
| **Octreotide** | For secretory diarrhoea |
| **Charcoal** | Absorbent agents |

# Anorexia-Cachexia

## *Definition*

**Anorexia:** Loss of appetite and poor caloric intake
**Anorexia-cachexia:** Diminished caloric intake, increased basal energy expenditure, progressive depletion of lean body mass and weight loss

## *Causes*

Common treatable causes of anorexia
- Xerostomia, mucositis, esophagitis, gastro-oesophageal reflux, pain, swallowing incoordination, dysphagia, early satiety, bulky organomegaly, intestinal obstruction

Cancer treatment related anorexia-cachexia:
- Anorexia, nausea, vomiting, decreased oral intake, and weight loss during cancer treatment

Anorexia-Cachexia syndrome during end stage disease:
- Pain, decreased function, immobility, stiffness, decubitus ulcers, oedema, ascites, shortness of breath, psychosocial distress, poor quality of life, poor prognosis

## *Management*

- Provide effective cancer-directed therapy
- Treat reversible causes
- Increase appetite and nutritional intake
- Improve functional status
- Provide interdisciplinary care to address nutritional, functional and psychological issues

## *Strategies to increase food intake*

- Offering the child favourite foods and nutritional supplements he or she enjoys
- Eliminating dietary restrictions
- Reducing portion sizes and increasing the number of meals
- Making food look more enticing
- Avoiding disliked food odours

### *Psychological approaches*

- Encouraging child and family interaction to reduce psychological distress
- Supporting the family to distinguish between things that they can and cannot control
- Exploring the emotion components and the meaning of their child not eating and losing weight
- Assessing the impact of symptoms on the child and his or her family
- Assessing the quality of life of the child and his or her family

### *Non-pharmacological management*

- Hypnosis
- Relaxation and Mental Imagery
- Massage
- Music Therapy

### *Pharmacological management*

Pharmacological treatment is adjunctive to integrative and supportive management

Examples of pharmacological treatment options for anorexia

| | |
|---|---|
| Appetite stimulants | Corticosteroids, progestogens |
| Anti-depressants | Mirtazapine |

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## Perinatal Palliative Care Pathway

Perinatal Palliative Care covers four distinct periods[1]:

**Early prenatal period:** Life threatening foetal diagnosis made weeks to months before birth

**Late prenatal period:** Life threatening foetal diagnosis made hours to days before birth

**Early neonatal period:** Neonatal death at the first hours until the first 7 days of life

**Late neonatal period:** Neonate's or infant's death from 7 until 28 days of life.

## *Scope and Flow of Care*

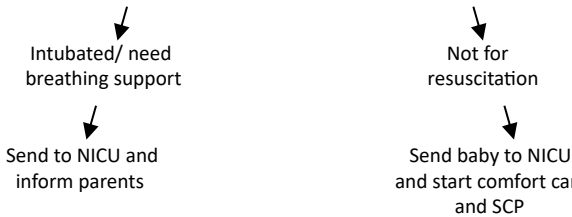
| Early Prenatal Period (weeks-months before birth) | |
|---|---|
| **Foetus, Parents and Family** | |
| **Care Plan Action Checklist** | **Content** |
| Birth Plan[2]<br>Resuscitation plan | Timing, location, route of baby's delivery and mother's pain management during delivery |
| -Plan A | -Plan A: For natural death and no resuscitation based on certain criteria at birth |
| -Plan B | -Plan B: For active resuscitation based on certain criteria at birth |
| -Pregnancy plan | -Pregnancy Plan: For parents to continue or terminate the pregnancy |
| **Flow of Care and Key Person** | |
| **Step 1:** Foeto-maternal specialist / obstetrician made the diagnosis of possible life-threatening conditions<br><br>**Step 2:** Perinatal meeting with neonatal and palliative care team regarding birth plan, resuscitation plan and pregnancy plan<br><br>**Step 3:** Foeto-maternal and palliative team meet with parents to discuss on the pregnancy and care plan.<br><br>**Step 4:** Offer the option of labour room, postnatal and NICU tour for parents and family if available.<br><br>**Step 5:** If parents opt for termination, obstetrician to discuss with parents about procedure of termination and grief support from palliative care team | |

| Late Prenatal Period (hours to days before birth) | |
|---|---|
| **Foetus, Parents and Family** | |
| **Care Plan Action Checklist** | **Content** |
| Symptom Care plan (SCP) Draft | SCP includes medication for pain, respiratory distress and feeding / hydration management plan draft |
| NICU preterm baby procedural plan | NICU preterm baby procedural plan include blood taking, ventilator support and blood transfusion |
| Preterm labour and emergency delivery plan | Mother needs to be prepared for possibility of preterm and emergency delivery<br>Need to decide on who is to be included in the delivery team on standby and key decision maker for resuscitation |
| **Flow of Care and key person** | |
| **Step 1:** If mother opts to continue with pregnancy, SCP and NICU preterm baby procedural need to be discussed. This should be done in a sensitive manner. Do not rush communication to avoid enhancing mother's guilt[3].<br><br>**Step 2:** Look into possibility of modifying environment to promote privacy, family togetherness and support grief in labour room and postnatal ward. | |

| Early Neonatal Period (hours to days of life) | |
|---|---|
| Neonate, Parents and Family | |
| **Care Plan Action Checklist** | **Content** |
| Place of Care Option | Place of care options either hospital (NICU or ward) or home (with hospice team support) |
| Comfort plan | Comfort plan include:<br>Warm<br>Minimal stimulation<br>Swaddling<br>Kangaroo care<br>Nesting<br>Massage<br>Music<br>Noise and light reduction<br>Nesting<br>Minimize painful procedure |
| Symptom care plan (finalized based on birth weight)<br>Letter to Police Department for cause of death | Symptom care plan at home need to include the contact details of primary NICU, palliative care and home hospice/domiciliary team |
| Grief support plan | Grief support plan including memory making, phone call, home visit and key person who can follow up the grief process |

**Flow of care and key person**

**Step 1:** Delivery standby team will decide on resuscitation plan




**Step 2:** For baby under conservative management, need to create NICU palliative corner or room equipped with bed for mother and newborn, memory making tools and space for family members to get together for family rituals.

**Step 3:** Discussion of place of care. If the parents chose their home for place of care, then palliative team needs to liaise with hospice / domiciliary team for home supports and prepare home symptom care plan, funeral, and death certificate/report plan (letter to police department)

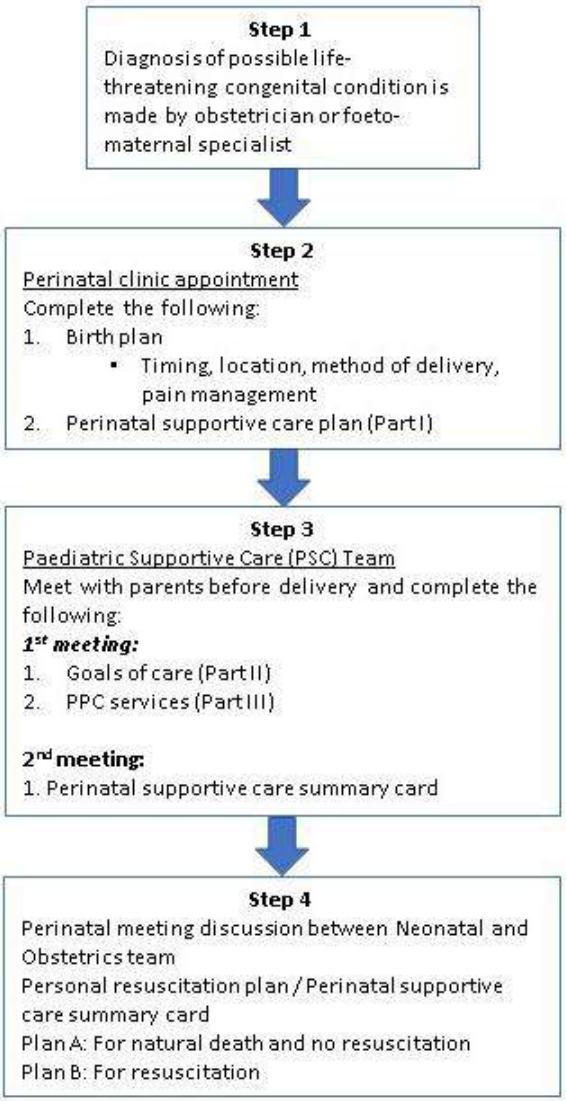
**Step 4:** If patient dies in hospital, explain to the parents the process of death management including transfer to mortuary and bringing the patient home.

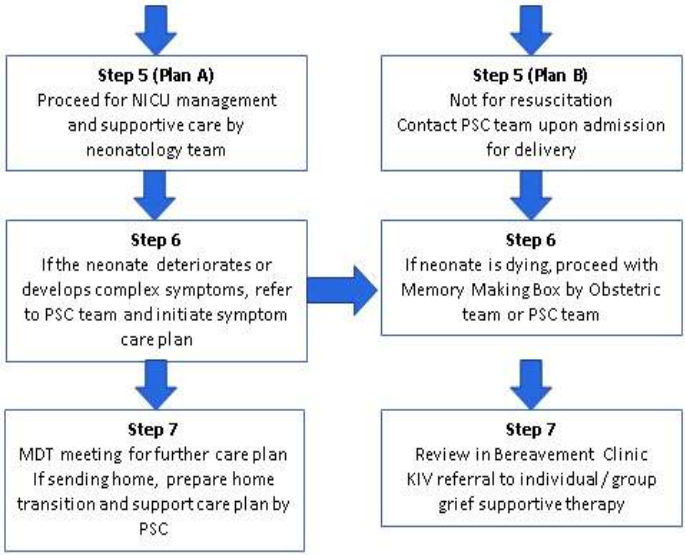
**Step 5:** Proceed with grief support plan

| Late Neonatal Period ( weeks to months) | |
|---|---|
| **Neonate, Parents and Family** | |
| **Care Plan Action Checklist** | **Content** |
| Symptom Care Plan | Need to relook and add more symptoms management in the care plan during the prolonged stay in hospital such as dystonia, nausea/vomit and seizure. |
| Grief support plan | To support parents and family to grief starting before the child's death in hospital and create avenue for bereavement follow up either phone call, mailings, memorial service or anniversary acknowledgements after child's death |
| Regular update meeting with parents | Regular meetings with parents help to assess parent's evolving needs including psychosocial care (by NICU and palliative care team) |
| Transition Home care plan | |
| Discussions on withholding and withdrawal of life-sustaining therapies [4] | Need to prepare a standard operating procedure (SOP) for:<br>- Hospital withholding and withdrawal<br>- Home withdrawal |

| Flow of care and key person |
| --- |
| **Step 1:** Palliative care team should be part of the team in managing complex symptom care with ongoing modification of symptom care plan while patient in NICU/ward/home.<br><br>**Step 2:** Regular meeting with parents by NICU and palliative care team would elicit more needs and supports for parents and family.<br><br>**Step 3:** Before transfer out baby from NICU, a contingency plan should be decided by MDT team (NICU, Palliative, General Paediatrician, Hospice) if clinical condition worsening outside NICU.<br><br>**Step 4**: If patient is stable to go home, a transition home care plan (refer module 3 of this handbook) need to be done and pass over to home care team.<br><br>**Step 5:** If patient's condition is worsening in NICU, withholding and withdrawing supports may need to be discussed among MDT team and with parents. Grief support plan need to be continued. |

## *Example of flow process for perinatal care*




Step 5 (Plan A)
Proceed for NICU management and supportive care by neonatology team
Step 5 (Plan B)
Not for resuscitation
Contact PSC team upon admission for delivery
Step 6
If the neonate deteriorates or develops complex symptoms, refer to PSC team and initiate symptom care plan
Step 6
If neonate is dying, proceed with Memory Making Box by Obstetric team or PSC team
Step 7
MDT meeting for further care plan
If sending home, prepare home transition and support care plan by PSC
Step 7
Review in Bereavement Clinic
KIV referral to individual / group grief supportive therapy

## Perinatal Supportive Care Plan

**PART I: PERSONAL DETAILS**

| | |
|---|---|
| Name: | Date completed: |
| Date of Birth: | Date for review:<br>(This document will not be valid after this date) |
| IC No: | Hospital RN No: |
| Home Address: | |
| Patient/family members/carers: | |
| Diagnosis / Clinical Issues: | |
| Birth plan *(route of delivery and pain management)*: | |

**PART II: Goal of Care**

| |
|---|
| |

**PART III: Paediatric Supportive service**

☐ Visiting labour room

☐ Family conference

☐ Anticipating grief assessment and management

☐ Memory making

☐ Symptom care plan for baby

☐ Home visit/Hospice care

☐ Grief & bereavement support

☐ Others _____

_____

_____

## Neonatal Supportive Care Plan (Summary) card

**Neonatal Supportive Care Plan**
**(Summary) card**

**Mother Name :** **Neonate RN No :**
**Mother RN No :**

Admission Diagnosis:
**Neonatal Resuscitation Plan**

☐ For active resuscitation upon delivery ☐ To decide upon delivery
☐ Do Not Resuscitate upon delivery

Overall Goals of Care

| |
|---|
| |

Preferred End of life care

| |
|---|
| |

### *Anticipatory Grief Support Plan*

Most parents and family members value the golden chance to make good and meaningful memories with their baby during the brief time before baby's death. Others may hesitate initially but may consider taking the offer with some time for them to decide[5].

| **Photography** |
|---|
| • Encourage protected photography of baby with family members |
| • Photography style: www.nilmdts.org www.toddhochberg.com |
| • Perinatal bereavement service guidelines for photographing babies at end of life[3] |
| **Plaster Moulds** |
| • Hand and feet 3D mould kits |

| **Ink Prints and Other Memories** |
|---|
| • Hands and feet prints on special birth certificates, baby book, cloth, shirts |
| **Personal items and memory box** |
| • Patient's voice record, hand-knit caps and blanket |
| **Interaction of baby with family** |
| • Touching and holding baby e.g. kangaroo care |
| • Rituals of blessing, naming, baptism |
| • Singing to baby or reading storybooks |
| • Taking baby for social outing |

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# Nursing care in Paediatric Palliative Care

## Oral Care

### *Introduction*

Oral problems such as pain, salivary gland dysfunction, dysphagia, and oral mucosal infections can occur during end of life. Therefore, oral hygiene and care should not be neglected even during active dying. Poor oral hygiene can result in multiple dental problems such as dental caries, halitosis, as well as a reservoir for infections.

Oral care is required even if the patient is no longer taking food orally, but on parenteral nutrition or tube feeding. Maintaining oral hygiene is important for patient's comfort.

### *Halitosis*

#### *What is it?*

Unpleasant foul-smelling breath

*Possible causes*

- Dry mouth
- Poor oral hygiene
- Infections of the upper respiratory tract and oral cavity
- Gastro-oesophageal reflux

*Non-pharmacological management*

- Brush teeth and tongue 2-3 times a day with a soft nylon toothbrush.
- Super soft toothbrushes or oral sponges which are soaked in 0.2% alcohol-free chlorhexidine mouthwash can be used if the child is unable to tolerate soft toothbrush.
- If the child can gargle, dissolve 1 teaspoon of sodium bicarbonate in a glass of water and use as mouthwash.
- Gauze soaked in recommended mouthwash can be used to clean the mouth for children who cannot gargle yet. This can be fastened to the end of a tongue depressor.

*Pharmacological management*

- Oral cavity infections can be treated with broad spectrum antibiotics (e.g. amoxicillin-clavulanate) and anaerobic coverage (metronidazole).
- Oral candidiasis can be managed with nystatin suspension.

## *Xerostomia*

***What is it?***

Excessively dry mouth

*Possible causes*

- Dehydration
- Hypercalcaemia
- Salivary gland dysfunction
- Infections
- Drugs (e.g. diuretics, anticholinergics, antihistamines)
- Mouth breathing
- Oxygen therapy

*Non-pharmacological management*

- Frequent sips of water
- Suck frozen lemon juice cubes
- Petroleum-based or beeswax-based lip balm
- Maintain oral hygiene
- Avoid medications that cause dry mouth

*Pharmacological management*

- Saliva stimulation (e.g. pilocarpine)
- Saliva substitution

# Stomatitis

## *What is it?*

Inflammation of the oral mucous membrane, leading to pain and ulcers

## *Causes*

- Radiotherapy
- Chemotherapy
- Infections, especially viral infections
- Drug-induced
- Physical irritation from oral appliances
- Nutritional deficiencies

## *Non-pharmacological management*

- Optimize oral hygiene
- Soft food
- Avoid irritating food e.g. spicy or acidic food, very hot food

## *Pharmacological management*

- Topical analgesics – Xylocaine viscous 4 hourly / prn, Topical anti-inflammatory - choline salicylate and cetalkonium chloride gel (e.g. Bonjela or Oral Aid)
- Topical hyaluronic acid gel – anti-inflammatory and angiogenic properties
- Topical triamcinolone oral paste – in children aged more than 7 years
- Treat infections – oral acyclovir for herpes simplex infections, nystatin suspension for oral candidiasis

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## Tube feeding

Feeding may need to be given to the child via tubes, such as nasogastric, gastrostomy or gastrojejunostomy tubes.

Caregivers need to be shown how to prepare feeding formula and to give tube feeding correctly before discharge. Ideally, the healthcare provider should observe the caregiver demonstrating correct tube feeding technique before discharge.

Incorrect tube feeding technique and feeding formula preparation can lead to various problems such as aspiration, tube occlusion or dislodgement.

Initiation of tube feeding also may present with diarrhoea due to hyperosmolarity or lactose intolerance. Volume of feeds should be increased gradually to prevent overdistention of the stomach.

### *Overdistention of the stomach*

*Signs of overdistention*
- Bloated abdomen
- Nausea and vomiting

*Possible causes*
- Gastroparesis
- Volume or rate of feeding is too high
- Squashed stomach syndrome – compression by liver tumour or other structures in the abdomen
- Delayed gastric emptying due to medications

*Management*
- Consult dietician on the appropriate volume and formula for feeding. May need to temporarily reduce feed and gradually increase until target volume is reached.
- Feeding volume may be reduced but frequency of feeding increased to compensate.
- Ensure patient is kept propped up 30$^{o}$ for at least 30 minutes after feeding.

### *Diarrhoea*

*Possible causes*
- Hyperosmolarity of the formula can result in temporary diarrhoea on initiation
- Intolerance to formula contents e.g. lactose, proteins
- Gastroenteritis due to poor hygiene in formula preparation

*Management*
- Refer to dietician to replace with other types of feed with similar calorie and nutritional content.
- Reduce the amount of feed and gradually increase dose when tolerated.
- Ensure feeds are prepared hygienically
- Maintain skin integrity – apply barrier cream over perineum to prevent skin breakdown

### *Aspiration*

*Signs of aspiration*
Can be silent – no choking or coughing
Symptoms of lung infection – coughing, fever, dyspnoea

*Possible causes*
- Gastro-oesophageal reflux
- Lying patient flat immediately after feeding
- Increased intra-abdominal pressure
- Tube displacement
- Worsening of dysphagia

*Prevention*
- Check tube placement before feeding
- Check tube placement after every tube change
- Prop patient 30$^{o}$ up for at least 30 minutes after feeding

*Management*
- If aspiration pneumonia has set in, treat with antibiotics.
- If GERD, start medications e.g. domperidone, omeprazole.

# Gastrostomy Tube Care

A gastrostomy tube is used to provide liquid feeds directly into the stomach. Gastrostomy tubes are preferred for long term feeding. Care for gastrostomy tubes is important to reduce risk of complications. After 3 months of creating the tract, the gastrostomy tube can be changed into button type or skin-level gastrostomy tube which is less conspicuous compared to normal gastrostomy tube.

## *Common problems related to gastrostomy feeding tube[1-3]*

### *Tube obstruction or blockage*

*Signs of tube obstruction*
- The tube cannot be flushed with water
- Prepared feeds or medications does not pass through the tube as usual
- Tube is bulging when bolus feeding is given

*Possible causes*
- Formula not prepared appropriately or too thick
- Medications not suitable for tube administration or inadequately crushed or dissolved
- Inadequate flushing
- Tube clamp is not released
- Defective tubing
- Infusion rate is too slow

*Management*
- Check that the tube clamp has been released.
- Do NOT force the feed or medication into the clogged tube.
- Flush the tube with 60ml of warm water, using a large syringe.
- Pull back the syringe plunger to create a vacuum before flushing again. This may help to dislodge the block.
- If this does not work, then the child needs to be referred to the hospital for reassessment of the tube and possibly replacement.

### *Tube displacement*

*Signs of tube displacement*
- The tube is apparently out of the tract
- Child has sudden breathing difficulty
- Child has sudden symptoms of obstruction such as nausea, vomiting and abdominal pain

*Possible causes*
- The tube was not adequately secured
- Excessive force on the tube
- Tube migrates beyond the pylorus due to peristalsis
- Balloon deflation or rupture

*Management*
- Stop feeding
- If tube has migrated inside, gently pull the tube until resistance is felt. Take note of the marking of the tube and secure tube.
- If tube has completely come out, replace the tube.

### *Leaking tube*

*Signs of leaking tube*
- Skin irritation around the site of insertion – may be painful, infected
- Visible hole or leak at the tube itself or around site of insertion.
- Dressing around site of insertion requires frequent change.

*Possible causes*
- Poorly fitted tube
- Excessive movement or tugging at exit site – resulting in enlarged tract
- Accidental cutting of the tube due to repeated clamping
- Defective or clogged tube
- Excessive pressure inside the stomach
- Skin infection surrounding the exit site

*Management*

- Prescribe proton pump inhibitors to reduce acidity of gastric secretion
- Barrier cream / stoma adhesive powder surrounding the insertion site.
- Secure the tube with tape.
- Possibility of using Foley's catheter temporarily to allow tract to shrink. In the meantime, other methods of feeding such as nasogastric tube feeding should be used.

### *Skin infection or over-granulation*

*Signs of infection / over-granulation*

- **Infection:** Redness, tenderness, increased purulent discharge, pustule, fever
- **Over-granulation:** Moist cauliflower-like pink tissue surrounding insertion site, bleeds easily

*Possible causes*

- **Infection:** Poor hygiene or site care, immunocompromised state
- **Over-granulation:** excessive movement of the tube or trauma to the site

*Management*

- Regular dressing with proper aseptic technique
- Warm saline compress over the site – cut Y shape over 2x2cm gauze, soak in warm saline, leave on site for 3-5 minutes, repeat 3-4 times a day
- Topical antibiotics for local infection and consider systemic antibiotics if fever is present
- Prevent excessive tube movement

## *Emergency gastrostomy tube replacement*

*Emergency gastrostomy kit*

Consists of:

- Foley's catheter of the same French size or smaller size and an extra G-tube button
- Water based lubricant (KY jelly)
- 5ml syringe (to fit into the balloon port) and 20ml syringe (to aspirate the stomach contents)
- Clamp from old extension set

**DO NOT PANIC** if the tube falls out or is pulled out.

*Foley's catheters*

- Insert the end of the tube into the opening of the abdominal wall gently about 3-4 inches.
- Use a 5ml syringe to fill the balloon with water into the part that inflates the balloon.
- Pull back gently on the tube until you meet some resistance.
- Slowly draw back stomach contents using 20ml syringe to assure proper placement of the tube.
- Then verify placement with free flow of small amount of water.

*G-tube button*

- Insert tube into stoma. *If there is any resistance, do not push. Go to the nearest hospital with your emergency kit.
- Using 5ml syringe, fill the balloon with cool boiled water or water for injection (amount depending on the G-tube button).
- Attach the extension set. Aspirate stomach content to assure placement of tube.
- Then verify placement with free flow of small amount of water.
- It is important to replace the tube as fast as possible because the tract that the G-tube enters through the stomach can close very quickly.

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# Tracheostomy Care

Tracheostomy tubes may be inserted when the child requires prolonged ventilation or when upper airway obstruction cannot be removed.

## Common problems with tracheostomy tubes

### *Obstruction or tube displacement*

| Causes | Management |
|---|---|
| • Early tracheostomy tube change when tract is not matured yet<br>• Tracheostomy stenosis<br>• Granulation tissue at tracheostoma<br>• Obese neck with deep seated trachea<br>• Restless or too anxious patient | • Obstruction or displaced tube leading to ventilation problems - Must remove and replace tracheostomy<br>• Can use a smaller diameter tracheostomy tube to replace the current tube using a bougie or fibre optic scope<br>• If track is immature (< 7 days old) blind replacement is contraindicated |

### *Bleeding*

| Causes | Management |
|---|---|
| • Tracheo-innominate fistula<br>• Bleeding from an invading tumour<br>• DIC<br>• Infection<br>• Local irritation or erosion | • Call for surgical backup<br>• All bleeding should be considered dangerous regardless of volume or cessation and should be evaluated in an OT setting.<br>• Manage and resuscitate the patient before sending to the OT.<br>• Over-inflate the cuff to tamponade the bleeding (successful in 85% of cases of trachea innominate fistula)<br>• If bleeding continues, secure the airway with endotracheal intubation<br>• Remove the tracheostomy and insert a finger into the stoma to compress the innominate artery<br>• Digitally compress the innominate artery anteriorly |

### *Emergency tracheostomy kit*

These items should always be present in a child's emergency tracheostomy kit:

- Two clean tracheostomy tubes :
  - o Tracheostomy tube of similar size to current tube
  - o Tracheostomy tube one size smaller than the current tube
- Tracheostomy ties
- Small blanket or towel roll
- Blanket for mummy restraint (if needed)
- Sterile water
- Water soluble lubricant
- Saline lavage (if used at home)
- Suction and catheter kits
- Portable suction machine
- Luer-Lock syringe (if tracheostomy tube is cuffed)
- Bandage scissors
- Tissues
- Ryle's tube size 12Fr
- Wipes or hand sanitizer
- Oxygen tank
- Emergency phone numbers

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# Urinary Care

## *Common problems in patient with diapers:*

*Diaper dermatitis*

Red and tender skin over the buttock and perineal area, may involve thighs.

*Causes*

- Contact irritant: Irritation from stool and urine, chaffing or rubbing with diapers – flexures are spared as it is worst over areas with direct contact to the irritant.
- Atopic: Triggered by food, new toiletries or fabric
- Bacterial infection: presence of pustules
- Candida yeast infection – usually the redness is over the flexural areas. Presence of satellite lesions.

*Non-pharmacological management*

- Change diapers regularly
- Rinse the buttocks with warm water and pat dry

*Pharmacological management*

- Topical barrier creams e.g. Drapolene, Bepanthen, zinc oxide, Vaseline- use at every diaper change
- Powders are not recommended
- Topical antifungal if due to fungal infection

## *Common problems in patient with urinary catheter (intermittent/indwelling)*

### *Bladder spasms[1]*

Lower abdominal pain associated with sensation of urgency, leading to leakage or incontinence

*Causes*

- Irritation from the catheter balloon
- Urinary tract infection

*Non-pharmacological management*

- Pelvic floor muscle exercises
- Avoid irritating food e.g. spicy food, citrus, carbonated beverages

*Pharmacological management*

- Antispasmodics – tolterodine, oxybutynin
- Tricyclic antidepressants e.g. desipramine

### *Catheter blockage*[2]

- Inability to advance the catheter into the bladder
- No urine flowing out from the catheter despite distended bladder
- Urinary leakage around the catheter

*Causes*

- Mineral deposits or crystals within the catheter
- Blood clots or sediments within the catheter
- Kinked catheter
- Constipation

*Non-pharmacological management*

- Check for and remove any kinks or obstruction in the catheter or the drainage bag tubing.
- Ensure the bag is positioned below the bladder when child is lying, sitting or standing.
- Check that the leg bag straps are fitted correctly and not causing bag obstruction.
- Increase fluid intake
- Increase citrate intake
- If heavy gross haematuria is seen, consider bladder irrigation
- Enema or digital evacuation of impacted stool

### *Urinary tract infections*[3,4]

Indwelling catheters predispose the child to urinary tract infections. It is important to distinguish between a catheter-associated urinary tract infection (CAUTI) and bacterial colonisation of the catheter.
Urinary tract infection is more likely if:

- Systemic symptoms such as fever, chills, vomiting, delirium
- Local symptoms – flank pain, abdominal pain, haematuria
- Change in urine – foul-smelling, increased leakage, cloudy urine

Pyuria (leucocyte +ve) is not reliable for diagnosing UTI.
Replace the catheter and take the sample from the new catheter for urine culture and sensitivity.
A significant growth of $>10^5$ colony-forming units (CFU)

#### *Pharmacological management*[4]

- Trimethoprim 4mg/kg bd x 7 days
- Nitrofurantoin 0.75mg/kg qid x 7 days
- Cephalexin 12.5mg/kg bd x 7 days (first choice if upper UTI is suspected)
- Co-amoxiclav

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# Bedbound patients

## *Common problems faced by bedbound patient*

### *Pressure ulcers*[1]

*Causes*

- Injuries to the skin that are caused by prolonged high pressure due to immobility.
- Aggravated by poor nutrition, shearing force during transfer, local perfusion, poor skin integrity, infection, anaemia.

*Prevention*

- Regular turning and repositioning of child in bed. Elevate bed head not more than 30° when not feeding.
- Cotton clothing and bedding to absorb sweat.
- Encourage time out of bed.
- Teach proper transfer techniques and use aids such as frames, slings or slide sheets to prevent shearing.
- Regular passive range of motion exercises to maintain joint flexibility.
- Ensure skin is moisturized adequately.
- Change clothing or diapers once soiled.

*Management*

- Dynamic pressure relieving surfaces eg ripple mattress.
- Repositioning chart to remind caregivers when to turn the patient.
- Appropriate dressing for ulcers. Minimize pain by giving analgesics before dressing and use non-adherent dressings.

### *Orthostatic pneumonia*

*Causes*

- Reduced lung expansion leading to atelectasis due to prolonged lying down position.
- Aspiration of gastric contents
- Reduced immunity

*Prevention*

- Frequent repositioning.
- 30° elevation of bed head except when sleeping or feeding.
- Keep patient propped up 30-45° after feeding.
- Maintain good oral hygiene
- Chest physiotherapy including use of incentive spirometry, percussion and inducing cough.

*Management*

Treat the infection if benefits outweigh the risks.
Manage symptoms.

### *Constipation*

*Causes*

- Reduced nutrition or fluid intake
- Reduced bowel motility due to medications / disease
- Immobility

*Management*

- Optimise feeding as tolerated
- Regular bowel habits
- Encourage mobilization
- Impacted stools may consider enema or digital evacuation
- Co-prescribing gut stimulant or laxatives if opioids are prescribed

### *Spasticity and contractures*[3]

*Causes*

Joint immobility resulting in tightening of muscles or tendons, associated with hyperreflexia.

*Prevention*

- Active and passive range of motion exercises for joints.
- Proper support and positioning of limbs, using splints, wedges, pillows etc.

*Management*

- Analgesics
- Muscle relaxants e.g. baclofen, clonazepam
- Spasticity can be managed with botulinum toxin injections
- Surgical release of contractures

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## Multidisciplinary Paediatric Palliative Symptom and Psychosocial Support Services

Symptom and psychosocial support services could be provided by the other co-opt MDT team members in paediatric palliative care service. Co-opt members is variable depending on the availability of resources of the corresponding hospital or community-based care. In this chapter, we are focusing on:

| Co-opt MDT service | Objectives in Palliative Care |
|---|---|
| Occupational therapy | To regain maximum physical, psychological, cognitive, social, and vocational functioning within the limit caused by the disease and its treatment to the patient.<br>Educate and empower patient and family to learn different assisted living techniques with and without the help of medical instruments. |
| Physiotherapy | Assist in improving quality of life by maximizing functional independence and helping to provide relief from distressing symptoms such as pain, breathing, problems, weakness or mobility issues. |
| Psychological support | Assist in psychological assessment including assessment of patient and parent's understanding of the disease, coping mechanism, and their spiritual needs.<br>Provide psychological therapy including cognitive behavioural therapy, play therapy, art therapy and counselling. |

# Occupational therapy

## *Role of the occupational therapist*

*Assessment*

The occupational therapist (OT) will use standardized tests, purposeful play and other planned activities to examine the child's practical ability to do the tasks that enable him or her to learn like other children of the same age.

*Management*

Once the assessment is complete, the therapists will provide treatment services or suggestions tailored to the client's needs. In occupational therapy, rehabilitation for children generally focuses on:

- Symptom control
- Motor training
- Sensory training
- Cognitive training

## *Symptom control*

*Problem-solving strategies*

This can range from physical, emotional, social and psychological problems.

If the client has any difficulty in terms of lifestyle challenges, fatigue, and self-esteem issues, OT could help to determine their priorities, gauge energy levels, to recognize that a client's inner feelings and values, to change behaviour, and to adapt to their changed lifestyle.

*Restoration activities*

**Relaxation**

Relaxation techniques appear to increase one's sense of mastery, reduce stress, relieve muscle tension, and distract one's attention from the pain. It can be achieved through:

**• Biofeedback-Assisted Relaxation**

Biofeedback techniques measure body functions and give you information about them so that you can learn to control them. Biofeedback-assisted relaxation uses electronic devices to teach you to produce changes in your body that are associated with relaxation, such as reduced muscle tension.

**• Deep Breathing or Breathing Exercises**

It helps children relax by slowing their breathing rate, decreasing the heart rate and normalizing blood pressure. This technique involves focusing on taking slow, deep, even breaths.

**• Guided Imagery**

For this technique, people are taught to focus on pleasant images to replace negative or stressful feelings. Guided imagery may be self-directed or led by a practitioner or a recording.

**• Progressive Relaxation**

This technique, also called the Jacobson relaxation or progressive muscle relaxation, involves tightening and relaxing various muscle groups. Progressive relaxation is often combined with guided imagery and breathing exercises.

For young children simple progressive relaxation needs to be adjusted for example "Toe Tensing" this is a method of drawing tension down to the toe. This is an exercise that involves lying on the back and allowing yourself to tense your toes. Ask the child to pull his toe muscles towards the body and hold the position for ten counts. Do 4-5 repetitions of the exercise.

*Pacing activities, work simplification and energy conservation Principles*

Work Simplification and Energy Conservation principles will allow the child to remain independent and be less frustrated by the illness, when their energy can last throughout the day.

Pacing involves breaking tasks down into small manageable sessions and resting between sessions to allow the body to recuperate before finishing the task. By using activity pacing, it can help the child to work with their body and understand its needs.

Example of pacing: By recording a daily log about his routine activity, a child can determine when the pain begins to worsen. The child can then reduce time for the tasks by 20%.

*Body Mechanics and Ergonomics (position adjustment)*
Pain can be alleviated through supportive positioning using a pressure cushion for seating, or positioning to counteract involuntary motor patterns, e.g. supporting children in a flexor position when they have a strong extensor pattern.

*Splints*
Making splints to help overcome various orthopaedic and neurological problems. Splint is a rigid support given to any part of the body. Functions of splint:
- to protect the affected part and thus reduce pain.
- to strengthen any weak muscles and thus assist to carry out its action.
- to prevent formation of contractures and deformities

Examples: Resting hand splint, cock-up hand splint, knee extension splint, ankle resting splint, anti spastic hand splint and elbow extension splint.

*Compensation activity*
This involves the use of assistive equipment (modifications, aids and adaptive tools). The equipment aids in decreasing symptoms such as fatigue and cancer pain, and also to increase client's participation in activities.
Example: Use of table to support arm during grooming to reduce fatigue.
Interventions are targeted toward minimizing barriers to performance, which include modifications for games or activities that clients enjoy as well as appropriate positioning strategies. This may involve modifications to their home in introducing adaptive equipment.

### *Motor training*

Motor skills are important for daily functioning of patients and strongly influences their quality of life. It can be divided into fine motor and gross motor skills.

#### *Fine motor skills*

Hand-strengthening with putty / playdough, speed improvement with competitive plays, and endurance training by increasing the time in activities are examples of mostly used trainings.

#### *Gross motor skills*

Children should develop gross motor skills as they participate in school and sports activities.

### *Sensory training*

- Hypersensitivity
- Hyposensitivity

Desensitization or sensory re-education should be done with materials children are familiar with.

If a client has severe problems, caregiver should be well educated to prevent injuries like burn, cut, etc.

### *Cognitive training*

#### *Attention*

Attention is needed for children to be successful in all areas of daily living but especially in school functioning.

Example: Attention should be handled in terms of selective attention, shifting attention, and divided attention. These attention parameters can be added to skills training, e.g. singing song while playing block-stacking games.

#### *Processing speed, short-term and long-term memory, and sequencing*

Processing speed, short and long-term memory, and sequencing ability should also be trained.

Examples: Memory cards, history telling, making animation, and memory training by watching cartoon and asking questions.

**The role of occupational therapists in different patient groups:**

| Category | Main symptoms/issues | Reason for referral to OT |
|---|---|---|
| Neuromuscular disorder | • Muscle weakness<br>• Easy muscle fatigue<br>• Muscle loss/atrophy<br>• Muscle pain<br>• Joint contractures<br>• Functional difficulty/disability | • Activities of daily living training(patient/caregivers)<br>• Splinting<br>• Wheelchair assessment<br>• Pacing<br>• Aids and adaptation/assistive devices (e.g. power-mobility device, buttoning aid, enlarged handle for keys, transfer boards, hoist for transfer etc.)<br>• Home modification/ Environmental modification (resizing bathroom door for wheelchair access/ mobile shower chair access)<br>• Body mechanics and ergonomics (Positioning)<br>• Motor training<br>• Sensory training<br>• Cognitive training |
| Severe neurological impairment | • Muscle weakness<br>• Spasticity or Hypotonia<br>• Joint Contractures<br>• Pain<br>• Impaired motor control<br>• Impaired sensory processing<br>• Functional difficulty/disability | • Activities of daily living training(patient/caregivers)<br>• Splinting<br>• Pacing<br>• Wheelchair assessment<br>• Aids and adaptation/assistive devices (e.g. power-mobility device, buttoning aid, enlarged handle for keys, transfer boards, hoist for transfer etc.)<br>• Home modification / environmental modification (resizing bathroom door for wheelchair access/ mobile shower chair access) |

| Category | Main symptoms/issues | Reason for referral to OT |
|---|---|---|
| Severe cyanotic heart disease and chronic respiratory disease | • Breathlessness<br>• Fatigue<br>• Anxiety/stress<br>• Functional difficulty | • Activities of daily living training(patient/caregivers)<br>• Pacing<br>• Aids and adaptation/assistive devices (e.g. light utensil, enlarge handle, cardiac table, push chair, etc.)<br>• Home modification / environmental modification (e.g. re-positioning the furniture to make walking around easier, keeping frequently used items close to hand, easy access storage to avoid bending and stretching, etc )<br>• Body mechanics and ergonomics (positioning) |
| Chronic Pain | • Pain<br>• Stiffness<br>• Fatigue<br>• Stress<br>• Functional difficulty | • Activities of daily living training(patient/caregivers)<br>• Pacing<br>• Aids and adaptation/assistive devices (grab sticks, big buttons, raised armchairs and highchairs, walking aids, etc)<br>• Home modification/ Environmental modification (A raised toilet seat)<br>• Activities of daily living training<br>• Relaxation<br>• Body mechanics and ergonomics (Positioning)<br>• Splinting<br>• Wheelchair assessment |

| Category | Main symptoms/issues | Reason for referral to OT |
|---|---|---|
| Syndromic children with slow learning | • School refusal<br>• Functional difficulty<br>• Developmental delay<br>• Sensory processing difficulties<br>• Cognitive problem/disability<br>• Stress<br>• Fatigue<br>• Fine motor delay/poor hand function<br>• Physical disabilities | • Activities of daily living training (patient/caregivers)<br>• Splinting<br>• Wheelchair assessment<br>• Pacing, energy conservation and work simplification.<br>• Aids and adaptation/assistive devices (e.g. power-mobility device, buttoning aid, enlarged handle for keys, transfer boards, hoist for transfer etc.)<br>• Home modification/ environmental modification (resizing bathroom door for wheelchair access/ mobile shower chair access)<br>• Body mechanics and ergonomics (Positioning)<br>• Motor training<br>• Sensory training<br>• Cognitive training<br>• Relaxation |

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# Physiotherapy in Paediatric Palliative Care

## *Referral for Physiotherapy*

| Indication for referral | Contraindication |
|---|---|
| • Trouble in breathing<br>• Pain<br>• Weakness<br>• Poor mobility | • Medical instability<br>• Shortness of breath at rest<br>• Resting angina<br>• Poorly controlled epilepsy<br>• Abnormal arterial blood gases<br>• Acute pulmonary embolism<br>• Acute haemorrhage |

| Chest physiotherapy | Indications of positive response to chest physiotherapy |
|---|---|
| • Breathing<br>• Postural drainage<br>• Percussion<br>• Vibration<br>• Active cycle breathing technique<br>• Incentive spirometry<br>• Suction | • Changes in breath sounds<br>• Improved chest x ray<br>• Increased oxygenation of the blood as measured by arterial blood gas sampling<br>• The child's report of increased ease in breathing |

| Limb physiotherapy, transferring and positioning | Why limb physiotherapy is important |
|---|---|
| • Active free exercise<br>• Active assisted exercise<br>• Passive movement<br>• Stretching<br>• Strengthening<br>• Balance training / proprioception training<br>• Postural stabilization<br>• Ambulation<br>• Mechanical exercise<br><br>**Transferring & positioning**<br>• Independent<br>• Stand by assist<br>• 1-person assist<br>• 2-person assist | • Reduces stiffness/relaxes tight muscle<br>• Minimise muscle wasting<br>• Prevent from contracture<br>• Maintain joint and connective tissue mobility<br>• Decrease restlessness<br>• Assist circulation and vascular dynamics<br>• Help patient awareness of movement<br>• Can give caregivers feeling of purpose if they can help with the exercises |

| Musculoskeletal pain | How physiotherapy management helps in musculoskeletal pain | How to perform |
|---|---|---|
| Active free exercise<br>Active assisted exercise | • Maintain elasticity and connectivity of muscle<br>• Increase circulation and prevent thrombus formation | The patient can assist with opposite extremity to perform the exercises |
| Passive movement<br>Passive stretching | • Maintain joint and connective tissue mobility<br>• Minimize the effects of the contractures | Provided by an external source by physiotherapist or carer. |
| Balance training<br>Proprioception training | • To establish an equilibrium of the body which is associated with a variety of movement and postural control | Stand with one foot on the ground while the other foot is lifted up or stand on a balance board |
| Ambulation | • Assisting a patient to walk safely and efficiently, it includes stairs climbing with or without assistance device. | Support with assistance devices such as parallel bar, walker, axillary crutches and forearm crutches |
| Electrotherapeutic modalities – heat, cold, electrical, hydrotherapy | • Management and reduction of pain or inflammation | Discuss with therapist to choose suitable modalities based on medical condition |

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# Communication Skills for Supporting the Child and Family

## *Introduction*

Communication skills are a basic but crucial component in supporting children in palliative care. Good communication skills facilitate human connection and promote psychological well-being.[1,2] This section will provide brief guidance on common techniques for communicating with children and family members, including presence, listening, and responding techniques.

## *Techniques for communication*

| Presence | |
|---|---|
| **Skills** | **Barriers** |
| • Physical, mind and spiritual presence.<br>• Attentiveness and empathy<br>• Inner quietude, calmness<br>• Body gestures / position e.g. sit at the same eye-level as the child | • Excessively task-oriented<br>• Lack of concern<br>• Cognitive/emotional reactive |

| Active listening | |
|---|---|
| **Skills** | **Barriers** |
| • Genuine and congruent<br>• Unconditional/acceptance positive regards<br>• Encourage expression of thoughts and feelings (e.g. nodding, maintain eye contact)<br>• Check for understanding<br>• Use child-appropriate level of language<br>• Other medium of expression for kids: e.g. drawing, stories, cards | • Interrupting<br>• Judging<br>• Explaining reactively<br>• Advising prematurely<br>• Blocking of expression<br>• Self-disclose/talk about own experiences |

**Useful ways to check understanding**

- Clarifying "Correct me if I'm wrong, I'm hearing…"
- Repeating
- Paraphrasing
- Summarizing
- Reflecting "Sounds like you are going through a tough time…"

| Boundary awareness | |
|---|---|
| **Skills** | **Barriers** |
| • Aware of own emotion/belief and its impact on therapeutic intervention<br>• Have healthy emotional boundary (e.g. attentive, rested; not in overworked/ fatigue)<br>• Have healthy relational boundary (e.g. not taking money from family) | • Projecting own value<br>• Burnout/ exhaustion |

**Responding to Emotion in End of Life Communication**

It is important for the health care team to be sensitive to child or family members' emotional expression, and to allow their emotional processes as part of the journey in the end of life.

| Technique | Example |
|---|---|
| Normalizing and Validation | "It is normal to feel sad…"<br>"It is understandable that you are upset…" |
| Empathic Observation | "You are making a difficult choice…"<br>"It is not easy to be in what you are in now…" |
| Name/Acknowledge Emotion | "You look frustrated…"<br>"You seem helpless…" |
| Encourage Expression | "Tell me more about how you are feeling today?"<br>"I wonder how you have coped all this while." |
| Praise | "You are very brave…" |
| Paraphrase and Repeat Back | "If I understand you correctly, you are angry because you were told that your child's condition would not respond to antibiotics…" |
| Express Regret | "I am sorry that things have not turned out as we would have wished…" |
| Elicit Feedback | "How did you feel about our meeting today? I know that is not easy discussing death and the process of dying…" |
| Silence | A non-verbal way to say, "I understand" e.g. nodding head slightly<br>Giving space for more expression |
| Gesture or Touch | Offering tissues; touching the patient's arm (be culturally sensitive and asked for permission before touching) |

### *Brief Multi-Dimensional Psychosocial Assessment*

The multi-dimensional psychosocial assessment helps us to understand the child's psychological state in relation to emotion, cognition, social, and spirituality.[1,3] Questions are best phrased in simple and direct manner, at child's level of understanding.

| **Emotions** | |
|---|---|
| **Area of Exploration** | **Example of Open-Ended Questions** |
| General mood / behavioural symptoms, psychological distress (e.g. aggression, anxiety, depression) | How are you feeling today?<br>I see your tears, would you want to share more?<br>What you would like to do today to feel better? |

| **Cognition** | |
|---|---|
| **Area of Exploration** | **Example of Open-Ended Questions** |
| Orientation: Time, Place, People, Situation | Do you know where you are?<br>Are you aware of what is going on now?<br>What do the doctors or people around you tell you about your illness? |

| **Social** | |
|---|---|
| **Area of Exploration** | **Example of Open-Ended Questions** |
| Sociocultural background, social support | Would you want to tell me about your family/ friends?<br>When you are in distress/pain, what can others do to make you feel better? |

| Spiritual | |
|---|---|
| **Area of Exploration** | **Example of Open-Ended Questions** |
| Religious background, beliefs, hope | **FICA spiritual history tool**<br>**F** - Tell me about your faith<br>**I** - What importance does your faith have in your life?<br>**C** - Are you part of a spiritual community?<br>**A** - How would you like me to address these issues? |

| Resilience | |
|---|---|
| **Area of Exploration** | **Example of Open-Ended Questions** |
| Coping mechanism, protective factors | 1. What do you usually do to make yourself feel better?<br>2. Who do you usually go to when you need help? |

### *Breaking Bad News*

Even though breaking bad news is difficult, it is crucial to provide essential information in accordance with the child and family's needs and desires, and to tailor a more suitable treatment plan.

The 6-step SPIKES protocol is one of the methods to guide disclosure of bad news.[4,5] It is important to note that not every episode of breaking bad news will require all of the steps of SPIKES, but when they do they are meant to follow each other in sequence.

- Discuss with parents how child is best approached, with consideration of multiple factors such as age, personality etc.
- Tell the information at child's level of understanding, check with child if he/she can grasp the new information, correct immediately if misunderstanding happens.
- Be sensitive towards the child's emotion, provide support e.g. pat on arms, hugs when necessary (depending on relationship with child).

**SPIKES Protocol**

| Step | Guidelines |
|---|---|
| **S**etting Up the Interview | Arrange for some privacy that involves significant others. Sit down and make connection with the child. And manage time constraints and interruptions. |
| **P**erception | Explore family's ideas, concerns and expectations. |
| **I**nvitation | Adjust how much information to give based on child/family's comfort (e.g. "Would you want to know full information or should I skip the result? We can focus more on treatment plan." |
| **K**nowledge and Information | Warn child/family to prepare for bad news that is coming, (e.g. "I'm sorry to tell you that…" |
| **E**motion with Empathic Responses | Observe and identify the emotion and the reason behind, give child period of time to express his/her emotion, be attentive and empathic |
| **S**trategy and Summary | Presenting treatment that is available and manage expectation to be realistic in sensible manner. |

### *How Do I Handle Difficult Questions?*[3]

Difficult questions may include, “Am I going to get better?” “Am I going to die?” “How long do I have?”

- Listen to and acknowledge the question and check the reason behind it and if the answer is really wanted.
- You might say, “Would you like us to talk about that today or would you like to leave it to another day?” May also answer: “That’s a difficult question, there are no simple answers. We can hope to control your illness but can’t hope to cure it.”

### *The issue of “time left”*

- Avoid giving a prognosis with a definite time scale or expressing the notion that “nothing more can be done.”
- It is important to offer hope at some level, for example, “We cannot cure you, but we hope to control your disease” or “We will do our best to keep you as comfortable as possible.” Do not be afraid to say, “I don’t know.”
- Communicate time in range, i.e. hours to days, days to weeks, weeks to months and months to years.
- Flexible time scale, for example, “You may have a number of months,” or “You may have months rather than years.”

### *Collusion*

Definition: Withhold truth from children
Strategy: Healthcare team will not withhold truth from child but will not disclose truth in proactive manner. Truth should be told if invited by child and depending on their level of understanding.

Provide immediate follow-up (e.g. 24 hour) after consultation to child/family/significant others and help them to bridge resources as per needed, such as pastoral care, disease-specific support groups, palliative care services, counselling services and social workers.

*Be aware of the temptation to overload a patient with information.
Document in the medical and nursing notes what the patient and/or the family members/significant others have been told and their reactions.

### *Post breaking bad news support for parents*

Common issues and concern:

- Families feel abandoned by primary team once DNAR has been signed.
- Frequently sent home by casualty thinking no more active management.

Strategies:

- Allow admission if needed.
- Give hope of ensuring comfort.
- Continue follow-up with paediatric palliative care.
- Health care workers need to be aware of their possible avoidance behaviour, either verbal or non-verbal language that might upset the family.

### *Procedure for referral for clinical psychology psychotherapy services:*

For all government general hospital with palliative services

1. Palliative specialist/medical officer to write referral to psychiatry department
2. Patient to obtain appointment from psychiatry department
3. Psychiatrist/medical officer from psychiatry department assess and review patients
4. Psychiatrist to write referral to clinical psychologist depending on services required after assessment and review
5. Referral will be reviewed and discussed with referrer if necessary
6. Patient to obtain appointment from clinical psychologist
7. Patient to attend appointment and follow-up on pre-agreed date

For National Cancer Institute Malaysia

1. Palliative specialist to write referral to clinical psychologist depending on the services required
2. Referral will be reviewed and discussed with referrer if necessary
3. Patient to obtain appointment from clinical psychologist
4. Patient to attend appointment and follow-up on pre-agreed date

## *Psychosocial Intervention*

The relief of suffering in palliative care patients needs a combination of good symptoms control and psychosocial care. This section provides brief interventions that healthcare professional can carry out with children for psychosocial care.[1,5-7]

### *Psychoeducation*

- Counselling about the pain, aggravating and alleviating factors, management strategies, lifestyle factors that may influence the pain.

### *Self- management for child to regulate emotional distress/ pain*

- 2-6y/o: Blow bubbles, watch cartoon, play with toys/friends
- 6-12y/o: Talk about favourite things/places, deep breathing and squeeze balls, guided imagery exercise and to have a hobby
- Teenagers: Self-distraction, deep breathing, squeeze balls, guided imagery relaxation/ meditation/ mindfulness and to have a hobby or interest.

*Deep breathing relaxation*

- Put hands on stomach and cough, the contracting muscle indicating location of diaphragm, to ensure deep breathing with expansion of diaphragm
- Shallow and fast breathing may cause adverse impact such as vertigo and breathlessness. Pacing is important based on the consistent counting.
- Counting based on 4-2-6-2
- 4 – Inhale using Nose
- 2 – Stop/ Pause
- 6 – Exhale using Mouth
- 2 – Stop
- And repeat the cycle until patient reports feeling calmer
- To be done in relaxed position (e.g. sitting, lying down)

*Mindfulness of Pain*

- Seek help from caregivers/doctor for analgesia
- Breathe in and out to centre yourself
- Breathe until you feel you are calmer
- Bring your attention to the pain
- Try to keep a curious mind to see what pain is
- Notice the sensations, emotions and thoughts of pain
- Pay particular attention to the unpleasantness of pain
- Notice how the mind resists pain
- Relax the resistance
- Smile to your pain

*Progressive Muscle Relaxation by Edmund Jacobson*[5]

Progressive muscle relaxation is an exercise that relaxes your mind and body by progressively tensing and relaxation muscle groups throughout your entire body.

- You will tense each muscle group vigorously, but without straining, and then suddenly release the tension and feel the muscle relax. You will tense each muscle for about 5 seconds.
- If you have any pain or discomfort at any of the targeted muscle groups, feel free to omit that step.
- Progressive Muscle Relaxation videos are available at: https://www.youtube.com/watch?v=t3uK039WdaM

*Guided Imagery Exercise*[6]

Guided imagery is a mindful and meditative process that uses visualization and imagination to bring awareness to the mind-body connection. Children can easily access this healing process because they're naturally imaginative.

By relaxing into a vivid story child gain tools to deal with stress, pain or difficult feelings by listening to his/her inner wisdom and access their own power of healing.

Examples of scripts are available at https://www.greenchildmagazine.com/free-meditation-guided-relaxation-scripts-kids/

*Expressive Art Session*

- Music
- Story telling
- Drawing / colouring
- Play

*Wish fulfilment*

If possible, help the child or family to decide what they would most like to do before their loved one dies. The process of fulfilling the wishes often leaves wonderful memories for the child and the family.

*Supporting child with procedural pain*[7]

- Preparing the caregiver and child of procedural pain
- Supportive role for caregiver, provides physical touch (e.g. stroking, hold hands) when possible
- Remain calm for the child
- "Your child needs you to keep calm for him/her, can you do it now?"
- Caregiver can take deep breaths to calm themselves and help direct child to take slow deep breaths
- Distract the child
- Singing to child/ telling a story or jokes
- Take focus away from needle
- Teaching child to recognize successful coping and praise them
- Make use of the placebo effect for child e.g. kissing or blowing away the pain
- Validate, then reframe, useful phrases for caregivers:
  > It's painful right now, but it's going to get better
  > The medicines are going to make you feel better soon
  > You're being very brave. I'm proud of you.

## *Caregiver and Palliative Health Care Provider Well Being*

### *Caregiver Burnout*

It is common for caregivers to experience physical, psychological and emotional burnout while taking care of child in illness. Therefore, this section provides understanding to increase the awareness of caregiver burnout so their physical and psychological well-being were taken care while giving care to their children or family members.[8,9]

### *Risk factor for fatigue and burnout*

- Care burden
- Restricted freedom/activities
- Feeling of insecurity/ loneliness / fear
- Facing death
- Lack of emotional, practical and information-related support
- Role confusion/ multiple roles (e.g. work, spouse, child)
- Unrealistic expectations
- Lack of control (e.g. money, resources, skills)
- Overly high demands on self
- Lack of awareness of burnout and fatigue

### *Signs of caregiver burnout*

- Emotional and physical exhaustion
- Socially withdrawn
- Low mood, irritable, sense of hopelessness and helplessness
- Loss of interest in activities previously enjoyed
- Changes in appetite, sleep pattern
- Getting sick more often
- Feelings of wanting to hurt yourself or the person for whom you are caring
- Excessive use of alcohol and/or sleep medications

*Protective factors to assist the caregiver*

- Good social support
- Continuing previous activities
- Hope
- Keeping control (problem solving if able to)
- Satisfaction

*Helpful Behaviour to Overcome Caregiver Burnout*

- Have "ME" time
- Know own's limitation, get support and help when needed (e.g. family, workplace)
- Stick to routine and consistency
- Get enough rest
- Join a support group
- Use organizers (e.g. timers and reminders)

### *Health care provider well-being*

Health care provider's well-being is easy to be overlooked when dealing with the emotional and physical demand as a professional when treating patients. This section provides understanding and brief assessment for burnout to ensure healthcare provider has healthy physical and emotional well-being is well taken care of to continue doing justice to their treating patients.[10,11]

*Risk factors for burnout among palliative care providers*

- Lack of self-confidence in professional's own communication skills with patients and relatives
- Pressure of time
- Problems with the transmission of bad news in relation to ineffective curative treatment
- Lack of education and training in palliative care
- Dealing with pain, suffering, dying and death
- Worry of patient's economic ability
- Team conflict in palliative management

*Signs of clinician/support staff burnout*

- Physical, psychological and emotional exhaustion
- Frequently sick
- Difficulty setting healthy boundaries
- Dreading going to work
- Feeling under-appreciated
- Lack of ambition due to burnout
- Compassion fatigue

*Helpful Behavior in Overcoming Burnout*

- Getting social support (family and friends).
- Keeping to a routine.
- Carve out time to relax.
- Do enjoyable activities (e.g. sports, classes)
- Read self-help books for insight and strategies for coping
- Going to see a doctor/ mental health professional/ support group.
- Reframe unhelpful thoughts to helpful one.

*Self-assessment on Professional Quality of Life (ProQOL, 2009)*

Healthcare professional may self-assess their workplace well-being using Professional Quality of Life Scale (ProQOL) by B. Hudnall Stamm (2009).

ProQOL consists of 3 scales, mainly Compassion Satisfaction- Pleasure a person derive from being able to do his/her work well; Burnout- Association with the feelings of hopelessness and difficulties in dealing with work or in doing one's job effectively; Compassion Fatigue- Also known as secondary traumatic stress (STS). It is about one's work related, secondary exposure to extremely or traumatically stressful events.

*Professional Quality of Life Scale (ProQOL)©*
*Compassion Satisfaction and Compassion Fatigue (ProQOL)© Version 5 (2009)*
Available from https://www.macmh.org/wp-content/uploads/2016/05/Wkshp22_handout.pdf,
Reproduced with permission and courtesy from Dr. Hudnall Stamm.

When you [help] people you have direct contact with their lives. As you may have found, your compassion for those you [help] can affect you in positive and negative ways. Below are some questions about your experiences, both positive and negative, as a [helper]. Consider each of the following questions about you and your current work situation. Select the number that honestly reflects how frequently you experienced these things in the last 30 days.

1=Never 2=Rarely 3=Sometimes 4=Often 5=Very Often

___ 1. I am happy.
___ 2. I am preoccupied with more than one person I [help].
___ 3. I get satisfaction from being able to [help] people.
___ 4. I feel connected to others.
___ 5. I jump or am startled by unexpected sounds.
___ 6. I feel invigorated after working with those I [help].
___ 7. I find it difficult to separate my personal life from my life as a [helper].
___ 8. I am not as productive at work because I am losing sleep over traumatic experiences of a person I [help].
___ 9. I think that I might have been affected by the traumatic stress of those I [help].
___ 10. I feel trapped by my job as a [helper].
___ 11. Because of my [helping], I have felt "on edge" about various things.
___ 12. I like my work as a [helper].

___ 13. I feel depressed because of the traumatic experiences of the people I [help].
___ 14. I feel as though I am experiencing the trauma of someone I have [helped].
___ 15. I have beliefs that sustain me.
___ 16. I am pleased with how I am able to keep up with [helping] techniques and protocols.
___ 17. I am the person I always wanted to be.
___ 18. My work makes me feel satisfied.
___ 19. I feel worn out because of my work as a [helper].
___ 20. I have happy thoughts and feelings about those I [help] and how I could help them.
___ 21. I feel overwhelmed because my case [work] load seems endless.
___ 22. I believe I can make a difference through my work.
___ 23. I avoid certain activities or situations because they remind me of frightening experiences of the people I [help].
___ 24. I am proud of what I can do to [help].
___ 25. As a result of my [helping], I have intrusive, frightening thoughts.
___ 26. I feel "bogged down" by the system.
___ 27. I have thoughts that I am a "success" as a [helper].
___ 28. I can't recall important parts of my work with trauma victims.
___ 29. I am a very caring person.
___ 30. I am happy that I chose to do this work.

**PROQOL SELF SCORING WORKSHEET**

This worksheet helps you to get an estimate of your score on the ProQOL. To make it easy for you to use on your own, scores are grouped into high, average and low. If your score falls close to the border between categories, you may find that you fit into one group better than the other. The scores are estimates of your compassion satisfaction and fatigue. It is important that you use this information to assist you in understanding how your professional quality of life is, not to set you into one category or the other. The ProQOL is not a medical test and should not be used for diagnosis.

What is my score and what does it mean?

In this section, you will score your test and then you can compare your score to the interpretation below.

**Scoring**
1. Be certain you respond to all items.
2. Go to items 1, 4, 15, 17 and 29 and reverse your score. For example, if you scored the item 1, write a 5 beside it. We ask you to reverse these scores because we have learned that the test works better if you reverse these scores.

| You Wrote | Change to |
|---|---|
| **1** | **5** |
| **2** | **4** |
| **3** | **3** |
| **4** | **2** |
| **5** | **1** |

To find your score on **Compassion Satisfaction**, add your scores on questions 3, 6, 12, 16, 18, 20, 22, 24, 27, 30.

| The sum of my compassion Satisfaction questions was | My Score Equals | My Level of Compassion Satisfaction |
|---|---|---|
| 22 or less | 43 or less | Low |
| Between 23 and 41 | Around 50 | Average |
| 42 or more | 57 or more | High |

To find your score on Burnout, add your scores questions 1, 4, 8, 10, 15, 17, 19, 21, 26 and 29. Find your score on the table below.

| The sum of my Burnout questions | My Score Equals | My Level of Burnout |
|---|---|---|
| 22 or less | 43 or less | Low |
| Between 23 and 41 | Around 50 | Average |
| 42 or more | 57 or more | High |

To find your score on **Secondary Traumatic Stress**, add your scores on questions 2, 5, 7, 9, 11, 13, 14, 23, 25, 28. Find your score on the table below.

| The sum of my Secondary Traumatic Stress questions | So My Score Equals | My Level of Secondary Traumatic Stress |
|---|---|---|
| 22 or less | 43 or less | Low |
| Between 23 and 41 | Around 50 | Average |
| 42 or more | 57 or more | High |

**YOUR SCORES ON THE PROQOL:**
**PROFESSIONAL QUALITY OF LIFE SCALE**

Based on your responses, your personal scores are below. If you have any concerns, you should discuss them with a physical or mental health care professional.

Compassion Satisfaction _____
Compassion satisfaction is about the pleasure you derive from being able to do your work well. For example, you may feel like it is a pleasure to help others through your work. You may feel positively about your colleagues or your ability to contribute to the work setting or even the greater good of society. Higher scores on this scale represent a greater satisfaction related to your ability to be an effective caregiver in your job. The average score is 50 (SD 10; alpha scale reliability .88). About 25% of people score higher than 57 and about 25% of people score below 43. If you are in the higher range, you probably derive a good deal of professional satisfaction from

your position. If your scores are below 40, you may either find problems with your job, or there may be some other reason—for example, you might derive your satisfaction from activities other than your job.

Burnout_____

Most people have an intuitive idea of what burnout is. From the research perspective, burnout is one of the elements of compassion fatigue. It is associated with feelings of hopelessness and difficulties in dealing with work or in doing your job effectively. These negative feelings usually have a gradual onset. They can reflect the feeling that your efforts make no difference, or they can be associated with a very high workload or a nonsupportive work environment. Higher scores on this scale mean that you are at higher risk for burnout. The average score on the burnout scale is 50 (SD 10; alpha scale reliability .75). About 25% of people score above 57 and about 25% of people score below 43. If your score is below 18, this probably reflects positive feelings about your ability to be effective in your work. If you score above 57 you may wish to think about what at work makes you feel like you are not effective in your position. Your score may reflect your mood; perhaps you were having a "bad day" or are in need of some time off. If the high score persists or if it is reflective of other worries, it may be a cause for concern.

Secondary Traumatic Stress_____

The second component of Compassion Fatigue (CF) is secondary traumatic stress (STS). It is about your work-related, secondary exposure to extremely or traumatically stressful events. Developing problems due to exposure to other's trauma is somewhat rare but does happen to many people who care for those who have experienced extremely or traumatically stressful events. For example, you may repeatedly hear stories about the traumatic things that happen to other people, commonly called Vicarious Traumatization.

You may see or provide treatment to people who have experienced horrific events. If your work puts you directly in the path of danger, for example due to your work as a emergency medical personnel, a disaster responder or as a medicine personnel, this is not secondary exposure; your exposure is primary. However, if you are exposed to others' traumatic events as a result of your work, such as providing care to people who have sustained emotional or physical injuries, this is secondary exposure. The symptoms of STS are usually rapid in onset and associated with a particular event. They may include being afraid, having difficulty sleeping, having images of the upsetting event pop into your mind, or avoiding things that remind you of the event. The average score on this scale is 50 (SD 10; alpha scale reliability .81). About 25% of people score below 43 and about 25% of people score above 57. If your score is above 57, you may want to take some time to think about what at work may be frightening to you or if there is some other reason for the elevated score. While higher scores do not mean that you do have a problem, they are an indication that you may want to examine how you feel about your work and your work environment. You may wish to discuss this with your supervisor, a colleague, or a health care professional.

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# Spiritual Care

***"There are a lot of people to help you usher a child into this world, but very few to help you gently accompany a child out."***
***- a patient's father -***

## *Introduction*

Spirituality refers to how individuals seek and express meaning and purpose in their lives, and the way they experience their connectedness to the moment, to self, to others, to nature, and to the significant or sacred.

Religion and spirituality are not the same thing, neither are they entirely distinct from one another. While spirituality may incorporate elements of religion, it is generally a broader concept. Although religion and/or spirituality are important values for many, the influence of religion and/or spirituality on treatment decision-making or personal response to significant events remains unclear. A strong sense of spirituality may bring about positive emotions such as peace, awe, contentment, gratitude, and acceptance.[1]

Palliative care provision in Malaysia needs to consider the cultural and religious diversity which affect understanding or approach to life and death. Patients from various religious groups express their faith, specific beliefs, and values in their own way. Therefore, religious and spiritual needs are different for each person or family. Palliative care providers should refrain from assumptions and judgments.
Spiritual care assessments therefore should focus on the specific needs of every patient.

## *Providing Spiritual Care*

The National Consensus Project for Quality Palliative Care, 2009 developed evidence-based clinical practice guidelines for managing spiritual suffering.[2]

"Spiritual screening or triage is a quick determination of whether a person is experiencing a serious spiritual crisis and therefore needs an immediate referral to a certified chaplain. Spiritual screening helps identify which patients may benefit from an in-depth spiritual assessment."[2]
Spiritual screening and assessment of the patient or family helps to uncover distress or suffering that impair the ability to experience meaning in life, connectedness with self, others, world or the Divine.

Offering spiritual care often involves creating a safe and secure or 'sacred' space, for the patient, where parents, siblings or the healthcare team are comfortable as well. In this space, the child and caregivers can express their inner emotions or suffering, know that it is all right to do so, and that they will be heard and taken seriously.

The art of good spiritual care is the art of empathetic listening - being able to be still and to hear what is not being said.
The gift of "being present" means settings aside the time to be fully available to discuss the needs and concerns of a patient. It may entail turning off your phone, or not looking at your watch.

You may practice a combination of any of the following, as appropriate to the patients' needs:

- Empathetic listening and seeking to understand worries and fears, which gives clues to their current state of spiritual health and journey.
- Touching, holding, and other forms of silent soothing – especially for those who are unable to articulate their needs and concerns.
- Addressing spiritual concerns and providing clear and consistent explanations about what is happening.

- Letting the child have a sense of control and empowerment with regards to their condition and treatment.
- Acknowledging and validating their emotions, reinforcing self-esteem and respecting privacy - especially for teenagers.
- Playing and praying together with the children and families.
- Fulfilling their secret wishes or unfinished matters they want to resolve.
- Encouraging them to explore their relationships with self / others / the Divine, along the themes of, “Thank you”, “Forgive me”, “I forgive you”, “I love you”.
- Performing religious rituals or rites together.

For patients, family members, and caregivers who draw strength from their faith, the following might be helpful for their coping:

- Remind them of the merciful loving qualities of the Divine.
- Create space for repentance, forgiveness, contemplation, reflection and gratitude.
- Refer to or bring in their community or personal religious leaders if they prefer.
- Help patients adjust by offering or teaching concessions for rituals in order to ease worship while sick – prayer, fasting, etc.
- Personalize connection with the Divine through their choice of verses of the Qur’an / Bible / other scripture. Offer to recite or listen to their recitation.
- For prayer – ask them what they want to ask the Divine for – empower them to verbalize their own wishes and prayers.
- Focus on being patient-centered, yet balancing the sensitivities of the family and culture.
- Meet patients at their own levels - no judgments / assumptions.
- Increase your own levels of spiritual, religious and cultural competency to be able to engage and connect deeper with the patient.

### *Understanding and Assessing Spiritual Suffering*

Patients are usually preoccupied with their physical illness and treatment, making them ignore or downplay spiritual suffering or concerns. For children, spirituality is often centered around their understanding of daily life.

Infants and children with limited verbal ability and no concept of death depend on input from their physical senses and their physical relationship to the surroundings. In the pre-school years, children may not be able to conceptualize their own death as they cannot grasp its irreversibility. Some may have "magical" thinking – and mention monsters, angels, imaginary friends, etc. Primary school age children would have more adult-like concepts of death and begin to understand their own mortality.

We should try to familiarize ourselves with the cues and metaphors which people may use to convey their concerns or distress, especially when facing a prolonged illness or anticipating death.

**Common spiritual suffering / concerns, and their corresponding verbal cues**

| Spiritual Suffering / Concern | Examples of verbal cues |
|---|---|
| Concern about life after death | • What happens after we bury a dead person?<br>• When do I get to go to Heaven? Will my cat be there? |
| Concern about the dying process | • Does it hurt to die? Will I die at home / hospital?<br>• Is dying like sleeping? Will I know if I'm dead? |
| Lack of meaning / purpose / sense of self | • Doesn't matter if I die anyway, I don't even know why I am alive.<br>• I can't go to school, I can't play, I can't even eat properly. I can't do anything good.<br>• I used to be cool and popular, now I have no hair / carry a poo-bag, etc. (change in any physical appearance due to the illness). |
| Loneliness / separation (from parents, siblings, pets, friends) | • Nobody comes to play with me anymore.<br>• Can I come back and play with Meow if I die?<br>• What if I don't wake up from sleep tomorrow? |
| Fear of not being remembered / no legacy | • I'm worried everyone will forget me.<br>• I haven't done much in my life yet. |
| Angry towards others / God | • Why did God let me get cancer? This is not fair.<br>• My friend is meaner than me, but why didn't he get sick? |
| Desires relationship with God | • Will God forgive me? Where is God? Will He listen to me? |

| Spiritual Suffering / Concern | Examples of verbal cues |
|---|---|
| Questions / confusion about God and/or belief and value system | • Mama keeps praying to God, but I'm still sick anyway.<br>• Why does anybody have to be sick? |
| Loss of future, relationships, self, sense of unfinished business | • Who is going to take care of Mama when she grows old, if I'm already gone?<br>• I won't get to graduate with my friends and go with them to Tioman. |
| Feels guilt from past actions / thoughts | • Am I sick because I was a bad brother to my siblings?<br>• Did my sister get cancer because I pushed her at the playground? |
| Feels guilt from present actions / thoughts | • Because of my sickness, Mummy and Daddy always fight about money.<br>• Mummy can't go to work and kakak can't go to school because they have to take care of me. |
| Loss of control / autonomy over own body / space | • They keep poking me and taking me for tests, but nobody asks me or explains what they are doing!<br>• Mama's friends come and pray for me, but I don't want them to. |
| Unfinished business | • I wish grandma knows I love visiting her at kampong, and I wanted to see the new babies from her pregnant cat. |

Non-verbal cues are important. Body language, facial expressions, or drawings provide creative way to assess and understand what the patient / caregiver is thinking. Skillful clinicians listen intently and ask open-ended questions, granting patients the safe space to share and express their inner thoughts. Explaining to parents / guardians the relevance and meanings behind their child's cues could help them in making sense of and addressing their child's concerns, which may indirectly comfort the parents / guardians themselves.

### *The Spiritual Care Cycle*


Spiritual care aims to build rapport and trust as a prerequisite to conducting a spiritual assessment. The process leads to the development of a care plan, taking the steps for intervention, and finally evaluating the outcome.

The assessment process is non-linear. It is agile and flexible, with no fixed time or iteration limit. There may be occasions where the assessment and interventions will happen immediately as you may have only one opportunity to meet with the patient. You may have a longer timeframe with other patients and conduct multiple visits and the opportunity for a more elaborate or comprehensive care and intervention plan.
It also creates awareness of how the patient's religious or spiritual beliefs and practices may impact their treatment choices. This will facilitate the development of an action plan for intervention to provide the best comforting care possible to the patient.

### *Spiritual conversations with children*

Some useful tips, phrases and activities to help spiritual conversation with children:

1. **Listen to their words:** For example: God, heaven, spirit, karma, hope, wish, anger, sad, ghost, lonely, strong, weak, guilty, brave or afraid. Explore these thoughts by asking what the words mean to the child.

2. **Listen to their dreams:** The story or fears coming from dreams can give a chance to look at worries that are difficult to look at in 'real' life. Ask the child what the dream means to him/her. Do not try to explain it yourself.

3. **Listen for 'searching' phrases:** Phrases that show the child is thinking or searching deeply can give you a chance to encourage the child to talk about it more. The child may ask, "Why me?" or "I wish..." or "I wonder if…". You can help the child explore this further by asking, "What else do you wish?" or "How do you think that may happen?"

4. **Listen to their journey:** Children who are beginning to sense that they are dying often talk about going home or leaving. Talking about these feelings and exploring the journey with the child is difficult, but it needs to be done. Do not give false reassurances that they are not dying.

### *Spiritual Care Assessment Tools*

There are several Spiritual Care Assessment tools and questionnaires publicly available, however these may be more suited to assess adolescents and adults, rather than children. But you may benefit from a general basic understanding of these tools in order to get to the heart of spiritual care, or while supporting families and caregivers. Further details on the tools are available online.

*S.P.I.R.I.T. (Maugans, Ambuel and Weissman)*

S - Spiritual belief system
P - Personal spirituality
I - Integration with a spiritual community
R - Ritualized practices and restrictions
I - Implications for medical care
T - Terminal events (death) planning

*F.I.C.A. (Puchalski and Romer)*

F - Faith
I - Importance or Influence of religious/spiritual beliefs & practices
C - Community Connections
A - Address or Action

*H.O.P.E. (Anandaraja and Hight)*

H - Sources of hope, meaning, comfort, strength, peace, love
O - Organized religion
P - Personal spiritual practices
E - Effects on medical care and end-of-life care

When all else fails, remember that just your comforting and compassionate presence and accompanying of the child and caregivers is one of the most important and impactful forms of spiritual care.

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# Module 3

## Transition Care

- Discharge planning
- Continuation of care in the community
- Home medications
- Transition to adult services
- Advance care plan

# Module 3: Transition Care

## *Introduction*

Children requiring palliative care service may need to be transitioned from the hospital to the community, or from paediatric service to adult service. Management of children with chronic and complex medical conditions require input from various teams, but with similar objectives and goals of care. Communication between team and parent, and documentation of previous or ongoing intervention would be vital as part of effective care transition for the patient.

## *Discharge planning*

Important issues that needs to be ironed out before discharge include:

- Decision on place of care and key healthcare workers involved
- Preparation of key documents: Advanced care plan including personal resuscitation plan, symptom care plan
- Caregiver preparation including essential knowledge and skills.
- Ensuring continuous supply of required medications
- Procuring equipment and consumable items.
- Financial support and community resources

Table 3.1 shows a checklist for tasks to be completed or issues to be discussed before discharge or transfer out from any service. For each item ticked “yes”, the date that it has been carried out is documented.

Table 3.2 shows another checklist for consumable items for parents. This list helps the family to prepare all necessary medical consumables before the patient is discharged and helps with cost-estimation for the family.

*Table 3.1: Checklist for discharge*

| Items | Yes (Date) | No | Not Relevant |
|---|---|---|---|
| **1. Patient / Child**<br>Medically stable for home care | | | |
| **2. Parents/ Caregiver**<br>Family desires to have child at home | | | |
| Family has learned the necessary skills<br>• Basic Life Support<br>• Suction<br>• Feeding (Ryle's tube/ Perfusor/ Gastrostomy)<br>• Stoma Care<br>• Pressure Sore Prevention<br>• Wound Care<br>• Tracheostomy Care<br>• Oxygen Therapy/ Ventilation (refer to Consensus on Paediatric Home Ventilation/LTOT guidelines)<br>• Dialysis (refer to Peritoneal Dialysis SOP)<br>• Acute seizure treatment<br>• Clean Intermittent Self Catheterization<br>• Care of indwelling catheter<br>• Care of central line / Hickman catheter<br>• Therapies (OT/PT/SLT)<br>• Others | | | |

| Items | Yes (Date) | No | Not Relevant |
|---|---|---|---|
| Family has the finances to provide care<br>(if not, referral made for financial assistance) | | | |
| Full time caregiver available | | | |
| Family has considered palliative care and end-of-life care options | | | |
| **3. Multidisciplinary team discussion**<br>• Advanced care plan discussion and documentation<br>• Follow-up plan for various disciplines<br>• Identification of key healthcare staff as contact person or reference point for parents<br>• Contingency measures if readmission is needed<br>• Arrangements for attending school | | | |
| **4. Home**<br>Home visit made to ensure that the home environment is adequate, safe, and accessible<br>(For those on oxygen therapy/ ventilation, please refer to the relevant home visit documents) | | | |

| Items | Yes (Date) | No | Not Relevant |
|---|---|---|---|
| **5. Equipment** (if applicable)<br>• Bag and mask set<br>• Suction machine<br>• Wheelchair<br>• Perfusor feeding machine<br>• Commode chair<br>• Ripple mattress<br>• Oxygen concentrator<br>• Portable oxygen cylinder<br>• Fire extinguisher<br>• Spacer device<br>• Others | | | |
| **6. Medical supplies**<br>• Suction catheters<br>• Nasogastric tube<br>• Feeding / Kangaroo bags<br>• Tracheostomy tube<br>• Dressing set<br>• Others | | | |
| **Medications** | | | |

| Items | Yes (Date) | No | Not Relevant |
|---|---|---|---|
| **7. Home Care Team**<br>• Hospital-based home care team<br>• Health clinic domiciliary care team<br>(contacted, briefed/ trained and logistic arranged) | | | |
| **8. Written document**<br>• Written consent for home care<br>• Written agreement on equipment loan<br>• Basic Life Support attendance<br>• Patient's summary (Book)<br>• Letter to local paediatrician/ FMS / community OT/PT<br>• Letter to school<br>• Personal Resuscitation Plan / Advance care plan / Contingency Plan<br>• Letter to police for certification of home death (if for end of life care)<br>• List of medications/ consumables/ equipment | | | |
| **9. Financial assistance** (if qualified or applicable)<br>• Refer hospital medical social worker | | | |

| Items | Yes (Date) | No | Not Relevant |
|---|---|---|---|
| • Fill up Borang OKU / Support letter for JKM Caregiver Allowance<br>• Fill up Borang C (to apply to TBP for medical and rehab equipment and milk (if on NG or gastrostomy tube feeding) for non-civil servant.<br>• Fill up JPA Borang Perubatan 1/09 (for civil servants)<br>• Support letter to Pusat Zakat (Baitulmal) for purchase of milk and disposable diapers<br>• Others | | | |
| **10. Contacts**<br>Provide contacts for:<br>• Key primary care provider<br>• Home care team (hospital or community-based)<br>• Hospice (if for palliative care)<br>• Biomedical company of equipment and supplies | | | |

*Checklist courtesy of Dr Khoo Teik Beng, Paediatric Neurology Unit, Kuala Lumpur Women and Children's Hospital

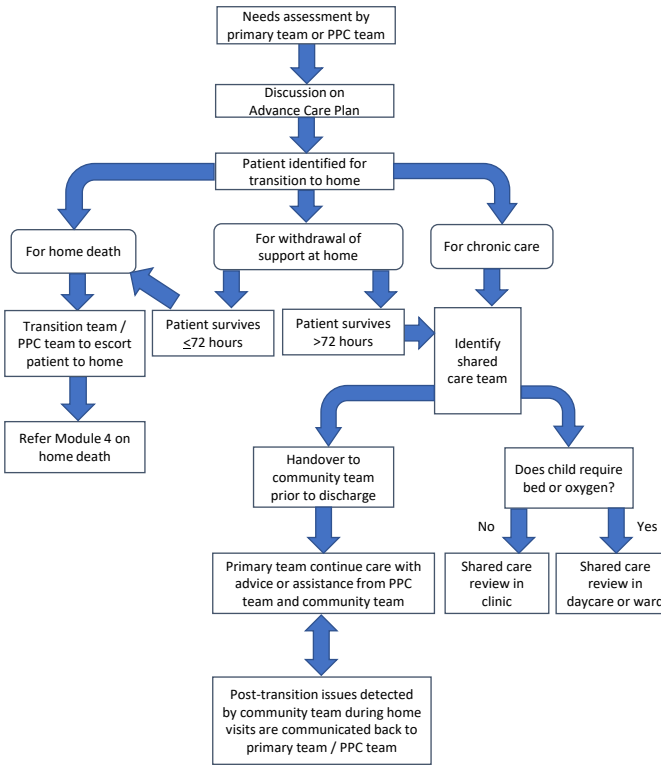
*Table 3.2: Template checklist for consumable items checklist and cost-estimation to be prepared prior to discharge home.*

| Category | No | Item | Size/Brand | Quantity Per Month | Tick Box |
|---|---|---|---|---|---|
| Feeding | 1 | Nasogastric tube | | | |
| | 2 | Feeding syringe (20/50cc) | | | |
| | 3 | Milk infusion bag+tube | | | |
| | 4 | Formula milk | | | |
| Respiratory | 1 | Suction tube | | | |
| | 2 | Normal saline for neb | | | |
| | 3 | Tracheostomy tube | | | |
| | 4 | Tracheostomy filter | | | |
| | 5 | Oxygen tubing and mask | | | |
| | 6 | Nebulizing set | | | |
| Dressing | 1 | One-use dressing set | | | |
| | 2 | Sterile cotton | | | |

| Category | No | Item | Size/Brand | Quantity Per Month | Tick Box |
|---|---|---|---|---|---|
| | 3 | Sterile gauze | | | |
| | 4 | Sterile glove | | | |
| | 5 | Latex glove (non-sterile) | | | |
| | 6 | Flavin /povidone | | | |
| | 7 | Saline 500ml/bottle | | | |
| Toileting | 1 | Urinary catheter | | | |
| | 2 | Diapers | | | |
| | 3 | Enema | | | |
| Medication | 1 | Alcohol swab | | | |
| | 2 | Medication syringes<br>20ml<br>10ml<br>5ml<br>3ml<br>1ml | | | |

| Category | No | Item | Size/Brand | Quantity Per Month | Tick Box |
|---|---|---|---|---|---|
| Skin | 1 | Lotion/moisturiser | | | |
| | 1 | Barrier cream | | | |
| Miscellaneous | 1 | Adhesive plasters / tape (to secure tubes / dressings) | | | |
| | 2 | Scissors | | | |

*Transition to home - flow process*



*Medical social worker in paediatric palliative care*

The Medical Social Worker Service's roles are:

a. To conduct the biopsychosocial assessment before the supportive therapy and practical assistance interventions are provided.
b. To provide practical assistance interventions e.g. purchase of medical equipment, purchase of medicines, funding treatment costs or general assistance, institutional placement and tracking down patients' relatives.
c. To provide supportive therapy interventions including consultation, emotional support and crisis interventions.
d. To facilitate application for eligible psychosocial assistance to patients and/or family members
e. Based on their assessment, they can recommend specific agencies or NGOs from whom the family are eligible to apply for required assistance.

**Examples of governmental and non-governmental agencies that can provide aid for patients**

| **Agency** | **Assistance** |
|---|---|
| Tabung Bantuan Perubatan (TBP) KKM | Medical equipment/ Medication/ Special formula |
| Majlis Kanser Nasional (MAKNA) | Medical equipment/ Medication<br>Transportation cost<br>Disposable items |
| National Cancer Society Malaysia | Living allowance/ Transportation cost |
| Yayasan Tunku Laksamana Johor | Medical equipment/ Medication<br>Transportation cost |
| Persatuan Paliatif Pediatrik Malaysia (MAPPAC) | Medical equipment<br>Transportation cost / Monthly financial assistance<br>Caregiver training / volunteer training<br>Respite care |

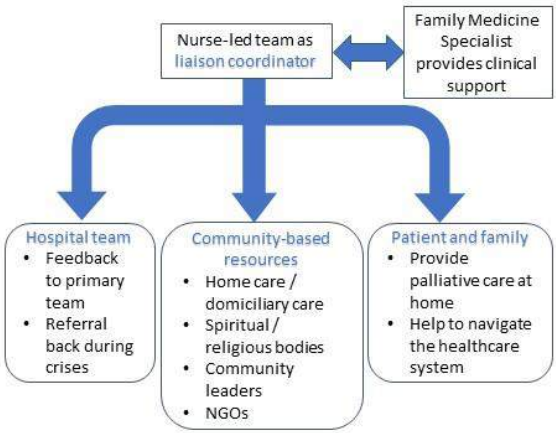
| Agency | Assistance |
|---|---|
| Baitulmal/ Lembaga Zakat Negeri | Medical equipment/ Medication<br>Transportation cost<br>Disposable items/ Special formula |
| Tzu Chi Foundation Malaysia | Medical equipment/ Medication<br>Disposable items/ Special formula |
| Tabung Kebajikan Perubatan Malaysia | Medical equipment/ Medication<br>Transportation cost |
| Jabatan Kebajikan Masyarakat | Monthly financial assistance |
| Persatuan Pemeliharaan dan Penyaraan Kanak-kanak Malaysia (MACAS) | Monthly financial assistance |

### *Continuation of care in the community (Post discharge)*

There are many models of collaboration between hospital and community healthcare providers, depending on resources and location. One example is the nurse-led community service. A trained nurse can become a liaison coordinator who can help the patient and family to navigate the local healthcare system. Community level palliative support may be coordinated with the local Family Medicine Specialist (FMS) or hospice. The hospital will provide additional support for crises.

It is vital for the hospital team to identify the available resources in the community before discharge. Availability of resources may be focused at urban communities. Special arrangements may be required if there are lack of necessary resources, particularly in rural communities.

**Example of nurse-led community team model**




## *Home medications*

### *Oral medications*

Continuous supply of medication can be arranged via the Centralised Medication Dispensing System or Sistem Pendispensan Ubat Bersepadu (SPUB).

The SPUB can be used for morphine or other drugs under Dangerous Drugs Act, provided the following conditions are met:

- the health clinic / district hospital can arrange to collect the medications from the tertiary hospital
- the pharmacist in the health clinic / district hospital has a system to store, monitor and dispense DDA drugs

### *Parenteral medications*

Medications delivered via the syringe driver may need to be constituted at the health clinic.

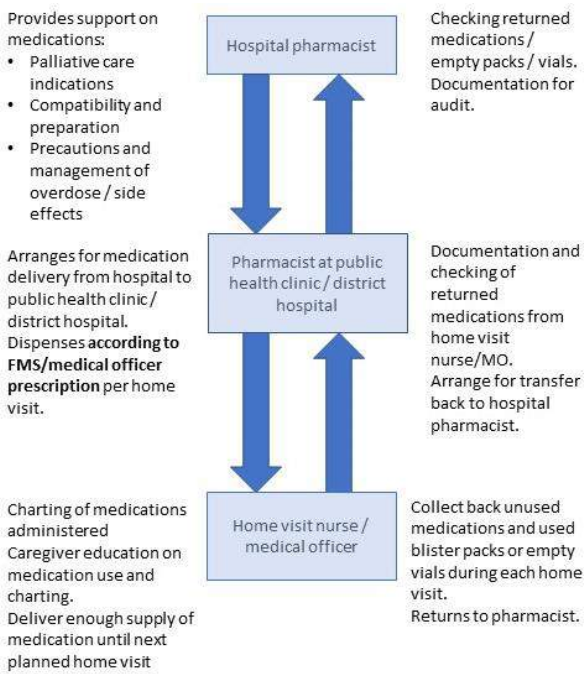
Discussions between hospital pharmacist with the local pharmacist is needed regarding:

- medications used for uncommon indications, which is common in palliative care
- compatibility of the drugs and preparation of parenteral medications
- steps to take in the event of medication error, side effects or overdose. (Careful documentation is essential.)

Arrangements should be made by local pharmacist to allow delivery of the medications from the tertiary hospital to their centre, and subsequently from their centre to patient's home.

There should also be a system in place for used / unused medications to be returned from the patient to the community pharmacy, and subsequently from the community pharmacy to the tertiary hospital. This allows for accountability of the medications that has been shared between hospital and community health centre.

**Example of flow process for medication provision from hospital to health clinic for PPC patients receiving home visits**




* different systems may be in place in different centres

Common drugs for home parenteral medications (SC bolus / infusion):

1. SC bolus / SC infusion Morphine sulphate for cancer pain, severe nociceptive pain, opioid-sensitive pain
2. Midazolam for terminal restlessness, anxiety, refractory seizures, dystonia
3. Dexamethasone for intestinal obstruction, raised intracranial pressure, anti-inflammatory for space-occupying lesion, severe pain, nausea and vomiting

4. Haloperidol for nausea and vomiting, terminal restlessness and hallucinations
5. Hyoscine butylbromide – for secretions, colicky pain,

**The medication should be integrated in the parallel planning with the primary team as part of the policy.**

Community pharmacist involvement is also helpful to ensure that family members learn how to manage the storage and administration of medications correctly.

Care must be taken for medication reconciliation every time patient is readmitted and discharged. Review all medications upon discharge from ward and ensure that caregivers are informed about changes to their usual regime.

### *Transition to adult services*

*Principles of transition to adult services*

1. Shared vision between adolescent and managing team
2. Collaboration with various agencies for health, education, housing, independent living, and social care.
3. Empowerment for the adult team to work with younger patients.
4. Engaging the community and lobbying the needs of people with life-limiting illness
5. Helping the young adult to talk about and plan for deterioration and crises, including dying.
6. Enabling adult health services to provide more patient-centred care including discussion on Advance Care Plan.
7. Improving the in-patient experience of young adults who are admitted to adult wards.
8. Supporting families during crises and bereavement.
9. Young people should have access to information.
10. Preparation for transfer should start before the child is 16 years old.

There are 3 phases of preparation for transfer to adult healthcare services:

| Phase | Process |
|---|---|
| Phase 1<br>(Before 16 years old) | To introduce the concept of transition to the patient and family, including introducing the patient to the key healthcare staff in the adult team. |
| Phase 2<br>(Age 16-18 years) | Combined patient review by paediatric team and adult team in the adult clinic |
| Phase 3<br>(After 18 years old) | Adult team provides subsequent care for patient, with the support of the paediatric team. |

Key information required during transfer of care to adult healthcare service:

1. Symptom profile, including pain
2. Patient's understanding of disease, preference and concerns of care
3. Support for caregivers
4. Patient's activities of daily living including mobility and nutrition
5. Multi-disciplinary assessment of needs
6. Advance care plan

### *Advance care plan*

The advance care plan (ACP) is a record of a discussion that has been taken place between a child or adolescent (where possible), their professional care givers and those close to them about their future care.[3]

Discussing the ACP allows patient and parents to retain their autonomy when facing uncertainty in patients' disease trajectories.[3] It improves the two-way communication between patients/parents and healthcare personnel when discussing short-term and long-term goals of care and treatment plan during a sudden serious event (personal resuscitation plan).[4]

The child and parents are given the opportunity to discuss their treatment or care plan options. Sometimes, treatment or care plan decision-making is required during sudden or unplanned serious events.[5] When the child is in a stable disease phase, the goals of care may still need to be re-discussed.

Hence, the ACP should be flexible as changes may be required later (parallel planning of life sustaining treatment and palliative care supports). The ACP should be reviewed regularly (every 6 to 12 months), even in the absence of changes.

The child's primary team paediatrician should usually be involved in the discussions. The first discussion should be led by the paediatrician. However, the paediatrician is not necessarily the chairperson for subsequent discussions.

Before the discussion, the teams should prepare information regarding confirmation of diagnosis and expected prognosis of the child's disease.

If the child's care involves many teams from local and referral hospital, the multidisciplinary teams may need to discuss among themselves even before discussions with the child and parents. Team discussion should involve all levels of staff, including the nurses. Nursing and junior staff can continue to support and follow through the ACP discussion and implementation.

*Timing of ACP discussion*

Discussion about ACP may be indicated if:

1. The child fulfils any of the criteria for the ACT/RCPH
2. categories for life-limiting or life-threatening conditions[5] (Refer Module 1)
3. The child's Paediatric Palliative Screening Scale (PaPaS) score is > 15[6] (Refer Module 1)
4. You would not be surprised if the child dies within a year[7,8]

OR

The child is not expected to live beyond 18 years of age

AND

Any of the following criteria:

- Previous admission to PICU
- Previous prolonged hospital admission >3 weeks
- Decline in underlying condition
- Increasing frequency of intercurrent illness and failure to return to prior baseline status
- Changes in treatment plans e.g. chemotherapy
- >3 unplanned hospital admissions in the past 12 months
- Child / family wishes to discuss ACP
- Admission from a long-term care facility
- Difficulty to control physical or emotional symptoms
- Patient, family or physician uncertainty regarding prognosis

In general, the ACP should be discussed as early as possible in the course of an illness, because it offers the greatest opportunity to explore the different possibilities that may happen as the child's illness progresses. However, the right time to introduce discussion about the ACP varies individually.

Timing of discussion should take the following into consideration:

- The preparedness and willingness to discuss by the child, parents and the physician.
- Availability of time to discuss, because the discussion should not be rushed.

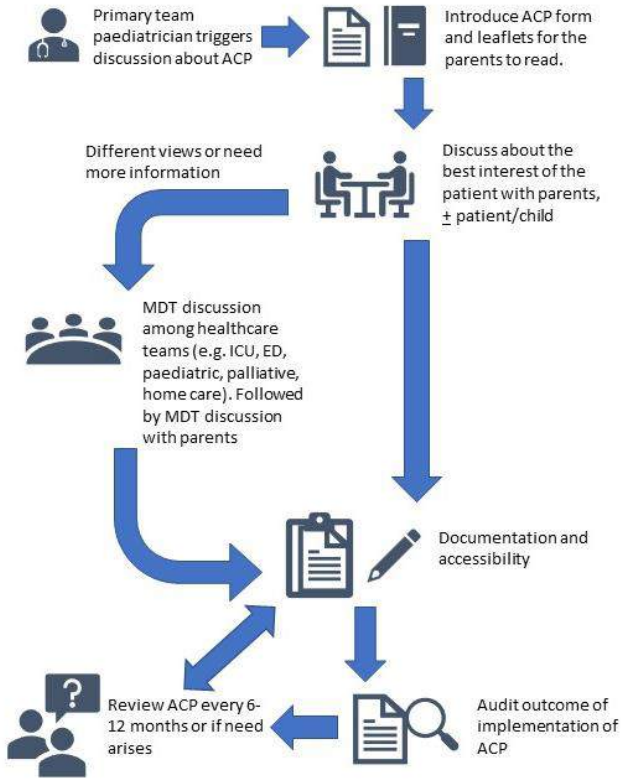
*Legality of the ACP*

It is the duty of clinicians, to act in the best interest of the patient. If the parent(s) or legal guardian is present when child collapses, they may wish to deviate from the previously agreed Advance Care Plan. Under these circumstances, the parent(s) or legal guardian's wishes should be respected, provided they are deemed to be in the best interests of the child/ young person.

The child/young person or parents/guardians may change their mind about any stated preferences in the care plan at any time. The documented ACP is just a record of prior discussions.

It is recommended that the ACP document is signed by both the primary team consultant and parents. This formality increases the likelihood that the document will be executed. However, signing the ACP itself is not strictly necessary.

*Flow process of discussing the ACP*




**Step 1**

- The primary team paediatrician identifies the need of ACP discussion for the children with life limiting disease.

**Step 2**

- The primary team paediatrician leads the first discussion to introduce the concept of ACP to the patient and parents.
- The blank ACP form and patient information leaflets is given to the patient and parents for further reading.

- An agreed time frame is given to the patient and parents for them to discuss with other family members before the next meeting.

**Step 3**

- The ACP discussion involves the primary team consultant / paediatrician, the patient (where possible) and the parents.
- If the child has no adequate cognitive ability and verbal capability to involve in the discussion, then the best interest of the child should be agreed upon between the paediatrician/clinician and the patient.

**Step 4**

- If the parents and patient (where possible) are unable to reach a consensus with the primary team consultant / paediatrician with regards to personal resuscitation plan and goals of care, then a multidisciplinary (MDT) team meeting should be arranged for further discussion among medical staffs.
- The MDT team members may include Paediatric Intensivist, Emergency physician, related subspecialty paediatricians, palliative care physician or paediatrician, nurse in charge and home care doctors or nurses.
- If the parents and patient (where possible) has the same decision with the paediatrician/clinician, then the ACP form should be documented and signed by both parents and the primary team paediatrician.

**Step 5**

- Review the ACP document regularly:
  > The child just being discharged from hospital admission
  > The child/parents wish to change or modify the ACP decision
  > Every 6 to 12 months duration from last review in the clinic appointment

**Step 6**

- Regularly audit (at least once every two years) to counter check if the ACP documented plans for a child were being carried out in your hospital whenever the child came to casualty or being admitted to ward.
- If the audit failed to prove the implementation of the ACP plan, then a root cause analysis should be sort out to look into the steps of failure and the strategy to improve the implementation.

*The ACP Form*

**Part I and II**

Fill in the personal details of the patient (name, age) and parents / legal guardian (name, contact telephone number, relationship) who are involved in the ACP discussion.

**Part III**

Fill in the diagnosis and the bio-psycho-social issues of the patient and family in this column.

**Part IV**

List down all major events or possible future emergency symptoms and signs related to the disease of the patient, especially those causing suffering and cardiorespiratory distress.

**Part V**

In the event of immediate reversible cause of acute life-threatening deterioration such as choking, tracheostomy blockage or anaphylaxis, active resuscitation must be carried out.

Decisions are required on treatment options for two scenarios:

- resuscitation during cardiorespiratory arrest (asystole and stop breathing)
- intervention plan for acute deterioration (not cardiorespiratory arrest)

**Part VI**

This part documents the patient's preferred place of death, the funeral arrangement and the care support for the family members after the patient deceased.

**PART VII**

This part documents the preference and goals of care process for patient and family members while patient is at the stable phase of disease.

**PART VIII**

This part contains the signatures from the paediatrician and the parent/legal guardian to signify the ACP discussion has been taken place. It also records the date that the ACP was signed.

# Template for advance care plan

**Paediatric Advance Care Plan (ACP)**

**PART I: PERSONAL DETAILS**

| | |
|---|---|
| Name: | Date completed: |
| Date of Birth: | Date for review:<br>(This document will not be valid after this date) |
| IC No: | Hospital RN No: |
| Home Address: | |

**PART II: PATIENT/FAMILY MEMBERS/CARERS INVOLVED IN ACP DISCUSSION**

| Name | Relationship to Patient | Age ( years) | Contact number |
|---|---|---|---|
| (Main) | | | |
| | | | |
| | | | |
| | | | |

**PART III: DIAGNOSIS / CLINICAL ISSUES**

**PART IV: SYMPTOMS & SIGNS TO EXPECT IN THE EVENT OF EMERGENCY**

*Please refer to symptom care plan (if available) for detailed management.*

The child/young person or parents /guardian can change their mind about any of the preferences on this care plan at any time. This document is a record of discussion. Version 1: August 2019

**PART V: PERSONAL RESUSCITATION PLAN**

**In the event of immediate reversible cause of acute life threatening deterioration such as choking, tracheostomy blockage or anaphylaxis, please intervene and treat actively.**

Clinicians have a duty to act in a patient's best interests at all times. If a parent or legal guardian is present at the time of their child's collapse, they may wish to deviate from the previously agreed Advance Care Plan and under these circumstances their wishes should be respected, provided they are thought to be in the best interests of the child/ young person.

**The child/young person or parents/guardian can change their mind about any of the preferences on this care plan at any time. This document is a record of discussion.**

**Resuscitation Status for Cardiorespiratory Arrest** ( Please tick (√) your preferred option)

- ☐ For active cardiopulmonary resuscitation (including bag and mask ventilation, chest compression, intubation and Intensive Care unit admission)
- ☐ Do not attempt cardiopulmonary resuscitation

Further Information (If any):

**Intervention plan for Acute Deterioration ( Non Cardiorespiratory Arrest)**
( Please circle either "Yes" or "No" option)

| | | |
|---|---|---|
| **YES** | **NO** | Oxygen (Face Mask or Nasal Cannula) |
| **YES** | **NO** | Airway clearance/suction ( Include Bag and Mask if required) |
| **YES** | **NO** | Analgesic / sedation for comfort |
| **YES** | **NO** | Tube feeding |
| **YES** | **NO** | Intravenous Access |
| **YES** | **NO** | Intraosseous Access |
| **YES** | **NO** | Intravenous antibiotic |
| **YES** | **NO** | Blood transfusion |
| **YES** | **NO** | Intubation and ventilation |

Further Information (If any):

*Further discussion is needed for any unforeseen condition that requires emergency surgical procedures.*

**PART VI: End of Life Care**

| **Preferred Place of Care** | **Priorities of Care** *(wishes, hope, organ donation, funeral, memories making, bereavement support)* |
|---|---|
| ☐ Hospital<br>☐ Home<br>☐ No preference<br>☐ Undecided<br>☐ Others:_____ | |

**PART VII: PREFERENCES DURING LIFE**

| |
|---|
| **Patient's Preferences** *(e.g. Place of care, wish, symptom management, people to be involved [professional/ non-professional], activities to be continued [including spiritual and cultural] and goal-directed outcomes)* |
| **Family's Preferences** *(e.g. who you would like to be involved, sibling needs (e.g medical, spiritual or cultural backgrounds).* |

**PART VIII: Agreement with Discussions**

Senior Clinician's agreement: I have discussed and support this care plan

Signature:

Name: Designation:
Date: Phone contact:

Parent / Guardian's agreement: I have discussed and support this care plan

Signature: Relationship:

Name: Phone contact:
Date:

## Template of letter to police officer for confirmation of death

Kepada
Pegawai Polis Daerah _____

Nama Pesakit :
No. K/P :
Penyakit :
Alamat :

Ayah :
No. K/P :
Ibu :
No. K/P :

Surat ini adalah untuk mengesahkan bahawa [nama pesakit] sedang mengidap penyakit [diagnosis] semenjak [tahun diagnosis dibuat] dan berada di bawah rawatan pihak kami di [nama hospital].
Bagaimanapun, semenjak [Tarikh], keadaan_[nama pesakit] telah menjadi semakin teruk, dan ibu bapa [nama pesakit] telah sedia maklum bahawa penyakit ini akan semakin melarat dan pesakit akan meninggal disebabkan penyakit ini.
Ibu, bapa dan [nama pesakit] telah menyatakan keinginan untuk menghabiskan masa akhirnya di rumah. Sekiranya ini terjadi, kami berharap agar surat ini dapat menerangkan situasi yang dialami oleh keluarga ini dan memudahkan mereka untuk mendapatkan sijil kematian dan permit pengebumian.
Pihak tuan boleh menghubungi kami sekiranya terdapat sebarang kemusykilan. Pihak kami akan membuat apa yang boleh untuk membantu keluarga ini mengharungi masa yang sukar ini. Pegawai yang boleh dihubungi semasa waktu pejabat ialah Jururawat / Pegawai Perubatan yang menjaga [wad atau klinik berkenaan] di nombor [nombor telefon] ext: [nombor sambungan] atau di talian terus [nombor talian terus].

Segala kerjasama dari pihak tuan adalah amat dihargai dan didahului dengan ucapan terima kasih.

Yang menjalankan tugas,

_____
Pegawai Perubatan
Jabatan Paediatrik
Hospital [ ]

## *References for this section*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4. Tsai E, Canadian Paediatric Society (CPS), Bioethics Committee. Advance care planning for paediatric patients. Paediatrics & child health. 2008 Nov 1;13(9):791-6.

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# Module 4

## End-of-Life Care

- Active dying
- Caring for the family
- Symptom management at end of life: pain, terminal restlessness or delirium, terminal seizures, excessive respiratory secretions, nausea and vomiting, breathlessness, terminal bleeding
- Basic nursing care at end of life: nutrition & hydration, oral care, skin care, home oxygen support
- Home parenteral medications
- Home extubation
- Home death
- Grief
- Ethical issues regarding end-of-life

### *Active dying*

Active dying is the final phase of dying, commonly referred to as the final 48-hours of life.[1,2] The following are common signs and symptoms that may occur in last few days or hours of life:[3]

| Physiological changes | Symptoms |
|---|---|
| **Neurological** | Increased lethargy<br>Drowsiness<br>Unable to talk<br>Failure of temperature regulation<br>Terminal delirium |
| **Respiratory** | Cheyne-Stokes breathing / apnoea<br>Mouth breathing<br>Death rattle / terminal congestion<br>Gasping |
| **Circulatory** | Cool peripheries<br>Dusky skin<br>Feeble pulse<br>Tachycardia / bradycardia |
| **Gastrointestinal** | Reduced appetite and thirst<br>Dysphagia<br>Gastric stasis<br>Bowel incontinence |
| **Renal** | Urinary incontinence<br>Reduced urine output |

### *Caring for the family*

Before the patient enters active dying phase:

- Discuss **goals of care** and **advance care plan** with family and patient.
- Take note of patient and family's **preferences and wishes**, eg. Place of care and death, spiritual rites.
- Management **plan** should incorporate patient and family's preferences.
- Explore and address patient and family members' concerns during end-of-life.

*What do I do when the child enters active dying phase?*[4]

- Any treatment or intervention given are not for prolonging life.
- Inform family members regarding impending death and expected signs or symptoms.
- Educate and prepare caregivers on how to manage the anticipated symptoms.
- As far as possible, provide a contact with a healthcare professional who can guide them during the active dying phase, especially if home death is desired.
- Take the family's cultural and religious beliefs into consideration on appropriate dying rituals.

*How to provide medications to the dying child?*

- Most medications need to be converted into subcutaneous, transdermal, sublingual or rectal route when the child is no longer able to take orally.
- Teach caregivers how to administer the subcutaneous medications and how to operate the syringe driver, if any.
- Provide medications for anticipated end-of-life symptoms to the family and educate family on indications.

*Preferred place of death*

- Discuss with family members regarding suitability of preferred place of death.
- Consider availability of equipment, feasibility of symptom control, and caregiver preparedness.
- Discuss about possibility of rapid transfer and whether it is in their best interest.

## *Pain*

### *Assessment of pain*

Child is unable to communicate verbally.

Determine most likely cause of pain and whether it is reversible (refer Module 2)

Use non-verbal pain scales such as FLACC (face, legs, activity, cry, consolability) scale to measure pain intensity.[5]

### *Management of pain*

Oral analgesics may be converted to subcutaneous morphine or transdermal fentanyl.

SC morphine can be given as bolus or as an infusion.

Transdermal fentanyl can be initiated if minimum daily oral morphine requirement is 15mg and above.[6]

Refer to opioid equivalence chart for dose conversion.

Continue oral or SC morphine for a further 8-12 hours when initiating transdermal fentanyl. After that, oral or SC morphine can be safely discontinued.[6]

### *Caregiver training*

Teach caregiver to administer bolus doses for breakthrough pain.

Teach caregiver how to operate the syringe driver (see Section IV).

Teach caregiver to maintain a simple pain diary and opioid charting (see Fig 4.1).

To convert oral morphine to SC morphine, divide oral morphine dose by 2.5.
e.g. oral morphine 10mg = SC morphine 4mg

**Fig 4.1 Suggested format of simple pain diary and medication log**

| **Prescription by doctor:**<br>Regular dose: Syrup morphine 2.5ml every 4 hours<br>Breakthrough pain: Syrup morphine 2.5ml when needed for pain | | | | |
|---|---|---|---|---|
| Date: 18 April 2019 | | | | |
| Time | Pain score | Name | Amount | Remarks |
| 0300 | 4/10 | Morphine | 2.5ml | |
| 0700 | 7/10 | Morphine | 2.5ml | |
| 0930 | 8/10 | Morphine | 2.5ml | Sudden worsening of pain |
| 1100 | 5/10 | Morphine | 2.5ml | |
| 1500 | 4/10 | Morphine | 2.5ml | |
| 1900 | 5/10 | Morphine | 2.5ml | Vomited after dose |
| 2300 | 5/10 | Morphine | 2.5ml | |

### *Terminal restlessness or delirium*[7]

*What is it?*

An abrupt increase in anxiety, agitation and confusion at end of life.

*Assessment*

- Any symptom that has not been relieved?
- Any medications that could have triggered the restlessness?
- Any fever or evidence of infection?

*Pharmacological management*

Palliative sedation may be given to alleviate patient suffering or caregiver distress without intention to shorten the patient's life.

*Refer to the appendix for the doses:*

- SC bolus or continuous SC infusion midazolam
- SC bolus, or SC/IV infusion haloperidol
- Sublingual lorazepam
- CSCI phenobarbitone

*Non-pharmacological management*

- Appropriate lighting to time of day (dark at night, bright during daytime)
- Reduce noise and light stimulation.
- Provide visual stimulus to remind of day, date and time. E.g. clock, newspaper
- Promote a familiar environment.
- Continue to talk as usual to comfort the child

### *Terminal seizures*[8]

*What is it?*

- Seizures may become more prolonged and frequent at end of life.
- Absorption of oral anticonvulsants is poor at this stage.

*Risk factors*

- Underlying epilepsy
- Neurological disorders
- Brain tumours
- Metabolic derangement
- Medications that lower seizure threshold e.g. amitriptyline, tramadol, baclofen

*Caregiver preparation*

- Provide oral midazolam (for buccal administration) or rectal diazepam.
- Educate on immediate actions during a seizure (remove potential hazards, left lateral position, head turned to lateral, not to insert objects into mouth)

*Pharmacological management*

- Buccal midazolam
- Rectal diazepam
- Consider SC midazolam if not controlled
- Consider CSCI midazolam or CSCI phenobarbital if not controlled with bolus SC midazolam

## *Excessive respiratory secretions*[9]

*What is it?*

Excessive salivation can occur at the end of life, due to failure of swallowing. Secretions can pool at the throat of the patient causing a rattling sound while breathing.

*Non-pharmacological measures*

- Head positioning (avoid flexed neck posture, lateral position)
- Bibs or absorbent towels

*Medications*

- Sublingual atropine 1% eyedrops
- Hyoscine hydrobromide (Scopoderm®) patch
- SC Glycopyrronium bromide bolus or infusion
- SC hyoscine butylbromide bolus or infusion

## *Nausea and vomiting*[9]

*Assess for causes*

Refer to symptom management module for assessment of causes.
At the end of life, nausea and vomiting can be due to:

- Gastric stasis
- Increased ICP in brain tumours
- Intestinal obstruction
- Side effects of medications

*Non-pharmacological management*

Reduce or withhold feeds if there is gastric stasis.
Nausea and vomiting is not usually a great problem at end of life unless there is bowel obstruction or it has not been controlled previously.

*Pharmacological management*

Choice of medications depends on underlying cause. At end of life, subcutaneous

- Haloperidol (first-line)
- Metoclopramide - not for intestinal obstruction
- Promethazine (subcutaneous infusion, not for bolus)
- Dexamethasone (increased ICP or intestinal obstruction)

## ***Breathlessness[9]***

*Assess for causes*

- Anxiety
- Physical discomfort
- Environmental factors
- Accumulated airway secretion
- Medical disorders (pneumonia, heart failure, sepsis, acidosis)

*General principles*

- Treat underlying cause if reversible.
- Oxygen supplementation may not be necessary or helpful, unless there is documented hypoxia.

*Pharmacological management*

- Bronchodilators if bronchoconstriction is present
- Nebulised saline
- Low dose short-acting morphine

*Non-pharmacological management*

- Direct a fan to the side of patient's face
- Open a window
- Repositioning – prop up to 45 degree
- Suctioning if necessary

### *Terminal bleeding*[10]

*Assess for causes*

- Coagulopathy and rupture of oesophageal varices from liver failure
- Tumour erodes to major blood vessel
- Thrombocytopenia

*General principles*

- Goal of care is patient comfort.
- Calm the patient and family members.
- Appropriate analgesia and sedation may be prescribed to reduce the child's anxiety.

*Pharmacological management*

- SC Morphine
- SC Midazolam
- Topical Adrenaline

*Morphine and midazolam should be considered as terminal sedation if the child is restless or anxious due to bleeding.

*Non-pharmacological management*

- Prepare dark cloth, linen and bucket near the bedside
- When the major bleed happens, compress adrenaline-soaked cloth at bleeding site.

### *Nutrition and hydration*[11]

- Nutrition and hydration at the end of life is for patient's comfort, and NOT for weight gain or sustaining life.
- Initiating tube feeding is not recommended during active dying.
- Gastric stasis occurs at end of life, may lead to vomiting.
- Subcutaneous fluid infusion can be started if dehydration is causing distress to the child, However, increasing hydration at end of life may increase secretions or oedema.
- Advise family members to perform oral care, even if the child is no longer able to take orally.
- Subcutaneous fluids can be given short term (≤10 days) via gravity infusion sets or syringe driver.

**Cultural considerations**

Food and drink play an important role in our culture and family members become concerned when someone is no longer able to eat or drink. Explain to family members that at the end of life, hunger and thirst is no longer an issue due to reduced physiological needs.

*Indications for subcutaneous hydration are:*

- Hypercalcaemia
- Nausea and vomiting
- Dysphagia
- To improve myoclonus (involuntary contractions of muscles)
- Assists sedation

### *Oral care*[12]

- Alleviates the discomfort from dry mouth, halitosis and excessive salivation.
- Active routine of mouth care is required.

*Caregiver training*

- Clean the mouth regularly or at least 4 times a day with wet gauze to maintain oral hygiene and prevent odour.
- Gently remove the plaque, debris or dry skin from oral mucosa with oral swab stick or wet gauze.
- Moisten the mouth regularly with water spray or ice chips as frequent as possible.
- Apply lip balm to prevent cracked lips.
- Avoid glycerine and lemon - increase dryness and may damage tooth enamel.

### *Skin care*

*Possible changes at end of life*[13]

- Higher risk of pressure sore due to immobility and reduced skin perfusion
- Difficult to maintain hygiene if unable to transfer to bathroom
- Oedema and dry skin increase risk of skin breakdown and infection
- Incontinence leads to irritant contact dermatitis

*Caregiver training:* [14]

- Regular re-positioning to prevent pressure sore.
- Use pressure-relieving mattress.
- Regular bedside sponging for hygiene.
- Apply emollients at pressure site or swollen peripheries to reduce friction.
- Apply moisturisers regularly on dry skin to reduce itchiness.
- Handle oedematous limb gently.
- Apply barrier cream at diaper area.
- Use of sliding sheet to prevent shearing force.

### *Home oxygen support*[15]

- Indicated for breathlessness due to hypoxaemia ($SpO_2$< 90%)
- The aim of home oxygen therapy is to **provide comfort** rather than prolong life.
- Routine checking saturations may not be necessary for palliative care.

### *Guidelines for prescribing home oxygen*

**Hospital and healthcare workers**

- Indication for the use of oxygen should be clearly documented in patient case note
- Oxygen prescription should include flow rate and route of delivery:

| Route of oxygen support | Oxygen flow rate |
|---|---|
| Nasal cannula | 1-2.5L/min |
| Face mask | 4-6L/min |

- Humidification of home oxygen is a must if oxygen is given via tracheostomy tube.
- For oxygen flow rate that is more than 2L/min, humidification helps to prevent drying effect on mucous membranes.
- Provide family members written information regarding dangers of using home oxygen near sources of fire.

**Home assessment**

- Should be arranged **BEFORE discharge** and commencement of home oxygen support.
- Regular reassessment at each home visit by community palliative care provider

**Assessments should include:**

- Home environment (proximity to naked flames from stoves/lamps/cigarettes)
- Attitude toward risks
- Smoking behaviour of family members
- Advice family regarding smoking cessation and location of oxygen tank in the home.

*Risks and adverse effects of home oxygen support:*

- Dry nose/eyes/mouth
- Pressure sores over cheeks, ears or nose
- Claustrophobia
- Hypercapnia respiratory failure
- Fire risk

*Home non-invasive ventilation (NIV)[16]:*

- The aim of the use of NIV is for symptom control, not for prolonging life.
- NIV improves symptoms by:
  > reducing respiratory effort by the patient
  > reducing carbon dioxide retention
- NIV can be used when withdrawing invasive ventilation support in ICU or the ward.
- Community palliative care providers require training to operate the ventilator prior to patient discharge from hospital.

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# Home parenteral medications

## *Subcutaneous route*[1–3]

Suitable for parenteral administration of medications when:

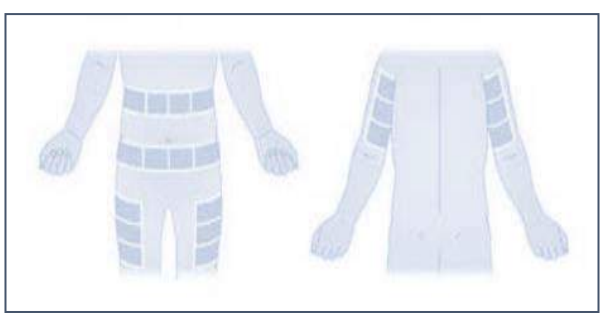
- Unable to take orally (nausea, vomiting, dysphagia)
- Poor gastrointestinal absorption
- Intestinal obstruction
- Reduced consciousness

Intravenous lines are not recommended for the home setting.

### *Insertion*[4,5]

- Use a fine gauge paediatric cannula (24G/yellow) or a butterfly needle
- For butterfly needle, grasp the textured sides of the wings and bring them together, pinching firmly.
- Using thumb and index finger, gently pinch the skin around the selected site to identify the subcutaneous tissue.
- Insert at 30-45o to the skin surface.

- Secure with adhesive tape.
- Connect to infusion line (for infusion) or yellow stopper (for bolus medications)



**Avoid** inserting the line at:

- Bony prominences
- Joints
- Oedematous, infected, broken or bruised skin
- Recently irradiated skin area
- Sites in contact with wheelchair harnesses or seatbelts
- Areas with a lot of body hair

### *Syringe driver*[6–8]

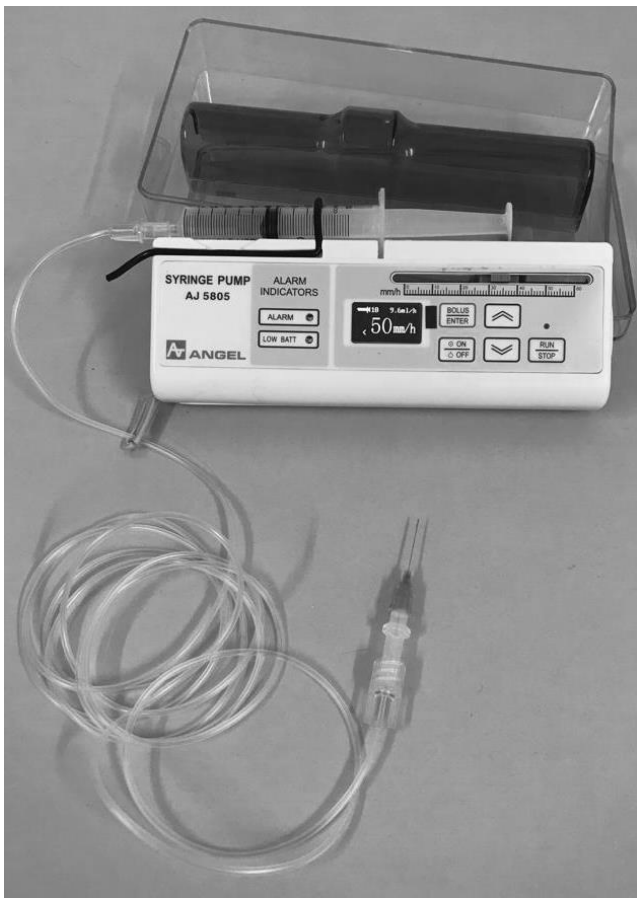
*Medication preparation for use with a syringe driver*

- Check for compatibility especially if combining drugs in single syringe
- Calculate the dose and volume needed for the infusion.

| Volume of syringe | Volume of diluent |
|---|---|
| 10ml | 10ml |
| 20ml | 18ml |
| 30ml | 22ml |
| 50ml | 33ml |
| Take note that larger syringes need to be under filled for the syringe driver to work! | |

- Label the prepared medications syringe (patient's name, name of drug(s), strength / dilution, rate ordered, date and time, name of staff who prepared the syringe).
- Both water for injection and normal saline can be used for diluting drugs. Normal saline is preferred when there is risk of skin irritation at the site of infusion but may not be suitable for some drugs. Water for injection is hypotonic and may cause skin irritation. However, it has less risk of drug incompatibility.

**Caution:** Promethazine and phenobarbitone cannot be given as a subcutaneous bolus due to high risk of severe irritation and tissue necrosis. However, it may be given as an infusion diluted with normal saline




**Syringe driver with infusion set**

*Combining medications in a single syringe*

- Check for compatibility before combining medications in a single syringe. Refer to your pharmacist!
- Common medications that can be combined include:
  > Midazolam
  > Morphine or other opioid
  > Hyoscine hydrobromide or Glycopyrrolate
  > Metoclopramide
  > Haloperidol

- Incompatible medications can result in:
  > Precipitation / crystallisation of the drugs
  > Cannula blockage
  > Skin / tissue irritation
  > Ineffective absorption of drug into the body

*Storage of the medications*[7,8]

- Most drugs diluted in normal saline are physically compatible and stable for 24 hours at ambient temperature.
- Unused prepared syringes should be stored in the refrigerator for not more than 7 days.

### *Operating the syringe driver*[9]

- Different models have different operations. Please refer to manufacturer's manual!
- Check that the delivery rates have been calculated correctly.
- For newly set up infusion line, let the medications to fill up the whole tubing before starting the infusion (Priming the line).
- Change the infusion tubing whenever the infused medication is changed.
- If doses are altered, use a new syringe. Altering the rate of delivery is not advisable.

| Caregiver education |
| --- |
| Educate caregiver on use of syringe driver at home on:<br>• Basic steps of operating the syringe driver<br>• Recognizing the occlusion alarm and almost empty alarm.<br>• How to replace empty syringes<br>• Steps to take if occlusion occurs<br>• How to eliminate air bubbles. |

*Monitoring of the infusion line*[9]

| Monitoring of the infusion line | Steps to take |
| --- | --- |
| Ensure line is secured with adhesive dressing. | Replace the adhesive dressing if dirty or less adhesive. |
| Check infusion site for redness, swelling, discomfort/pain and leakage. | Remove current line and insert a new subcutaneous line at a different location. |
| Check the diluted medications for precipitation, cloudiness, big air bubbles or colour change. | Replace the syringe immediately. |

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# Withdrawal of life support

In certain groups of severely ill children, prolonged ventilation and intensive care may no longer be in their best interests.[1]
These may include:

- No chance for survival, or imminent death despite further treatment.
- Permanent severe disabilities or incapacitating conditions, resulting high burden of pain and suffering.
- The decision to withdraw support is led by the consultant, supported by the team of healthcare professionals involved in the care of the child and the child's parents.[1] Early involvement of a palliative care team is advisable in planning and communicating decisions with family members.

## *Introduction of withdrawal*

- Consult palliative care team specialist.
- Identify the appropriate clinicians and healthcare professionals to be present during family meeting to discuss withdrawal.

Important points to be discussed with family:

- Options for
  > continuing current intensive care support vs
  > withholding escalation of support vs
  > withdrawal of care
  > place for withdrawal of care (home vs hospital)
  > pros and cons of withdrawal of care – child may die faster if care is withdrawn, but withdrawal allows the team to plan for better quality of end-of-life care
- Shared decision that there will be no more reintubation or cardiopulmonary resuscitation in the process of withdrawal.
- Management of symptoms after withdrawal
- Preferred place for extubation
- Timing of death is variable, child may survive beyond expected time frame.
- Wishes family may have before extubation, e.g. taking family portraits, legacy work (hand mould, handprints etc.)
- Ensure family's concerns and values are addressed appropriately.
- Shared decision making on timing of:
- Extubation
- Discontinuation of essential life-sustaining medications

Document discussions and agreed steps in case notes.

## Inpatient ventilator withdrawal

Inpatient ventilator withdrawal can be conducted in 2 ways:[2]

- **Immediate extubation**
  > Endotracheal tube is immediately removed and humidified oxygen is given instead.
  > Preferred method if patient is conscious, minimal secretions, and airway patency can be maintained.

- **Terminal weaning**
  > Gradual decrease in ventilator settings (ventilation rate, PEEP and oxygen settings) while endotracheal tube is left in place.

### *Immediately before withdrawal*

- Allow time for family rituals or memory-making.
- Turn off all alarms and monitors.
- Remove any restraints and medical devices such as nasogastric tubes.
- Discontinue parenteral medications e.g. intravenous infusions of inotropes, muscle relaxants, antibiotics, or hydration as agreed in pre-withdrawal discussions.
- Wean down any morphine and/or midazolam infusion.
- Keep intravenous access for palliative medications.
- Establish adequate symptom control before extubation.
- Prepare additional sedation for use if required after extubation.
- Give IV/SC glycopyrronium 1-2 mcg/kg/dose stat, OR IV/SC hyoscine butylbromide 0.5mg/kg around 10-15 minutes before extubation to reduce airway secretions.
- Consider IV/SC dexamethasone 0.15-0.25mg/kg stat if the child is expected to have post-extubation stridor due to prolonged intubation.

### *During withdrawal*

- Reduce $FiO^2$ to 0.21 and observe for respiratory distress. If respiratory distress is present, adjust medications for symptom control.
- Give a short trial of stopping ventilator assistance before removal of endotracheal tube.
- When removing the endotracheal tube, ensure towels and suction are available in case of secretions.
- Turn off ventilator alarms.
- Provide emotional support and presence for the family members during this process.
- Arrange for provision of grief and bereavement support for family members.

### *Medications to be given after extubation*

- IV/SC morphine 0.1 mg/kg stat and PRN (maximum 2mg per dose)
- IV/SC midazolam 0.025mg/kg stat and PRN (maximum of 2mg per dose)
- IV/SC glycopyrronium 1-2 mcg/kg if additional dose is needed, OR
- IV/SC hyoscine butylbromide 0.5mg/kg stat if additional dose is needed

Consider to convert all these medications to 24 hours infusion if a few repeated doses are required.

## Home extubation

### *Pre-transfer*

- Discontinue unnecessary medications and parenteral access to maximise comfort and facilitate transfer.
- Identify and engage with local services to meet child and family at home, preferably during the time of extubation.
- These may include: general practitioners, family medicine specialist, hospice doctor, community / hospice nurse.
- Facilitate arrangements for transport and equipment e.g. home oxygen, suction machine, essential medications, healthcare personnel to escort in ambulance.

### *Caregiver preparation*

- Educate regarding expected symptoms and signs at end-of-life.
- Symptom care plan – to guide caregivers and community health team for home management, if patient survives beyond expected time
- If patient dies during transfer – extubation will take place at the home. It is not recommended to extubate in the ambulance.
- Essential medications and how to administer
- Letter to facilitate home death certification, what to do in event of home death
- Communicate child's location and status, advance care plan to local hospice and emergency services.
- Provide a letter to inform the police about the likely cause of death / primary diagnosis, to facilitate death certification.
- Provide a copy of the child's advance care plan to the family.

### *During transfer*

Before starting the journey home, give:

- IV/SC morphine 0.1 mg/kg stat (maximum 2mg per dose) for breathlessness, **AND**
- IV/SC midazolam 0.025mg/kg stat (maximum of 2mg per dose) as anxiolytic, **AND**
- IV/SC glycopyrronium 1-2 mcg/kg/dose stat or IV/SC hyoscine butylbromide 0.5mg/kg to reduce airway secretions

Consider IV/SC dexamethasone 0.15-0.25mg/kg stat if the child is expected to have post-extubation stridor due to prolonged intubation.

### *Extubation*

Provide the family with time and privacy to perform cultural rituals or religious ceremony.

Give medications to manage symptoms that are expected to occur around the time of extubation.

- IV/SC midazolam 0.025mg/kg stat (maximum of 2mg per dose)
- IV/SC glycopyrronium 1-2 mcg/kg stat if additional dose is needed, **OR**
- IV/SC hyoscine butylbromide 0.5mg/kg stat if additional dose is needed
- IV/SC morphine 0.1 mg/kg stat (maximum 2mg per dose) if additional dose is needed

### *Post-extubation*

If child develops restlessness or anxiety post-extubation:

- Repeat IV/SC midazolam 0.025mg/kg stat after 15 minutes, **OR**
- Set up IV/SC midazolam infusion 1 to 5mg/24 hours
- Provide a contact for symptom management support.

Refer to home death transition flow process in Module 3.

### *After death*

- Death certification by local authorities.
- Funeral arrangements by family.
- Bereavement support for family members.

**Checklist for home extubation**

| No. | Medication/items | Amount / quantity | Check (√) |
|---|---|---|---|
| 1 | IV/SC Morphine | 3 prepared doses +<br>2 vials for infusion if needed | |
| 2 | IV/SC Midazolam | 3 prepared doses +<br>1 vial for infusion if needed | |
| 3 | IV/SC Dexamethasone | 1 prepared dose | |
| 4 | IV/SC Glycopyrronium | 2 prepared doses | |
| 5 | IV/SC Hyoscine butylbromide | 3 prepared doses | |
| 6 | Infusion set | 1 set | |
| 7 | Letter to police to support death certification | 1 | |
| 8 | A copy of advanced care plan | 1 | |
| 9 | Oxygen face mask and oxygen tank | 1 | |
| 10 | Portable ventilator (if available) | 1 | |
| 11 | Symptom care plan with contact number | 1 | |
| 12 | BIPAP or oxygen concentrator (optional) | 1 | |

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# Home death

## *Preparation for home death*

- Explore what patient and family already knows about the condition.
- Discuss on agreed goals of care for the patient and family.
- Explain what symptoms to expect or anticipate during end of life phase. Provide medications for the symptoms.
- Provide information on what to do in case of emergencies.
- Provision of support number to call for help / guidance
- Discuss spiritual needs – identify spiritual leader, funeral arrangements
- Provide the family with a letter for purpose of death notification to police (Refer to template in Module 3)
  > Identification details of patient
  > Patient's diagnoses
  > Most likely cause of death
  > Doctor's name, institution and contact number for verification

## *Communication issues*

### *Talking about death and dying with children*[1,2]

Children have different understanding of death over different age groups. Use different approaches to talk about death with children based on their age group and understanding of death.[3,4]

| Age | Understanding of Death | Supportive intervention |
|---|---|---|
| **1-2 years** | A dying person is sleeping and will wake up.<br>Fear of separation from caregiver. | Keep child's daily routine unchanged. Talk to them, hold them, comfort them. |
| **2-6 years** | Death is temporary and reversible.<br>Continuous with life—becoming less alive.<br>Life goes on under changed circumstances.<br>Death is personified | Provide concrete information about death.<br>Don't use misleading terms for death, like "sleep".<br>Young children may be afraid to go to sleep if it is associated with death.<br>Tell the child that death is not the child's fault. |

| Age | Understanding of Death | Supportive intervention |
|---|---|---|
| | and a punishment. (magical thinking) | Reassure sense of security by maintaining consistent daily routine. |
| **7-12 years** | Death is final and irreversible.<br>Unpredictable, personal and can happen to them.<br>Concrete reasoning with cause-and-effect relationships. | Reassure the child.<br>Help the child to express their emotions through activities eg art, music or conversations<br>Acknowledge their feelings. Give honest and consistent responses. |
| **Above 12 years old** | Death is accepted as a part of life.<br>Explore theological explanations and unrealised plans. | Acknowledge and explore their feelings.<br>Support independence and privacy.<br>Peer support. |

Suggested books for further reading when working with children on grief issues:

- The Goodbye Book by Todd Parr; for kids 3-6 years
- How I Feel: A Coloring Book for Grieving Children by Alan Wolfelt; for kids 3-9 years.
- The Invisible String Patrice Karst; for kids 4-9 years
- When Someone Very Special Dies by Marge Heegaard; for kids 6-12 years.
- When Something Terrible Happened by Marge Heegaard; for kids 6-12 years.

Good communication skills, especially listening with empathy is vital when discussing death.

*Talking about death and dying with parents*[5,6]

| Things to avoid | Suggestions |
|---|---|
| Saying "I know how you feel" | "It must be very difficult for you." "I can see how sad you are." |
| Avoid talking about the deceased | Allow the family to talk about their memories of the deceased as this helps with the grieving process. |
| Taking angry comments personally or being defensive | "I can see you are very upset. Would you like to share with me more on this?" |
| Saying the deceased is in a better place (unless voiced out by parents) | Explore regarding parents' spiritual values and beliefs. Do not impose own beliefs on them. |
| Placing blame e.g. "You should have brought him/her to see a doctor earlier." | Emphasize on what can be done to comfort and support the child. |

*Prognostication of survival time*[7,8]

When parents ask, "How much time is left?", assess the underlying reason for the question.

Providing an estimated prognosis to parents is important and valued because[7]:

- Parents want to know the child's prognosis
- Builds trust between clinician, parent and child
- Enable child and family to make decisions regarding their care plan
- Promotes hope and peace of mind
- Reduces uncertainty and distress
- Sets the platform for important discussions on child and family's concerns, values and preferences to support subsequent care planning

*Communicating prognosis to the child*[8]*:*

- Children should be given the opportunity to initiate discussion on prognosis in a safe and open environment
- Children should know they will not be lied to
- Children should not be forced into disclosure discussions against their wish

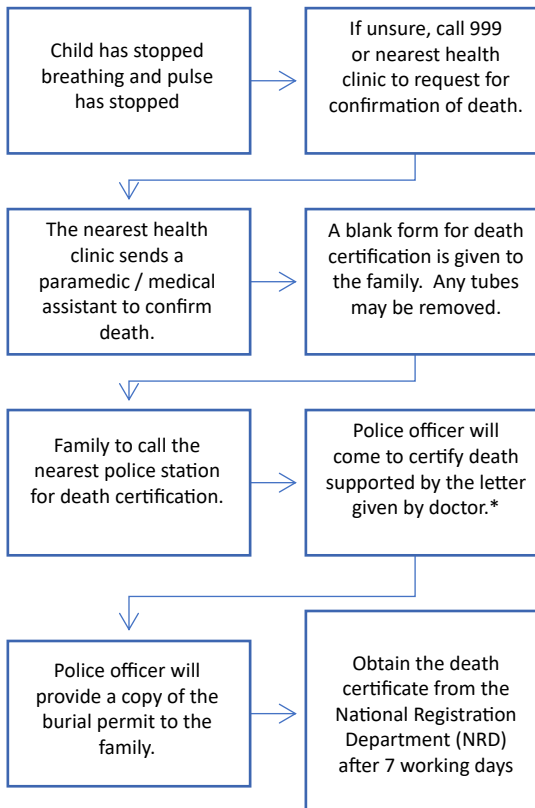
Prognostication is inexact and difficult[9]. There is still lack of studies to support prognostication in paediatric population.8 Tools such as the "Surprise Question" are being tested on its value for prognosis.[10]

Prognosis can be affected by various factors[11]:

- Inherent trajectory pattern of the primary diagnosis
- Acute conditions (eg sepsis, delirium, diarrhoea, vomiting)
- Comorbid organ failure
- Rate of disease progression
- Clinicians' experience in assessment
- If requested, give an estimate in units eg days to a week, weeks to a month.

## *Home death*[12]

**Process of obtaining death certification**




*The police may request that the child is sent to the nearest hospital, if they are not confident to confirm the cause of death.

Alternatively, **funeral service providers** may assist the family with the documentations for death.

In Sabah and Sarawak, death must be notified to the NRD within 24 hours. There are different set of forms for notification within 24 hours and late notification of death. In Sarawak, deaths among indigenous tribes require a certification of death by their community leaders, and police report for home deaths.12

About a month after death, the family may receive a visit from healthcare staff from the nearest health clinic who will be responsible to interview the family members regarding possible cause of death, as part of a **verbal autopsy**.[13] This occurs in deaths that have not been medically certified.

*Tips for healthcare providers when informed of patient's death*

- May attend funeral on a personal basis if invited
- Contact family about a week after funeral to allow for family to complete funeral proceedings
- May express own personal sorrow to family members
- Identify if any assistance or needs that can be provided to family
- Allow family members to express their grief
- Plan for follow up review for family members, more importantly if at risk of pathological grief[5]
- Offer contact information and advice to come to clinic if having symptoms of pathological grief

## *Grief*

| Normal acute grief | Complicated grief |
|---|---|
| Varies between individuals. Usually 6-12 months. | Lasts **beyond culturally accepted duration** (compare the grief symptoms with other family members, friends of the deceased), usually beyond 6 months. Also includes increasing / persistent grief intensity and living dysfunction. |
| • Yearning for the deceased (core symptom)<br>• Depressed mood and guilt related to the deceased<br>• Pangs of sadness, interspersed with periods of joy<br>• Frequent thoughts of the deceased, including hallucination of the deceased<br>• Somatic symptoms: insomnia, loss of appetite, dry mouth | • **Persistent** and intense symptoms of acute grief that are **excessive**. (Unable to feel positive mood)<br>• **Affects the functioning** of the bereaved e.g. personal, family, occupational, social functioning.<br>• Similar to mild post-traumatic stress disorder, where the stressor is the death of the deceased. |
| Symptom intensity reduces with supportive environment for grieving over time.<br>Grief support should begin before the child dies (anticipatory grief). | Grieving intensity persists if supportive environment is not given.<br>Require further intervention:<br>• Screening for complicated grief (to differentiate between complicated vs prolonged grief)<br>• Interpersonal / group psychotherapy<br>• Treat comorbid major depression / anxiety disorder |

*Screening for complicated grief*[14,15]

The Brief Grief Questionnaire is shown in the following page. This screening tool can be used in adults bereaved for at least 12 months or children who have been bereaved for at least 6 months

Refer family members to a mental health specialist, e.g. psychiatrist / clinical psychologist if they scored >5.

Initial:_____

Date: ___/___/____

THE CENTER FOR
COMPLICATED GRIEF

## Brief Grief Questionnaire (BGQ)

Katherine Shear M.D. and Susan Essock Ph.D.


1. How much are you having trouble accepting the death of _____?

| 0 | 1 | 2 |
|---|---|---|
| Not at all | Somewhat | A lot |

2. How much does your grief still interfere with your life?

| 0 | 1 | 3 |
|---|---|---|
| Not at all | Somewhat | A lot |

3.How much are you having images or thoughts of _____ when he/she died or other thoughts about the death that really bother you?

| 0 | 1 | 3 |
|---|---|---|
| Not at all | Somewhat | A lot |

4. Are there things you used to do when _____ was alive that you don't feel comfortable doing anymore, that you avoid? Like going somewhere you went with him/her, or doing things you used to enjoy together? Or avoiding looking at pictures or talking about _____? How much are you avoiding these things?

| 0 | 1 | 3 |
|---|---|---|
| Not at all | Somewhat | A lot |

5. How much are you feeling cut off or distant from other people since _____ died, even people you used to be close to like family or friends?

| 0 | 1 | 3 |
|---|---|---|
| Not at all | Somewhat | A lot |

*Brief Grief Questionnaire (reproduced with permission from Center for Complicated Grief, Columbia School of Social Work)

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## Ethical issues regarding end-of-life care

The four pillars of medical ethics are:
- Beneficence (do good)
- Non-maleficence (do no harm)
- Patient autonomy (patient's free will)
- Justice (fair distribution of limited medical resources)

### *Common issues at end of life*

*Disclosure of diagnosis or prognosis to the child*

| Ethical principle(s) | Explanation |
|---|---|
| Patient autonomy, beneficence, non-maleficence | Parents may wish to withhold the diagnosis from their child to protect them from the suffering.[1]<br>However, many children do have some capacity to understand their condition.[2]<br>Discuss the pros and cons of diagnosis disclosure with the child.<br>If disclosure is done, ensure that it is given at a level that the child can understand, and the amount that is needed for the child to understand. |

*Withdrawal of treatment, nutrition and hydration*[3]

| Ethical principle(s) | Explanation |
|---|---|
| Non-maleficence and justice | Withdrawal of treatment is done when treatment is futile. Futile treatment is when treatment provides no further benefit to the patient and will not cause harm if not given.[4]<br>Some resources can be used for other patients who may benefit from it.<br>Children who are able to and wish to take orally should be given food and drink.<br>Medically provided food and drink should only be withheld if it prolongs or causes more symptoms to the dying process. |

*Euthanasia*[5]

| Ethical principle(s) | Explanation |
|---|---|
| Non-maleficence<br>Patient autonomy | In Malaysia, giving medications with intent to hasten death is not legal.[5]<br>If patient request for euthanasia, explore underlying reasons and optimise symptom control.<br>Supporters of euthanasia claim that patients who request for it are suffering from existential suffering, rather than physical. However, this is still strongly debated in various countries.[6,7] If there is suspicion of existential suffering, refer to psychotherapist (narrative therapy or hypnotherapy) or pastoral care. |

*Preferences for place of death*[8] *(home vs hospital)*

| Ethical principle(s) | Explanation |
|---|---|
| Patient autonomy, beneficence and non-maleficence | Patient may prefer to die at home, however there may be challenges if the community lack resources to support home death.[9]<br>Adequate caregiver preparation is required to allow home death.<br>Family members may bring patient back to the hospital if they are unable to cope with the symptoms of active dying. |

*Conflict between child's and parents' preferences*[2,10]

| Ethical principle(s) | Explanation |
|---|---|
| Patient autonomy, decision-making competency | Have a family conference to discuss the discrepancy in attempt to reconcile the preferences.<br>If conflict persists after adequate discussion and deliberation, the parents' preferences take precedence due to the Child Act which states that children <18 years old are under the care of their parents or legal guardians. |

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## Index

# The Association of Paediatric Palliative Medicine Master Formulary

**5th edition**

**2020**

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## Contents

# Abbreviations

SRE= strong research evidence

WRE= some weak research evidence

NoRE= no published evidence but has clinical consensus

ARE= evidence (research or clinical consensus) with adults

SC = subcutaneous

IV = intravenous

IM= intramuscular

CSCI = continuous subcutaneous infusion

CorGA = corrected gestational age

In general (and when available), this Formulary includes, for palliative care, the same doses as those recommended in one or more of: British National Formulary (BNF) [1], British National Formulary for Children (BNFC)[2], Neonatal Formulary[3], WHO Guidelines on the Pharmacological Treatment of Persisting Pain in Children with Medical Illnesses[4], Palliative Care Formulary[5]and Medicines for Children[6]. Readers outside the UK are advised to consult any local prescribing guidelines in addition to this Formulary.

The authors have made every effort to check current data sheets and literature up to September 2019, but the dosages, indications, contraindications and adverse effects of drugs change over time as new information is obtained. It is the responsibility of the prescriber to check this information with the manufacturer's current data sheet and we strongly urge the reader to do this before administering any of the drugs in this document. In addition, palliative care uses a number of drugs for indications or by routes that are not licensed by the manufacturer. In the UK such unlicensed use is allowed, but at the discretion and with the responsibility of the prescriber.

# Formulary

**Acetazolamide**
Use:
- Epilepsy
- Raised Intracranial Pressure – to reduce CSF production in obstructive causes, as an alternative to steroids
- Potential GABAA mediated analgesia at the spinal level

Dose and route:
Epilepsy
By mouth or slow intravenous injection:
- **Neonates** : Initially 2.5 mg/kg 2-3 times daily, followed by 5-7 mg/kg 2-3 times daily (maintenance dose)
- Child 1 month–11 years: initially 2.5 mg/kg 2-3 times daily, followed by 5-7 mg/kg 2-3 times daily, max 750 mg daily (maintenance dose)
- Child 12-18 years: 250 mg 2-4 times daily max 1 g per day

Raised Intracranial Pressure
By mouth or slow intravenous injection: 8mg/kg three times a day, increased as necessary to max 100mg/kg/day.
Notes:
- Carbonic anhydrase inhibitor. Licensed for raised intracranial pressure and epilepsy in childhood. Also used outside of licence for glaucoma.
- Acetazolamide may give symptomatic benefit in the case of CSF obstruction.
- This may translate to benefit in cases of inoperable brain tumours, causing obstruction to drainage of CSF, rather than just mass effect (where pulses of steroid may be more appropriate).
- There have also been suggestions of GABAA receptor mediated analgesia at the spinal level, as a consequence of carbonic anhydrase inhibition.
- Do NOT use IM / SC as very painful due to alkaline pH.
- May cause electrolyte disturbance with prolonged use (can be corrected with potassium bicarbonate). GI disturbances reported, associated with paraesthesia at higher doses.
- Note contraindications include sulphonamide sensitivity, adrenocortical insufficiency, hypokalaemia, hyponatraemia. (Monitor blood count and electrolytes in prolonged use).
- Has considerable drug interactions with other medications.
- Peak plasma concentration 1-2 hours after administration of tablet.
- Available as 250 mg tablets; modified release capsules 250 mg; 500 mg injection (sodium salt, powder for reconstitution) Diamox®.
- Can be used via feeding tubes without causing blockage: tablets are scored and can be halved or quartered. Dissolving tablet in 10ml water produces a coarse dispersion that settles rapidly. Syringe and container should therefore be well rinsed and the residue administered to ensure the full dose is given. No specific data for jejunal administration: monitor for increased side effects or lack of efficacy. Injection can theoretically be used via feeding tubes, but costly. NB modified release capsules unsuitable for feeding tube administration.

Evidence: [1, 2, 5, 7-11] NoRE

**Adrenaline** (topical) (also known as Epinephrine)

Use:
Small external bleeds
Upper airway obstruction (inflammatory/oedema cause)

Dose and routes:
For bleeding: Soak gauze in 1:1000 (1mg/mL) solution and apply directly to bleeding point for up to 10 minutes. (Short term use only due to risk of ischaemic necrosis and rebound vasodilatation).

For upper airway obstruction: By inhalation of nebulised solution

**1 month-11 years**: 400 micrograms/kg (max: 5 mg per dose).
Can repeat in 30 mins. Clinical effect 2-3 hours. 1:1000 (1 mg/mL)solution diluted with 0.9% saline nebulised.

Evidence: [1-3, 5] NoRE

**Alfentanil**

Use:

- Short acting synthetic lipophilic opioid analgesic derivative of fentanyl.
- Used as analgesic especially intra-operatively and for patients in intensive care and on assisted ventilation (adjunct to anaesthesia).
- Alternative opioid if intolerant to other strong opioids; useful in renal failure if neurotoxic on morphine, or stage 4 to 5 severe renal failure.
- Useful for breakthrough pain and procedure-related pain.

Dose and Routes:

***1. Analgesic especially intra-operatively and for patients in intensive care and on assisted ventilation (adjunct to anaesthesia).***
***SEEK SPECIALIST ADVICE***

By IV/SC bolus (**these doses assume** assisted ventilation is available)

- **Neonate:** 5-20 micrograms/kg initial dose, (slow bolus over 30 seconds) up to 10micrograms/kgsupplemental doses
- **1 month-17 years:** 10-20 micrograms/kg initial dose, (slow bolus over 30 seconds). Up to 10micrograms/kg supplemental doses

By continuous IV or SC infusion (these doses assume assisted ventilation is available)

- **Neonate:** 10-50 micrograms/kg over 10 minutes then 30-60micrograms /kg/ hour
- **1 month-17 years:** 50-100 microgram/kg loading dose over 10 minutes, then30-60microgram/kg/hour as a continuous infusion

***2. Alternative opioid if intolerant to other strong opioids; useful in renal failure if neurotoxic on morphine, or stage 4 to 5 severe renal failure. SEEK SPECIALIST ADVICE.***

Doses should be based on opioid equivalence with the following suggested as safe and practical conversion ratios.
Oral morphine to CSCI alfentanil: 1/30 of the 24 hour total oral morphine dose
e.g. oral morphine 60 mg/24 hours = alfentanil 2 mg/24 hours CSCI.

CSCI/IV morphine to CSCI alfentanil: 1/15 of the 24 hour total CSCI/IV morphine dose
e.g. morphine 30 mg/24 hours CSCI/IV = alfentanil 2mg/24 hours CSCI.

CSCI diamorphine to CSCI alfentanil: 1/10 of the 24 hour total diamorphine dose
e.g. diamorphine 30 mg/24 hours = alfentanil 3 mg/24 hours CSCI.

If conversion is due to toxicity of the previous opioid, lower doses of alfentanil may be sufficient to provide adequate analgesia.
Opioid naïve Adults: CSCI 500 microgram-1 mg over 24 hours.

***3. Breakthrough pain SEEK SPECIALIST ADVICE***

SC / Sublingual / Buccal

Suggest 10-16% of the total CSCI dose. However there is a very poor relationship between the effective PRN dose and the regular background dose, so start with low dose and titrate. Alfentanil has a quick onset of action (within 5 minutes after subcutaneous bolus injection), but short duration of action (under 60 minutes). Even with an optimally titrated PRN dose, frequent dosing (even every 1-2 hours) may be required. Dose and frequency of administration should be regularly reviewed.

***4. Procedure-related pain SEEK SPECIALIST ADVICE***

SC / Sublingual / Buccal

- **Adults** (assuming spontaneous unsupported respiration): 250-500 microgram single dose over 30 seconds. Subsequent doses 250microgram. Doses differ if assisted ventilation.
- **Child:** 5 microgram/kg single dose.
  Give dose at least 5 minutes before an event likely to cause pain; repeat if needed.

Notes:

- Licensing: Alfentanil injection is licensed for use in children as an analgesic supplement for use before and during anaesthesia. Use for pain relief in palliative care is unlicensed. Buccal, sublingual or intranasal administration of alfentanil for incident/breakthrough pain is an unlicensed indication and route of administration.
- Useful for incident and breakthrough pain as faster onset, shorter acting, smaller volumes required compared with fentanyl.Dose required for breakthrough pain does not correlate with background analgesia requirement.
- There is limited information / evidence for analgesic doses in palliative care, especially in children. Doses are largely extrapolated from suggested equianalgesic doses with other opioids.
- Potency: 10-20 times stronger than parenteral morphine, approximately 25% of the potency of fentanyl.
- Very useful in patients with severe renal failure (no dose reduction is needed). May need to reduce the dose 30-50% in severe hepatic impairment.
- In order to avoid excessive dosage in obese children, the dose may need to be calculated on the basis of ideal weight for height, rather than actual weight.
- Pharmacokinetics: half-life is prolonged in neonates, so can accumulate in prolonged use. Clearance may be increased in patients from 1 month to 12 years of age, so higher infusion doses may be needed.
- Contraindication: not to be administered concurrently with MAOIs (monoamine oxidase inhibitors) or within 2 weeks of their discontinuation.
- Interaction: alfentanil levels are increased by inhibitors of Cytochrome P450.
- Adverse effects include respiratory depression, hypotension, hypothermia, muscle rigidity (which can be managed with neuromuscular blocking drugs).
- Metabolised by CYP3A4 and CYP3A5, so note potential interactions (including midazolam).
- For SC or IV infusion, alfentanil is compatible with 0.9% NaCl or 5% glucose as a diluent. For CSCI alfentanil appears physically compatible with most drugs used in a syringe driver. There is evidence for compatibility with midazolam. Note possible concentration-dependent incompatability with cyclizine: use water for injection as diluent and observe for crystallisation. Like diamorphine, high doses of alfentanil may be dissolved in small volumes of diluent which is very useful for SC administration.

- Available as: injection (500 microgram/mL in 2 ml and 10 ml ampoule); Intensive care injection (5 mg/mL in 1ml ampoule which must be diluted before use). Nasal spray with attachment for buccal / SL use (5 mg/5 mL bottle available as special order from Torbay Hospital Manufacturing Unit Tel: 01803 664707. Each 'spray' delivers 0.14 ml = 140 microgram alfentanil. More costly than using injection preparation).
- Schedule 2 CD

Evidence: [1, 2, 5, 6, 12-15]
ARE, SRE (for PICU settings), NoRE (in palliative care settings outside ICU)

**Amitriptyline**

Use:

- Neuropathic pain
- Drooling, refractory cough (same dosing)

Dose and routes:

By mouth:

- **Child 2–11 years:** Initial dose of 200 microgram/kg (maximum 10mg) given once daily at night. Dose may be increased gradually, if necessary and beneficial, to a suggested maximum of 1mg/kg/dose twice daily (under specialist supervision).
- **Child 12–17 years:** Initial dose of 10mg at night increased gradually, if necessary, every 3-5 days to a suggested initial maximum of 75 mg/day. Higher doses up to 150 mg/day in divided doses may be used under specialist advice.

(Twice daily dosing rarely needed, if used then give 25-30% of daily dose in morning and 30-75% at night).

Notes:

- Not licensed for use in children with neuropathic pain, drooling or cough.
- Analgesic effect unlikely to be evident for several days. Potential improved sleep and appetite which are likely to precede analgesic effect.
- Patient information; see Medicines for Children leaflet: 'Amitriptyline for neuropathic pain'. https://www.medicinesforchildren.org.uk/amitriptyline-neuropathic-pain-0
- For intractable cough, benefit probably relates to reducing cough reflex hypersensitivity.
- Drug interactions: not to be administered concurrently with MAOIs (monoamine oxidase inhibitors) or within 2 weeks of their discontinuation. Caution with concurrent use of drugs which inhibit or induce CYP2D6 enzymes. Concurrent carbamazepine use reduces plasma amitriptyline by up to 60%.
- Contraindicated in severe liver impairment and arrhythmias.
- Main side effects limiting use in children include: constipation, dry mouth, blurred vision and drowsiness.
- Absorbed slowly from gastrointestinal tract. Peak plasma concentration occurs 4-8 hours after oral administration. Liquid may be administered via an enteral feeding tube (mix with equal volume of water; no data for some of the preparations). No specific data available for tablets via enteral feeding tube: they can be crushed to disperse in water for immediate administration but don't easily disperse.
- No specific data available for jejunal administration: monitor for increased side effects or loss of efficacy.
- Available as: tablets (10 mg, 25 mg, 50 mg) and oral solution (10 mg/5 mL, 25 mg/5 mL, 50 mg/5 mL; other strengths may be available as 'specials').

Evidence: [1, 2, 5, 10, 16-20]

**Aprepitant**

Use:

- Prevention and treatment of nausea and vomiting associated with moderate or highly emetogenic cancer chemotherapy.

Dose and route:

For oral administration:

- **Child 6 months–11 years:** 3 mg/kg (max 125 mg)as a single dose on Day 1(1 hour before chemotherapy) followed by 2 mg/kg (max 80 mg) as a single dose on Day 2 and Day 3
- **Child >12 years:** 125 mg as a single dose on Day 1 (1 hour before chemotherapy) followed by 80 mg as a single dose on Day 2 and Day 3

Aprepitant is used in combination with a corticosteroid (usually dexamethasone) and a 5-HT3 antagonist such as ondansetron.

Notes:

- Aprepitant is licensed for the prevention of acute and delayed nausea and vomiting associated with highly or moderately emetogenic cancer chemotherapy in adults, children and infants from 6 months of age (>6kg). Role in palliative care unclear.
- Aprepitant also has a role in treating pruritus, particularly due to chemotherapy or mixed causes.
- Aprepitant is a selective high-affinity antagonist at neurokinin NK1 receptors (in Vomiting Centre and Chemoreceptor Trigger Zone).
- Aprepitant is a substrate, a moderate inhibitor and inducer of the CYP3A4 isoenzyme system. It is also an inducer of CYP2C9 and therefore has the potential to interact with any other drugs that are also metabolised by these enzyme systems including rifampicin, carbamazepine, phenobarbital, itraconazole, clarithromycin, warfarin and dexamethasone. Please note this list is not exhaustive – seek advice.
- Common side effects include hiccups, dyspepsia, diarrhoea, constipation, anorexia, asthenia, headache and dizziness.
- Available as: capsules 80 mg and 125 mg. Powder for an oral suspension (25 mg/ml) has recently been approved by the European Medicines Agency, but there is not currently a UK launch date. In the interim, a formulation is available for extemporaneous preparation of an oral suspension.

Evidence: [1, 5, 21-26]

**Arachis Oil Enema**

Use:

- Faecal softener
- Faecal impaction

Dose and route:

By rectal administration

- Child 3-6 years: 45-65 mL as required (~1/3 to 1/2 enema)
- Child 7-11 years: 65 mL - 100 mL as required (~1/2 to 3/4 enema)
- Child 12 years and over: 100-130 mL as required (~3/4 to1 enema).

Notes:

- Caution: as arachis oil is derived from peanuts, do not use in children with a known allergy to peanuts.
- Generally used as a retention enema to soften hard, impacted faeces. May be instilled and left overnight to soften the stool. Can be followed by use of a stimulant suppository or osmotic enema the following morning.
- Warm enema before use by placing in warm water.
- Administration may cause local irritation.
- Licensed for use in children.
- Available as: enema, arachis (peanut) oil in 130mL single dose disposable packs.

Evidence: [1, 2, 5, 6] NoRE

**Atropine**

Use:

- Reductionof death rattle
- Hypersalivation / Hypersecretion

Dose and route:

By sublingual administration

- **Neonates:** Injection solution, 20-40 micrograms/kg/dose 2-3 times a day as required,
- **Child 10-19kg:** Eye drop solution 0.5%, 1 drop three times a day at 6 hourly intervals.
- **Child 5-18 years (>20 kg):** Eye drop solution 0.5-1%,1-2 drops 4-6hourly intervals

Notes:

- Not licensed for this condition.
- Research evidence based on 0.5% eye drops, not avaliable in UK but available in other parts of world.
- Use only where symptom is affecting quality of life. Used 3rd line if glycopyrronium or hyoscine are not avaliable or effective.
- Concurrent treatment with 2 or more antimuscarinic drugs increases risk of side effects and central toxicity. Children are particularly susceptible.
- In palliative care patients, the number of antimuscarinic drugs used is associated with worsening quality of life.
- Monitor for anticholinergic side effects.
- Sublingual administration: use eye drops unless neonate (in which case use injection solution sublingually).
- Available as 1% (10 mg/ml) eye drops. 10 ml or 0.5 ml pack size. ). 0.5% eye drops in other parts of world. Injection 400 micrograms/mL, 600 micrograms /mL, 1 mg/mL ampoules.

Evidence: [1, 27-34] WRE

**Baclofen**

Use:

- Chronic severe spasticity or spasms of voluntary muscle
- Considered as third line neuropathic agent
- Hiccup (strong evidence in adults but none in children)

Dose and routes:

By mouth:

- **Initial dose for child under 18 years:** 300 microgram/kg/day in 4 divided doses, increased gradually at weekly intervals to a usual maintenance dose of 0.75-2 mg/kg/day in divided doses with the following maximum daily doses:
- **Child 1 month-7 years:** maximum total daily dose 40 mg/day
- **Child 8-18 years:** maximum total daily dose 60 mg/day

By Intrathecal injection:

- By specialist teams only. Maintenance 25-200micrograms daily via intrathecal pump.

Notes:

- Review treatment for spasticity if no benefit within 6 weeks of achieving maximum dose, and withdraw over 1-2 weeks if ineffective.
- Patient information: See Medicines for Children leaflet 'Baclofen for muscle spasm': www.medicinesforchildren.org.uk/baclofen-muscle-spasm
- Dependence and tolerance are unlikely, so preferable to diazepam.
- Likely onset of action for hiccups 4-8 hours, for muscle spasm in 1-2 days, for spasticity 3-4 days.
- For severe intractablehiccups –lower dose range to be used. May have direct effect on diaphragm.
- Balance efficacy against unwarranted additional effects of baclofen.
- There is very limited clinical data on the use of baclofen in children under the age of one year. Use in this patient population should be based on the physician's consideration of individual benefit and risk of therapy.
- Administer after food to reduce risk of gastric irritation.
- Monitor and review reduction in muscle tone and potential adverse effects on swallow, airway protection, posture and function. Drowsiness and nausea are common side effects.
- Impact of undesirable hypotonia may be minimised by reducing daytime and increasing evening doses.
- Intrathecal use may be considered, by specialist only, for severe chronic spasticity, if enteral treatment does not achieve control, is poorly tolerated, or higher doses are required.
- Avoid abrupt withdrawal as can precipitate serious psychiatric reactions and (especially after intrathecal use), life-threatening withdrawal syndrome including hyperactivity, increased spasticity, autonomic dysfunction. See PCF6 for management of this.
- Baclofen CSCI (using intrathecal preparation) may be used short term (after a test dose) to avoid sudden withdrawal when enteral and/or intrathecal routes become impossible.
- Risk of toxicity in renal impairment; use smaller oral doses and increase dosage interval if necessary.

- Contraindicated if there is a history of active peptic ulceration.

- Administration with or after food may minimise gastrointestinal irritation side effects.
- Peak plasma concentration achieved 0.5-1.5 hours after oral dose (site of absorption not documented).
- May be administered via enteral feeding tubes including gastrostomy or jejunostomy. (Specific data only available for some makes of liquid and tablet). Use liquid formulation for small doses; dilute prior to use to reduce viscosity. Consider dispersing tablets in water for higher doses owing to the sorbitol content of the liquid formulation. (Teva brand tablets produce a fine dispersion in 10 ml water).
- Available as: tablets (10 mg) and oral solution (5 mg/5 mL). Also intrathecal solution for infusion, for specialist 500 microgram/ml and 2 mg/ml.

Evidence: [1, 2, 5, 10, 35-44]

**Bethanechol**

Use:

- Opioid induced urinary retention

Dose and routes:

By mouth:

- **Child over 1 year:** 0.6 mg/kg/day in 3 or 4 divided doses. Maximum single dose 10mg.
- **Adult dose:** 10-25 mg per dose 3 to 4 times a day. Occasionally it may be felt necessary to initiate therapy with a 50 mg dose.

Subcutaneous:

- **Child over 1 year:** 0.12 to 2 mg/kg/day in 3 or 4 divided doses. Maximum single dose 2.5mg,
- **Adult dose:** 2.5 to 5 mg per dose 3 to 4 times a day.

Notes

- The safety and efficacy of bethanechol in children has not been established (bethanechol is not licensed for use in children).
- Preferably taken 1 hour before or 2 hours after food to reduce potential for nausea and vomiting.
- Contraindicated in hyperthyroidism, peptic ulcer, asthma, cardiac disease and epilepsy.
- Tablets may be crushed and dispersed in water for immediate administration via an enteral feeding tube; formulation for extemporaneous oral suspension is available.
- No specific data for jejunal administration: monitor for increased side effects or loss of efficacy.
- Poorly absorbed by gastrointestinal tract. Therapeutic effect seen within 1 hour of oral administration.
- Available as: 10 mg and 25 mg tablets licensed in UK, other strengths via importation companies and NOT licensed in UK.

Evidence: [1, 10, 45, 46]

**Bisacodyl**
Use:
• Constipation

Dose and routes:
By mouth:
• **Child 4–17 years:** 5-20 mg once daily (recommended to be taken at night) adjust according to response.

By rectum (suppository):
• **Child 2–17 years:** 5-10 mg once daily; adjust according to response.

Notes:
• Tablets act in 10–12 hours. Suppositories act in 20–60 min; suppositories must be in direct contact with mucosal wall.
• Tablets should not be crushed.
• Stimulant laxative. Acts by topical effect on the colonic mucosa.
• Prolonged or excessive use can cause electrolyte disturbance.
• Tablets not suitable for enteral tube administration.
• Available as: gastro-resistant tablets (5 mg) and suppositories (5 mg, 10 mg).

Evidence: [1, 2, 47]

**Buprenorphine**
Use:
• Moderate to severe pain

Dose and routes:
By sublingual route (starting doses; we recommend starting at the lower recommended dose of the range):
• **Child body weight 16–25 kg:** 100 micrograms every 6–8 hours
• **Child body weight 25–37.5 kg:** 100–200 micrograms every 6–8 hours
• **Child body weight 37.5–50 kg:** 200–300 micrograms every 6–8 hours
• **Child body weight over 50 kg:** 200–400 micrograms every 6–8 hours

By CSCI
• **Adult/ older adolescents** starting dose of 300 micrograms/24 hours, dilute with WFI NaCl or 5% glucose
• Stable with glycopyrronium and haloperidol

By transdermal patch:
• By titration or as indicated by existing opioid needs.

Buprenorphine patches are approximately equivalent to the following 24-hour doses of oral morphine

| | | | |
|---|---|---|---|
| morphine salt 12 mg daily | ≡ | BuTrans® '5' patch | 7-day patches |
| morphine salt 24 mg daily | ≡ | BuTrans® '10' patch | 7-day patches |
| morphine salt 48 mg daily | ≡ | BuTrans® '20' patch | 7-day patches |
| morphine salt 84 mg daily | ≡ | Transtec® '35' patch | 4-day patches |
| morphine salt 126 mg daily | ≡ | Transtec® '52.5' patch | 4-day patches |
| morphine salt 168 mg daily | ≡ | Transtec® '70' patch | 4-day patches |

**NB There are higher strength SL tablets also available but these are indicated as an adjunct in the treatment of opioid dependence. Take care with prescribing.**

Notes:
• Sublingual tablets not licensed for use in children < 6 years old.
• Patches not licensed for use in children.
• Patches may cause contact allergies. Pre-treatment topically with budenoside inhalation spray to the area the patch is applied to may help.
• Causes less constipation than some other opioids.
• Athough no actual published evidence, in theory has both opioid agonist and antagonist properties and may precipitate withdrawal symptoms, including pain, in children dependant on high doses of other opioids.
• Not fully reversible with naloxone at least not with the regular dose since the binding capacity is so high you have to use much higher doses than regularly used.
• Sublingual duration of action 6-8 hours.
• Caution with hepatic impairment and potential interaction with many drugs including anti-retrovirals.
• Available as: tablets (200 microgram, 400 microgram) for sublingual administration. Tablets may be halved.

Available as: several brands (and generics) of transdermal patches with 72 hour, 96 hour and 7 day release profiles. Only matrix patches can be cut.

1. BuTrans®, Butec®, Bupramyl®, Panitaz®, Reletrans®, Sevodyne®—applied every 7 days.
   Available as 5 (5 micrograms /hour for 7 days), 10 (10 micrograms /hour for 7 days), 15 (15 micrograms/hour for 7 days) and 20 (20 micrograms /hour for 7 days).
2. Bupeaze®, Buplast®, Relevtec®, TransTec®, —applied every 96 hours.
   Available as 32.5 (32.5 micrograms /hour for 96hours), 52.5 (52.5 micrograms / hour for 96hours), and 70 (70 micrograms /hour for 96hours).
3. Hapactasin® – applied every 72 hours.
   Available as 35 (35 micrograms/hour for 72 hours), 52.5 (52.5 micrograms/hour for 72 hours) and 70 (70 micrograms/hour for 72 hours)
4. IV/SC solution 300 micrograms/ml

For patches, systemic analgesic concentrations are generally reached within 12–24 hours but levels continue to rise for 32–54 hours (pharmacokinetic profile may differ slightly between preparations, check SPC for full details).

If converting from:

- 4-hourly oral morphine - give regular morphine doses for the first 12 hours after applying the patch.
- 12-hourly slow release morphine - apply the patch and give the final slow release dose at the same time.
- 24-hourly slow release morphine - apply the patch 12 hours after the final slow release dose.
- Continuous subcutaneous infusion - continue the syringe driver for about 12hours after applying the patch.

- Rate of absorption from patch isaffected by temperature, so caution with pyrexia or increased external temperature such as hot baths: possibility of accidental overdose with respiratory depression.
- Patches are finding a use as an easily administered option for low dose background opioid analgesia in a stable situation, for example in severe neurological impairment.
- Schedule 3 CD (CD No Register).

Evidence: [1, 2, 5, 48-62]

**Carbamazepine**
Use:
- Neuropathic pain
- Some movement disorders
- Anticonvulsant

Dose and routes
By mouth:
- **Neonates:** Experience is limited. Initial dose 5 mg/kg twice daily.
- **Child 1 month–11 years:** Initial dose of 5 mg/kg at night or 2.5 mg/kg twice daily, increased as necessary by 2.5-5 mg/kg every 3–7 days; usual maintenance dose 5 mg/kg 2–3 times daily. Doses up to 20 mg/kg/day in divided doses have been used.
- **Child 12–17 years:** Initial dose of 100–200 mg 1–2 times daily; increased slowly to usual maintenance of 200-400 mg 2–3 times daily. Maximum 1.8 g/day in divided doses.

By rectum:
- Child 1 month–17 years: Use approximately 25% more than the oral dose (maximum single dose 250 mg) up to 4 times a day.

Notes:
- Not licensed for use in children with neuropathic pain.
- Can cause serious blood, hepatic, and skin disorders. Parents should be taught how to recognise signs of these conditions, particularly leucopoenia.
- Numerous interactions with other drugs including chemotherapy drugs.
- May cause hyperalgesia on abrupt withdrawl.
- Patients taking carbamazepine alone or in combination with phenytoin appear to need more fentanyl than those not taking these antiepileptics. Carbamazepine appears to increase the production of a more potent metabolite of codeine, normorphine. Carbamazepine reduces tramadol concentrations, appears to reduce oxycodone concentrations and is predicted to reduce the concentration and efficacy of buprenorphine.
- Different preparations may vary in bioavailability so avoid changing formulations or brands.
- Suppositories of 125 mg are approximately equivalent to 100 mg tablets.
- Oral liquid has been administered rectally – should be retained for at least 2 hours if possible but may have a laxative effect.
- For administration via an enteral feeding tube use the liquid preparation. Dilute with an equal volume of water immediately prior to administration. Due to high viscosity it needs to be pushed through with a syringe. If giving doses higher than 400 mg/day, divide into 4 equal doses. Doses above 800 mg/day may cause bloating due to the sorbitol content of the liquid.There is no specific data relating to jejunal administration of carbamazepine. Administer using the above method. An increase in side-effects such as dizziness is possible owing to the rapid delivery into the small bowel. Monitor for increased side-effects or loss of efficacy. Consider decreasing the dose and increasing the dosing frequency if side-effects are problematic.
- Available as: tablets (100 mg, 200 mg, 400 mg), liquid (100 mg/5 mL), suppositories (125 mg, 250 mg), and modified release tablets (200 mg, 400 mg).

Evidence: [2, 10, 63-68]

**Celecoxib**

Use:

- Pain, inflammatory pain, bone pain, stiffness. Not used first line.
- Dose based on management of juvenile rheumatoid arthritis.

Dose and routes

By mouth:

- **Child over 2 years:**
  - Weight 10-25 kg: 2-3 mg/kg/dose twice a day (Maximum 50 mg twice daily or 100 mg daily)
  - Weight more than 25 kg: 100 mg twice daily
- **Over 16 years:** Adult dose of 100 mg BD. Can be doubled in severe pain to 200 mg BD

Notes

- Celecoxib is a cyclo-oxygenase-2 selective inhibitor.
- Not licensed in the UK for use in children.
- All NSAID use (including cyclo-oxygenase-2 selective inhibitors) can, to varying degrees, be associated with a small increased risk of thrombotic events (e.g. myocardial infarction and stroke) independent of the baseline cardiovascular risk factorsor duration of NSAID use. However, the greatest risk may be in those receiving high doses long term. COX-2 inhibitors are also associated with an increased risk of thrombotic effects.
- All NSAIDs are associated with serious gastro-intestinal toxicity. COX-2 inhibitors are associated with a lower risk of serious upper gastro-intestinal side-effects than non-selective NSAIDs. May exacerbate Crohn's disease.
- No difference in tolerability or efficacy has been shown between etoricoxib, naproxen and celecoxib.
- Use with caution in patients with renal impairment and avoid in severe renal impairment.
- Use with caution in hepatic impairment.
- Celecoxib interacts with a great many commonly used drugs. Check BNF (current version on-line). Reduce dose by 50% if using fluconazole.
- Capsules may be opened and contents mixed with soft food immediately before administration.For administration via an enteral feeding tube, the capsule may be opened and the contents mixed with water to form a milky suspension. For a 50 mg dose, approximately halve the 100 mg capsule contents to give a best estimate of a 50 mg dose. However, as the capsules are small, this is difficult to do accurately.
- Available as: capsules 100 mg, 200 mg.
- For SC /IM use use parecoxib adolescents 40-80 mg/24 hr CSCI or 20 mg SC PRN. For CSCI give parecoxib alone and diluted to a volume of 22 ml in 0.9% NaCl to reduce the risk of site reaction.

Evidence: [1, 69-76] WRE

**Chloral hydrate**
Use:
- Insomnia
- Agitation
- Seizures in severe epileptic encephalopathy (seek specialist advice)
- Status Dystonicus (seek specialist advice)
- Neonates; Sedation for procedures

Dose and routes:
By mouth or rectum:
- **Neonate:** Initial dose of 30 mg/kg as a single dose at night. May be increased to 45mg/kg at night or when required.
- **Neonates- for sedation for procedures in NICU:** 30–50 mg/kg 45–60 minutes before procedure; doses up to 100 mg/kg may be used with respiratory monitoring.

- **Child 1 month–11 years:** Initial dose of 30 mg/kg as a single dose at night. May be increased to 50 mg/kg at night or when required.
  Maximum single dose 1 g.
- **Child 12–17 years:** Initial dose of 500 mg as a single dose at night or when required. Dose may be increased if necessary to 1-2 g. Maximum single dose 2 g.

Notes:
- Not licensed for agitation or in infants <2 years for insomnia.
- Prolonged half-life in neonates.
- Oral use: mix with plenty of juice, water, or milk to reduce gastric irritation and disguise the unpleasant taste. Light-sensitive so needsto be given as soon as it is drawn up.
- For rectal administration use oral solution or suppositories (available from 'specials' manufacturers).
- Chloral hydrate oral solution may be administered via enteral feeding tubes although there is little information and it is important to remember it can cause gastric irritation. Suggest the dose is diluted with water to minimise this.There is no specific data relating to the jejunal administration of chloral hydrate. Monitor for loss of efficacy or increased side-effects.
- Accumulates with prolonged use and should be avoided in severe renal or hepatic impairment.
- Available as: tablets (chloral betaine 707 mg = choral hydrate 414 mg—Welldorm®), oral solution (143.3 mg/5 mL—Welldorm®; 200 mg/5 mL, 500 mg/5 mL both of which are available from 'specials' manufacturers or specialist importing companies), suppositories (available as various strengths 25 mg, 50 mg, 60 mg, 100 mg, 200 mg, 500 mg from 'specials' manufacturers).

Evidence: [2, 3, 6, 77-87]

**Chlorpromazine**

Use:

- Hiccups
- Nausea and vomiting of terminal illness (where other drugs are unsuitable)
- Agitated delirium at the end of life

Dose and routes:

Hiccups

By mouth:

- **Child 1–5 years:** 500 micrograms/kg every 4–6 hours adjusted according to response (maximum 40 mg daily)
- **Child 6–11 years:** 10 mg 3 times daily, adjusted according to response (maximum 75mg daily)
- **Child 12–17 years:** 25 mg 3 times daily (or 75 mg at night), adjusted according to response, higher doses may be used by specialist units.

Nausea and vomiting of terminal illness (where other drugs are unsuitable)

By mouth:

- **Child 1–5 years:** 500 micrograms/kg every 4–6 hours; maximum 40 mg daily
- **Child 6–11 years:** 500 micrograms/kg every 4–6 hours; maximum 75 mg daily
- **Child 12–17 years:** 10–25 mg every 4–6 hours.

By deep intramuscular injection:

- **Child 1–5 years:** 500 micrograms/kg every 6–8 hours; maximum 40 mg daily
- **Child 6–11 years:** 500 micrograms/kg every 6–8 hours; maximum 75 mg daily
- **Child 12–17 years:** initially 25 mg then 25–50 mg every 3–4 hours until vomiting stops.

Notes:

- Not licensed in children for intractable hiccup.
- Caution in children with hepatic impairment (can precipitate coma), renal impairment (start with small dose; increased cerebral sensitivity), cardiovascular disease, epilepsy (and conditions predisposing to epilepsy), depression, myasthenia gravis.
- Caution is also required in severe respiratory disease and in children with a history of jaundice or who have blood dyscrasias (perform blood counts if unexplained infection or fever develops).
- Photosensitisation may occur with higher dosages; children should avoid direct sunlight.
- Antipsychotic drugs may be contra-indicated in CNS depression.
- Risk of contact sensitisation; tablets should not be crushed and solution should be handled with care.
- Oral solution may be administered via an enteral feeding tube.There is no specific data relating to the jejunal administration of chlorpromazine. Monitor for loss of efficacy or increased side-effects.
- Available as: tablets, coated (25 mg, 50 mg, 100 mg); oral solution (25 mg/5 mL, 100 mg/5 ml ; injection (25 mg/mL and 2 mL ampoules).
- Over 16 years may have 100 mg base rectally. For equivalent therapeutic effect 100 mg chlorpromazine base given rectally as a suppository
- 20–25 mg chlorpromazine hydrochloride by intramuscular injection ≡
- 40–50 mg of chlorpromazine base or hydrochloride given by mouth.But ≡ rectal administration is unlicensed use.

- Suppositories from specials manufacturers.

Evidence: [1, 2, 88-97]

**Clobazam**

Uses:
- Adjunctive therapy for epilepsy
- Short term 'add on' therapy for epilepsy exacerbations related to hormonal changes or intercurrent illness

Dose and route:
For oral administration:
- **Child 1 month–5 years:** Initial dose of 125 micrograms/kg twice daily. Increase every 5 days as necessary and as tolerated to a usual maintenance dose of 250 micrograms/kg twice daily. Maximum dose 500 micrograms/kg (15 mg single dose) twice daily.
- **Child 6-17 years:** Initial dose of 5 mg daily. Increase every 5 days as necessary and as tolerated to a usual maintenance dose of 0.3-1 mg/kg daily. Maximum 60 mg daily. Daily doses of up to 30 mg may be given as a single dose at bedtime, higher doses should be divided.

Notes:
- Not licensed for use in children less than 6 years of age.
- Once titrated to an effective dose of clobazam, patients should remain on their treatment (except when being used for short courses) and care should be exercised when changing between different formulations.
- Tolerance in longer term use may be managed by 'switching/rotating' benzodiazepines.
- Tablets can be administered whole, or crushed and mixed in apple sauce. The 10mg tablets can be divided into equal halves of 5 mg. Clobazam can be given with or without food. Both oral liquid and normal tabletsdispersed in water may be administered via an enteral feeding tube.
- Age of patient and othe medication may impact on kinetic variability.
- Possible side-effects as would be expected from benzodiazepines. Children are more susceptible to sedation and paradoxical emotional reactions.
- Available as: tablets 10 mg (Frisium(R)) tablets; (5 mg – unlicensed and available on a named-patient basis); oral liquid (5 mg in 5 ml and 10 mg in 5 ml – care with differing strengths).
- Frisium(R) tablets are NHS black-listed except for epilepsy and endorsed 'SLS'. Schedule 4 CD (CD-Benz).

Evidence: [2, 6, 98-100]

**Clonazepam**
Use:
- Tonic-clonic seizures
- Partial seizures
- Cluster seizures
- Myoclonus
- Status epilepticus (3rd line, particularly in neonates)
- Neuropathic pain
- Restless legs
- Gasping
- Anxiety and panic
- Oral dysaesthesia in the adolescent
- Has been used in Neonatal units to control severe continuous seizures resistant to other anticonvulsants

Dose and routes:
By mouth (anticonvulsant doses: reduce for other indications):
- **Child 1 month–11 months:** Initially 250 micrograms at night for 4 nights, increased over 2–4 weeks to usual maintenance dose of 0.5–1 mg at night (may be given in 3 divided doses if necessary).
- **Child 1–4 years:** Initially 250 micrograms at night for 4 nights, increased over 2–4 weeks to usual maintenance of 1–3 mg at night (may be given in 3 divided doses if necessary)
- **Child 5–11 years:** Initially 500 micrograms at night for 4 nights, increased over 2–4 weeks to usual maintenance dose of 3–6 mg at night (may be given in 3 divided doses if necessary)
- **Child 12–17 years:** Initially 1 mg at night for 4 nights, increased over 2–4 weeks to usual maintenance of 4–8 mg at night (may be given in 3 divided doses if necessary).

For oral dysaesthesia [burning mouth syndrome] rinse with 0.1mg/ml solution
For status epilepticus: (SR)

Continuous subcutaneousinfusion:
- **Child 1 month–17 years:** Starting dose 20-25 micrograms/kg/24 hours
- Maximum starting doses:
  **1-5 years:** 250 micrograms/24 hours;
  **5-12 years:** 500 micrograms/24 hours.
- Increase at intervals of not less than 12 hours to 200 micrograms/kg/24hours (maximum 8 mg/24 hours)
- Doses of up to 1.4 mg/kg/24 hours have been used in status epilepticus in PICU environment.

By intravenous injection over at least 2 minutes, or infusion:
- **Neonate:** 100 micrograms/kg intravenous over at least 2 minutes, repeated after 24 hours if necessary (avoid unless no safer alternative). Used for seizures not controlled with phenobarbital or phenytoin.
- **Child 1 month-11 years:** Loading dose 50 micrograms/kg (maximum 1 mg) by IV injection followed by IV infusion of 10 micrograms/kg/hour adjusted according to response; maximum 60 micrograms/kg/hour.

- **Child 12-17 years:** Loading dose 1 mg by IV injection followed by IV infusion of 10 micrograms/kg/hour adjusted according to response; maximum 60 micrograms/kg/hour.

Notes

- Licensed for use in children for status epilepticus and epilepsy. Not licensed for neuropathic pain. Tablets licensed in children.
- Not licensed in the UK for SC use.
- Very effective anticonvulsant, usually 3rd line due to side effects and development of tolerance.
- Use lower doses for panic, anxiolysis, terminal sedation, neuropathic pain, and restless legs.
- Do not use in acute or severe respiratory insufficiency unless imminently dying. Be cautious in those with chronic respiratory disease.
- As an anxiolytic/sedative, clonazepam orally is approximately 20 times as potent as diazepam (i.e. 250micrograms clonazepam equivalent to 5 mg diazepam orally).
- Multiple indications in addition to anticonvulsant activity can make clonazepam particularly useful in the palliative care of children with neurological disorders.
- Many children with complex seizure disorders are on twice daily doses and on higher than recommeded dosages.
- Tolerance in longer term use may be managed by 'switching/rotating' benzodiazepines.
- The dose may be increased for short periods of 3-5 days during times of increased seizures e.g. from viral illness.
- Elimination half-life of 20-40 hours means that it may take up to 6 days to reach steady state; there is a risk of accumulation and toxicity with rapid increase of infusion; consider loading dose to reach steady state more quickly.
- Avoid abrupt withdrawal.
- Associated with salivary hypersecretion and drooling.
- For administration via an enteral feeding tube, tablets may be dispersed in at least 30ml water or consider a liquid formulation (especially for fine-bore tubes). Extra flushing with water is required to stop drug adhering to the wall of the tube. There are no specific data relating to jejunal administration. Administer using the above method. Monitor for loss of efficacy or increased side-effects.
- IV formulation may be diluted and given via enteral tube. Flush tube well following administration.
- Stability of diluted clonazepam is up to 12 hours so prescribers should consider 12 hourly infusions.
- Use non-PVC tubing when administering by subcutaneous infusion.
- Compatible with most drugs commonly administered via continuous subcutaneous infusion via syringe driver. Dilute with WFI or NaCl 0.9%.
- Available as: tablets (500 micrograms scored, 2 mg scored); liquid (0.5 mg in 5 mL and 2 mg in 5 mL now available as licensed preparations from Rosemont, but not indicated in children due to high alcohol content; other unlicensed oral liquids are available from specials manufacturers); injection (1 mg/mL unlicensed). CD Schedule 4 (CD-Benz).

Evidence: [2, 3, 41, 65, 98, 101-106]

**Clonidine**

Uses:

- Anxiety / sedation (prior to procedure)
- Pain / sedation / opioid sparing / prevention of opioid withdrawal effects
- Regional nerve block
- Spasticity / dystonia
- Status dystonicus
- Behavioural symptoms of irritability, impulsiveness, aggression

Doses and routes:

Anxiety / Sedation / Pre-procedure:
Oral / Intranasal /Rectal:

- **Neonate:** 4 micrograms/kg orally (or intranasally, although this does tend to sting and offers little advantage over the oral route), and in doses of 5 micrograms/kg rectally provides adequate sedation.
- **Child >1 month:** 4 micrograms/kg as a single dose.
  (suggested maximum 150 micrograms single dose).
  If used as premedicant prior to a procedure give 45-60 minutes before.

Pain / Sedation / Opioid sparing / Prevention of opioid withdrawal effects
(most experience on PICU):
Oral / IV Bolus:

- **Child >1 month:** Initial dose 1 microgram/kg/dose 3-4 times daily. Increase gradually as needed and tolerated to maximum of 5 micrograms/kg/dose four times a day.

IV infusion: Can also be used as CSCI

- **Neonates from 37 weeks CorGA: (only if ventilated)**
  Initially 0.25 micrograms/kg /hour, increasing in 0.1 microgram/kg/hour increments until adequate sedation achieved. Most will require 1 microgram/kg per hour, but doses up to 2 micrograms/kgper hour are sometimes necessary.
- **Child >1 month:** 0.1-2 micrograms/kg/hour.
  Usual starting doses:
  ~ Child <6 months: 0.4 micrograms/kg/hour
  ~ Child >6 months: 0.6 microgram/kg/hour

For chronic long-term pain, and once an effective oral dose has been established, conversation to transdermal patches can be considered using a patch size that will give a roughly equivalent daily dose of clonidine (see notes below).

Regional nerve block – only in situations where specialist input is available:

- **Child >3 months:** 1-2 micrograms/kg clonidine in combination with a local anaesthetic.

Spasticity / Movement Disorder:
Oral:

- **Child > 1 month:** 1-5 micrograms/kg/dose three times a day. Frequency of dosing may need to be increased and/or alternative route of administration considered if the enteral route is not possible.

Behavioural problems / Tics / Tourette's syndrome:
Oral:
- **Child > 4 years:** Oral: Initial dose of 25 micrograms at night. Increase as necessary after 1-2 weeks to 50micrograms at night. Dose can be further increased by 25 micrograms every 2 weeks to suggested maximum of 5 micrograms/kg/day or 300 micrograms/day

**When using patch (for children over 10 kg)**
- 2.5 mg clonidine patch delivers 100 micrograms/day
- 5m g clonidine patch delivers 200 micrograms/day
- 7.5 mg clonidine patch delivers 300 micrograms/day

Therapeutic plasma clonidine levels are achieved 2 to 3 days after initial application of patch.

If more than 2.5 mg patch to be used i.e.200 micrograms/day, consider using 2 smaller patches to be changed on different days of the week to reduce end of dose effect.

Conversion of patients on IV or oral clonidine:
- For patients on IV/oral dose less than 150 micrograms/day, select the clonidine 2.5mg patch. Then follow IV/oral tapering dose below.
- For patients on IV/oral dose between 150 micrograms and 250 micrograms/day, select the 5 mg clonidine patch.

IV/Oral tapering doses:
- Apply patch on day 1.
- Day 1 give 100% of oral/IV dose
- Day 2 give 50% of oral/IV dose
- Day 3 give 25% oral/IV dose [107]
- Day 4 patient will only need patch

Notes
- Clonidine is a mixed alpha-1 and alpha-2 agonist (mainly alpha-2). Appears to have synergistic analgesic effects with opioids and prevents opioid withdrawal symptoms. Also useful for its sedative effect. Use established in ADHD, behavioural problems and tics.
- Not licensed for use in children.
- Licensed indication of clonidine is for the treatment of hypertension, so reduction in BP is a likely side effect of use. Titrate the dose of clonidine against the symptoms and monitor BP and pulse on starting treatment and after each dose increase.
- When used for longer than a few days, clonidine should be withdrawn slowly on discontinuation, to prevent acute withdrawal symptoms including rebound hypertension.
- Use with caution in those with bradyarrhythmia, Raynaud's or other occlusive peripheral vascular disease.
- Remove patch if having MRI scan as risk of heating up and causing a burn.
- Common side effects include constipation, nausea, dry mouth, vomiting, postural hypotension, dizziness, sleep disturbances, headache.

- Effects of clonidine are abolished by drugs with alpha-2 antagonistic activity e.g. tricyclics and antipsychotic drugs. Antihypertensive effects may be potentiated by other drugs used to lower BP.
- Oral bioavailability 75-100%; generally 1:1 conversion IV:oral is suggested as a starting point (largely adult data. Note: it has been suggested that oral bioavailability may be lower in children [108]).
- Some reports of use of rectal clonidine. Pharmacokinetic studies suggest almost 100% bioavailability via this route. Single rectal doses of 2.5-4 micrograms/kg have been used.
- Onset of effect: oral 30-60 mins. Time to peak plasma concentration:

oral 1.5-5 hours; epidural 20 minutes; transdermal 2 days.

- CSCI can be useful to maintain control of dystonia in difficult cases.
- Clonidine has been used successfully by SC injection and infusion – seek specialist advice.
- Oral solution may be administered via an enteral feeding tube. Alternatively, if the required dose is appropriate to the available tablet strengths, the tablets may be crushed and dispersed in water for administration via an enteral feeding tube. The 25 microgram tablets do not appear to disperse in water as readily as the 100 microgram tablets. IV solution may also be given via the enteral tube. There is no specific information for jejunal administration. Administer as above but observe for any loss of efficacy or increased side effects.
- Chronic conditions – for older children the use of transdermal patches may be considered when an effective oral dose has been established which is great enough to allow an approximate conversion (1:1) to the transdermal route.
- Available as:
  tablets 25 micrograms, 100 micrograms;
  injection150 micrograms/mL;
  transdermal patch
  2.5 mg (=100 micrograms clonidine/day for 7 days),
  5 mg (=200 micrograms clonidine/day for 7 days) or
  7.5 mg (= 300 micrograms clonidine/day for 7 days),
  (transdermal patches not licensed in UK – available via importation company); oral solution (special) 50 micrograms/mL.

Evidence: [3, 84, 108-130]

**Co-danthramer (dantron and poloxamer 188)**
Use:
• Constipation in terminal illness only

Dose and routes:
By mouth:
Co-danthramer 25/200 suspension 5 mL = one co-danthramer 25/200 capsule(Dantron 25 mg, poloxamer '188' 200 mg):
• **Child 2–11 years:** 2.5–5mL at night
• **Child 6–11 years:** 1 capsule at night
• **Child 12–17years:** 5–10mL or 1–2 capsules at night. Dosage can be increased up to 10-20 mL twice a day

Strong co-danthramer 75/1000 suspension 5 mL = two strong co-danthramer 37.5/500 capsules:
• **Child 12–17 years:** 5 mL or 1–2 capsules at night.

Notes
• Co-danthramer is made from dantron and poloxamer '188'.
• Acts as a stimulant laxative.
• Avoid prolonged skin contact due to risk of irritation and excoriation (avoid in urinary or faecal incontinence, or children with nappies).
• No longer used in adult palliative care patients due to excoriation of skin around anus.
• Dantron can turn urine red/brown.
• Suspension can be used with enteral feeding tubes but is quite viscous, needing some pressure on syringe and to be flushed well after administration. Administration into the jejunum is unlikely to affect pharmacological response.
• Rodent studies indicate potential carcinogenic risk.

Evidence: [1, 2]

**Co-danthrusate (Dantron and Docusate Sodium)**
Use:
• Constipation in terminal illness only

Dose and routes:
By mouth:
Co-danthrusate 50/60 suspension 5 mL = one co-danthrusate 50/60 capsule(Dantron 50 mg/ Docusate sodium 60 mg)
• **Child 6–11 years:** 5 mL or 1 capsule at night
• **Child 12–17 years:** 5–15 mL or 1–3 capsules at night

Notes
• Not recommended for under 6 years.
• Co-danthrusate is made from dantron and docusate sodium.
• Acts as a stimulant laxative.
• Avoid prolonged skin contact due to risk of irritation and excoriation(avoid in urinary or faecal incontinence, or children with nappies).
• Dantron can turn urine red/brown.
• No specific data on enteral tube administration are available for this preparation. If necessary use the suspension and flush tube well after use. Consider diluting with water to aid administration.
• Rodent studies indicate potential carcinogenic risk.

Evidence: [1, 2, 131]

**Codeine Phosphate**
Codeine is no longer indicated for palliative care in children. It has been replaced by other opioids, particularly oral morphine and buccal diamorphine or fentanyl.

Evidence: [1-3, 65, 132, 133]

**Cyclizine**
Use:
- Antiemetic of choice forraised intracranial pressure.
- Nausea and vomiting where other more specific antiemetics (metoclopramide,5HT3 antagonists) have failed.

Dose and routes:
By mouth or by slow IV injection over 3–5 min:
- **Child 1 month–5 years:** 0.5–1 mg/kg up to 3 times daily, maximum single dose 25 mg
- **Child 6–11 years:** 25 mg up to 3 times daily

**Child 12–17 years:** 50 mg up to 3 times dailyBy rectum:
- **Child 2–5 years:** 12.5 mg up to 3 times daily
- **Child 6–11 years:** 25 mg up to 3 times daily
- **Child 12–17 years:** 50 mg up to 3 times daily

By continuous IV or SC infusion: **Some evidence 50% bioavailability when given orally.**
- **Child 1 month-23 months:** 1.5-3 mg/kg over 24 hours (maximum 25 mg/24 hours),
- **Child 2-5 years:** 25-50 mg over 24 hours
- **Child 6–11 years:** 37.5-75 mg over 24 hours
- **Child 12–17 years:** 75-150 mg over 24 hours

**NB** Care should be taken with subcutaneous or intravenous use of cyclizine, whichis acidic and can cause injection site reactions.

Notes:
- Antihistaminic antimuscarinic antiemetic.
- Tablets are not licensed for use in children < 6 years old.
- Injection is not licensed for use in children.
- Antimuscarinic side-effects include dry mouth, drowsiness, headache, fatigue, dizziness, thickening of bronchial secretions, nervousness.
- Increased sedative effect when given with tricyclics, anxiolytics, MAOI's.
- Increased antimuscarinic effect when given with tricyclics, antimuscarinics, MAOI's
- Theoretically antagonises betahistine, histamine.
- Avoid in patients on midodrine and children with severe liver disease. In severe cardiac failure may cause fall in cardiac output. Increased risk of transient paralysis with intravenous use in patients with neuromuscular disorders.
- Rapid SC or IV bolus can lead to 'lightheadness' –disliked by some and enthralling to others leading to repeated requests for IV cyclizine.
- For CSCI or IV infusion, dilute only with water for injection or 5% dextrose;incompatiblewith 0.9 %NaCland will precipitate.
- Concentration dependent incompatibility with alfentanil, dexamethasone, diamorphine and oxycodone.
- Suppositories must be kept refrigerated.
- Tablets may be crushed for oral administration. The tablets do not disperse well in water, but if shaken in 10 mL water for 5 minutes, the resulting dispersion may be administered immediately via an enteral feeding tube. There is no specific information for jejunal administration. If this route is used monitor for any loss of efficacy or increased side-effects.
- Available as: tablets (50 mg), suppositories (12.5 mg, 25 mg, 50 mg, 100 mg from 'specials' manufacturers) and injection (50 mg/mL).

Evidence: [2, 10, 134-137]

**Dantrolene**
Use:
- Skeletal muscle relaxant.
- Chronic severe voluntary muscle spasm or spasticity.

Dose and routes:
The dose of dantrolene should be built up slowly
By mouth:
- **Child 5–11 years:** Initial dose of 500 micrograms/kg once daily; after 7 days increase to 500 micrograms/kg/dose 3 times daily. Every 7 days increase by a further 500 micrograms/kg/dose until response. Maximum recommended dose is 2 mg/kg 3–4 times daily (maximum total daily dose 400 mg).
- **Child 12–17 years:** Initial dose of 25 mg once daily; after 7 days increase to 25 mg 3 times daily. Every 7 days increase by a further 500 microgram/kg/dose until response. Maximum recommended dose is 2 mg/kg 3–4 times daily (maximum total daily dose 400 mg).

Notes:
- Not licensed for use in children.
- Hepatotoxicity risk; consider checking liver function before and at regular intervals during therapy.
- Contraindicated in hepatic impairment: avoid in liver disease or concomitant use of hepatotoxic drugs.
- Can cause drowsiness, dizziness, weakness, nausea and diarrhoea.
- Cautious use in patients with impaired cardiac or pulmonary function: side effects include pericarditis, pleural effusion, respiratory depression, exacerbation of cardiac insufficiency, tachycardia and blood pressure changes.
- Available as: capsules (25 mg, 100 mg), oral suspension (extemporaneous formulation 5 mg/mL).

Evidence: [2, 36, 37, 42, 138, 139]

**Dexamethasone**
Use:

Dexamethasone has a wide range of potential uses associated with its capacity to reduce inflammation. They include:

- Headache associated with raised intracranial pressure caused by a tumour.
- Anti-inflammatory in brain and other tumours which cause pressure on nerves or bone or obstruction of hollow viscus.
- Analgesic role in nerve compression, spinal cord compression and bone pain.
- Antiemetic either as an adjuvant or in highly emetogenic cytotoxic therapies.

Dose and routes
Prescribe as dexamethasone base.

Headache associated with raised intracranial pressure
By mouth or IV:
**Child 1 month–12 years:** 250 micrograms/kg twice a day for 5 days; then reduce or stop.
To relieve symptoms of brain or other tumour
Numerous other indications in cancer management such as spinal cordand/or nerve compression, some causes of dyspnoea, bone pain, superior vena caval obstruction etc,, only in discussion with specialist palliative medicine team.High doses < 16 mg/24 hrs may be advised.

Antiemetic
By mouth or IV:
- **Child < 1 year:** Initial dose 250 micrograms 3 times daily. This dose may be increased as necessary and as tolerated up to 1mg 3 times daily
- **Child 1–5 years:** Initial dose 1 mg 3 times daily. This dose may be increased as necessary and as tolerated up to 2 mg 3 times daily
- **Child 6–11 years:** Initial dose 2 mg 3 times daily. This dose may be increased as necessary and as tolerated up to 4 mg 3 times daily
- **Child 12–17 years:** 4 mg 3 times daily

Notes:
- The adverse effects of dexamethasone quickly outweigh its benefits. Ideally it should be given as short courses of 48 hours or five days, but that is not always possible in the palliative phase, and many patients find themselves on dexamethasone for long periods.
- Dexamethasone can be stopped abruptly if it has been given for less than two weeks, but otherwise should be weaned down over a number ofweeks to allow recovery of the hypo-pituitary axis and avoid an Addisonian crisis.
- Not licensed for use in children as an anti-emetic.
- Dexamethasone has high glucocorticoid activity but relatively insignificant mineralocorticoid activity so is particularly suited for high dose anti-inflammatory therapy.
- Dexamethasone can be given in a single daily dose each morning for most indications. Whether in a single dose or two divided doses, giving the total daily dose of dexamethasone before midday reduces the likelihood of corticosteroid induced insomnia and agitation.

- Dexamethasone has an oral bioavailability of >80%; it can be converted to SC or IV on a 1:1 basis.
- Dexamethasone 1 mg = dexamethasone phosphate 1.2 mg = dexamethasone sodium phosphate 1.3 mg.
- Dexamethasone 1 mg = 7 mg prednisolone (anti-inflammatory equivalence).
- Dexamethasone has a long duration of action.
- Problems of weight gain and Cushingoid appearance are major concerns specifically in children. All specialist units therefore use pulsed dose regimes in preference to continual use. Regimes vary with conditions and specialist units. Seek local specialist advice.
- Other side effects include: diabetes, osteoporosis, muscle wasting, peptic ulceration and behavioural problems and agitation, also extreme exacerbation of and lability of mood (tearfulness, physical aggression).
- Tablets may be dispersed in water if oral liquid unavailable. Oral solution or tablets dispersed in water may be administered via an enteral feeding tube.
- Available as: tablets (500 micrograms, 2 mg), soluble tablets 2 mg, 4 mg, 8 mg, oral solution (2 mg/5 mL 10 mg/5 mL and 20 mg/5 mL and injection as dexamethasone sodium phosphate (equivalent to 3.8 mg/mL dexamethasone base or 3.3 mg/mL dexamethasone base.

Evidence: [6, 95, 140-143]

**Diamorphine**
Use:
• Moderate to severe pain.
• Dyspnoea

Dose and routes:

As background opioid for chronic pain
Normally convert using oral morphine equivalent (OME) from previous analgesia.
Use the following starting doses in opioid naive patient. The maximum dose stated applies to starting dose only.

By continuous subcutaneous or intravenous infusion
• **Neonate:** Initial dose of 60 micrograms/kg/24 hours which can be increased as necessary to a suggested maximum of 150 micrograms/kg/24 hours
• **Child 1 month-18 years:** 50-600 micrograms/kg/ 24 hours (initial maximum 10 mg/24 hours)adjusted according to response
By IV /SC or IMinjection:
• **Neonate:**15 micrograms/kg every 6 hours as necessary, adjusted according to response
• **Child 1-2 months:** 20 micrograms/kg every 6 hours as necessary, adjusted according to response
• **Child 3-5 months:** 25-50 micrograms/kg every 6 hours as necessary, adjusted according to response
• **Child 6-11 months:** 75 micrograms/kg every 4 hours as necessary, adjusted according to response
• **Child 1-11 years:** 75-100 micrograms/kg every 4 hours as necessary, adjusted according to response. Suggested initial maximum dose of 2.5 mg
• **Child 12-17 years:** 75-100 micrograms/kg every 4 hours as necessary, adjusted according to response. Suggested initial maximum dose of 2.5-5 mg.

By intranasal or buccal route:
• **Neonate:** 50 micrograms/kg/dose every 6-8 hours
• **Child over 10 kg:** 50-100 micrograms/kg every 4 hours as necessary adjusted according to response; maximum single dose 10 mg.
Injection solution can be used by intranasal or buccal routes or Nasal spray (Ayendi(R)) now available and licensed for use in children aged 2 years and over (weight 12 kg upwards) for the management of severe acute pain.

720 micrograms/actuation (Ayendi$^{(R)}$)
• 12-17 kg: 2 sprays as a single dose
• 18-23 kg: 3 sprays as a single dose
• 24-29 kg: 4 sprays as a single dose

1600 micrograms/actuation (Ayendi$^{(R)}$)
• 30-39 kg: 2 sprays as a single dose
• 40-49 kg: 3 sprays as a single dose

Intermittent pain without background opioids

Buccal, IV or SC route
- 30 micrograms/kg 1–4 hrly as needed.

Breakthrough pain

By buccal, subcutaneous or IV routes
- For breakthrough pain use 10-16% of total daily diamorphine dose every 1-4 hours as needed.
- Contact the medical palliative team if someone has needed three doses consecutively as they will need a review of their pain control.

Dyspnoea

By buccal, subcutaneous or IV routes
- **Neonates:** 10 micrograms/kg/dose
- **Child 1 month-11 years:** Dose as for pain, but at 25-50% of breakthrough dose

Notes:
- Diamorphine injection is licensed for the treatment of children who are terminally ill.
- For intranasal or buccal administration of diamorphine use the injection powder reconstituted in water for injections (unlicensed route of administration) or the nasal spray may be used (licensed for use in the management of severe acute pain from 2 years of age).
- In neonates, dosage interval should be extended to 6 or 8 hourly depending on renal function and the dose carefully checked, due to increased sensitivity to opioids in the first year of life.
- In poor renal function, dosage interval may be lengthened, or opioids only given as required and titrated against symptoms. Consider changing to fentanyl.
- For CSCI usually dilute with water for injections, as concentration-related incompatibility occurs at high doses with 0.9% saline (if above diamorphine 40 mg/ml).
- Diamorphine can be given by subcutaneous infusion up to a concentration of 250 mg/mL.
- Morphine injection is rapidly taking over from diamorphine, as the only benefit of diamorphine over morphine is its better solubility when high doses are needed and this is rarely a problem in paediatric doses.
- Spray has a significant volume and shelf life is very short. Thiscan make the spray difficult to use in practice.
- Available as: injection (5 mg, 10 mg, 30 mg, 100 mg, 500 mg ampoules); nasal spray 720 micrograms/actuation and 1600 micrograms/actuation (Ayendi Nasal Spray(R)).
- Schedule 2 CD.

Evidence: [1, 2, 6, 65, 144-146]

**Diazepam**
Use:
- Short term anxiety relief
- Agitation
- Panic attacks
- Relief of muscle spasm
- Treatment of status epilepticus.

Dose and routes
Short term anxiety relief, panic attacks and agitation
By mouth:
- **Child 2–11 years:** 0.5-2 mg 3 times daily
- **Child 12–18 years:** Initial dose of 2 mg 3 times daily increasing as necessary and as tolerated to a maximum of 10 mg 3 times daily.

Relief of muscle spasm
By mouth:
- **Child 1–11 months:** Initial dose of 250 micrograms/kg twice a day
- **Child 1–4 years:** Initial dose of 2.5 mg twice a day
- **Child 5–11 years:** Initial dose of 5m g twice a day
- **Child 12–17 years:** Initial dose of 10 mg twice a day; maximum total daily dose 40mg.

Status epilepticus
By IV injection over 3–5minutes:
- **Neonate:** 300-400 micrograms/kg as a single dose repeated once after 10 minutes if necessary
- **Child 1 month–11 years:** 300-400 micrograms/kg (max 10 mg) repeated once after 10 minutes if necessary
- **Child 12–17 years:** 10 mg repeated once after 10 minutes if necessary.

By rectum (rectal solution):
- **Neonate:** 1.25–2.5 mg repeated once after 10 minutes if necessary
- **Child 1 month–1 year:** 5 mg repeated once after 10 minutes if necessary
- **Child 2–11 years:** 5–10 mg repeated once after 10 minutes if necessary
- **Child 12–17 years:** 10-20 mg repeated once after 10 minutes if necessary.

Notes
- Do not use in acute or severe respiratory insufficiency unless in the imminently dying.
- Rectal tubes not licensed for children < 1 year old.
- Use with caution in mild-moderate hepatic diseaseand children with muscle weakness, respiratory depression or sleep apnoea.
- Metabolised via the cytochrome P450 group of liver enzymes: – potential for interaction with any concurrent medicine that induces or inhibits this group of enzymes. Enhancement of the central depressive effect may occur if diazepam is combined with drugs such as neuroleptics, antipsychotics, tranquillisers, antidepressants, hypnotics, analgesics, anaesthetics, barbiturates or sedative antihistamines.
- Can cause dose-dependent drowsiness and impaired psychomotor and cognitive skills.
- Almost 100% bioavailable when given orally or by rectal solution.

- Onset of action: apprx 15 minutes given orally and within 1-5 minutes given intravenously. Given as rectal solution, diazepam is rapidly absorbed from the rectal mucosa with maximum serum concentration reached within 17 minutes.
- Long plasma half-life of 24-48 hours. The active metabolite, nordiazepam, has a plasma half-life of 48-120 hours.
- The oral solution may be administered via a gastrostomy tube. For administration via a jejunostomy tube, consider using tablets dispersed in water to reduce osmolarity.
- Available as: tablets (2 mg, 5 mg, 10 mg), oral solution/suspension (2 mg/5 mL, 5 mg/5 mL), rectal tubes (2.5 mg, 5 mg, 10m g), and injection (5 mg/mL solution and 5 mg/mL emulsion).Schedule 4 (CD Benz).

Evidence: [1, 2, 6, 10, 36, 42, 102, 147-152]

**Diclofenac Sodium**
Use:
• Mild to moderate pain and inflammation, particularly musculoskeletal disorders.

Dose and routes
By mouth or rectum:
• **Child 6 months-17 years:** Initial dose of 0.3 mg/kg 3 times daily increasing if necessary to a maximum of 1 mg/kg 3 times daily (maximum 50mg single dose).

By IV infusion:
• **Child 2–17 years:** 0.3-1 mg/kg 1–2 times daily; maximum of 150 mg/day and for a maximum of 2 days.

Notes:
**Will cause closure of ductus arteriosus; contraindicated in duct dependent congenital heart disease**
• Not licensed for use in children under 1 year; suppositories not licensed for use in children under 6 years (except for use in children over 1 year for juvenile idiopathic arthritis); solid dose forms containing more than 25mg not licensed for use in children; injection(IV infusion only) not licensed for use in children.
• The risk of cardiovascular events secondary to NSAID use is undetermined in children. In adults, all NSAID use (including cyclo-oxygenase-2 selective inhibitors) can, to varying degrees, be associated with a small increased risk of thrombotic events (e.g. myocardial infarction and stroke) independent of baseline cardiovascular risk factors or duration of NSAID use. However, the greatest risk may be in those patients receiving high doses long term. A small increased thrombotic risk cannot be excluded in children.
• All NSAIDs are associated with gastro-intestinal toxicity. In adults, evidence on the relative safety of NSAIDs indicates differences in the risks of serious upper gastro-intestinal side-effects: piroxicam and ketorolac are associated with the highest risk; indometacin, diclofenac, and naproxen are associated with intermediate risk, and ibuprofen with the lowest risk (although high doses of ibuprofen have been associated with intermediate risk).
• Use with caution in children with cardiac, hepatic or renal impairment and those with asthma.
• Smallest dose that can be given practically by rectal route is 3.125 mg by cutting a 12.5 mg suppository into quarters (CC).
• For IV infusion, dilute in 5% glucose or 0.9% NaCl (previously buffered with sodium bicarbonate) and infuse over 30-120 minutes.
• Dispersible tablets may be administered via an enteral feeding tube. Disperse immediately before administration. There should be no reduction in bioavailability from jejunal administration.
• Available as: gastro-resistant tablets (25 mg, 50 mg), modified-release tablets (25 mg, 50 mg, and 75 mg), modified release capsules (75 mg and 100 mg), injection (25 mg/mL VoltarolR for IV infusion only), and suppositories (12.5 mg, 25 mg, 50 mg and 100mg).

Evidence: [2, 6, 10, 89]

**Dihydrocodeine**

Use:

- Alternative to low dose morphine on WHO pain ladder, mild to moderate pain in patients known to be able to benefit. Step 2 pain (i.e. moderate and/or intermittent) that is opioid sensitive.

Dose and routes:

By mouth or deep subcutaneous or intramuscular injection:

- **Child 1-3 years:** 500 micrograms/kg every 4-6 hours
- **Child 4-11 years:** Initial dose of 500 micrograms/kg (maximum 30 mg/dose) every 4-6 hours. Dose may be increased if necessary to 1 mg/kg every 4-6 hours (maximum 30 mg/dose)
- **Child 12-17 years:** 30 mg (maximum 50 mg by intramuscular or deep subcutaneous injection) every 4-6 hours.Oral doses up to 40-80 mg 3x daily can be given (maximum 240 mg/day).
- Modified release tablets used 12 hourly (use ½ of previous total daily dose for each modified release dose).For children age 12-18 years doses up to 60-120 mg every 12 hours can be given.

Notes:

- Most preparations not licensed for children under 4 years.
- Potency around one fifth of oral morphine (OME 0.2).
- Relatively constipating compared with morphine / diamorphine.
- Dihydrocodeine is itself an active substance, not a pro-drug.
- Oral bioavailability 20%, so probably equipotent with codeine by mouth (but opinion varies). Twice as potent as codeine by injection.
- Time to onset of action 30 minutes, duration of action 4 hours for immediate release tablets.
- Side effects as for other opioids, plus paralytic ileus, abdominal pain, paraesthesia.
- Precautions: avoid or reduce dose in hepatic or renal failure.
- Oral solution may be administered via an enteral feeding tube. Dilute with an equal volume of water before administration.
- Available as: tablets (30mg, 40mg), oral solution (10 mg/5 mL), injection (Schedule 2 CD), (50 mg/mL 1 mL ampoules) and m/r tablets (60 mg, 90 mg, 120 mg). Other than the injection, other forms of dihydrocodeine are CD Schedule 5 (CDInv).

Evidence: [2, 5, 65, 89] ARE, NoRE for injection

**Docusate**
Use:
• Constipation (faecal softener).

Dose and routes
By mouth:
• **Child 6 months–1 year:** Initial dose of 12.5 mg 3 times daily; adjust dose according to response
• **Child 2–11 years:** Initial dose of 12.5 mg 3 times daily. Increase to 25 mg 3 times daily as necessary and then further adjust dose according to response
• **Child 12–17 years:** Initial dose 100 mg 3 times daily. Adjust as needed according to response up to 500 mg/day in divided doses.

By rectum:
• **Child 12–17 years:** 1 enema as single dose.

Notes:
- Adult oral solution and capsules not licensed in children < 12 years.
- Oral preparations act within 1–2 days.
- Rectal preparations act within 20mins.
- Mechanism of action is emulsifying, wetting and mild stimulant.
- Stimulant laxatives should be avoided in intestinal obstruction.
- For administration by mouth, solution may be mixed with milk or squash.
- Oral solution may be administered via an enteral feeding tube. Administration directly into the jejunum will not affect the pharmacological response.
- Doses may be exceeded on specialist advice.
- Available as capsules (100 mg), oral solution (12.5 mg/5 mL paediatric, 50 mg/5 mL adult), and enema (120 mg in 10 g single dose pack).

Evidence: [2]

**Domperidone**
MHRA April 2014: Domperidone is associated with a small increased risk of serious cardiac side effects. Its use is now restricted to the relief of symptoms of nausea and vomiting and the dosage and duration of use have been reduced.
Domperidone is now contraindicated for use in those with underlying cardiac conditions and other risk factors.
The use of domperidone in palliative care is excluded from these recommendations HOWEVER caution should be exercised nevertheless.

The indications and doses below are therefore largely unlicensed usage in a particular population. Use the minimum effective dose. Do not use in those with known cardiac problems or other risk factors.

Obtain ECG prior to starting and follow QTc interval to ensure safety.

Use:
- Nausea and vomiting where poor GI motility is the cause.
- Gastro-oesophageal reflux resistant to other therapy.

Dose and routes
For nausea and vomiting
By mouth:
- **Neonates:** 250 micrograms/kg 3 times a day increase if necessary to 400 micrograms/kg 3 times a day
- **Child >1 month and body-weight ≤ 35 kg:** Initial dose of 250 micrograms/kg 3–4 times daily increasing if necessary to 500 micrograms/kg 3-4 times daily. Maximum
- 2.4 mg/kg (or 80 mg) in 24 hours
- **Child of body-weight> 35 kg:** Initial dose of 10 mg 3-4 times daily increasing if necessary to 20 mg 3-4 times daily. Maximum 80 mg in 24 hours

For gastro-oesophageal reflux and gastrointestinal stasis
By mouth:
- **Neonate:** Initial dose of 100 micrograms/kg 4–6 times daily before feeds. Dose may be increased, if necessary, to maximum of 300 micrograms/kg 4-6 times daily
- **Child 1 month–11 years:** Initial dose of 200 micrograms/kg (maximum single dose 10mg) 3-4 times daily before food. Dose may be increased, if necessary, to 400 micrograms/kg 3-4 times daily. Maximum single dose 20 mg
- **Child 12–17 years:** Initial dose of 10 mg 3–4 times daily before food. Dose may be increased, if necessary, to 20 mg 3-4 times daily

Notes
- Domperidone may be associated with an increased risk of serious ventricular arrhythmias or sudden cardiac death.
- Domperidone is contraindicated in those:
  > With conditions where cardiac conduction is, or could be, impaired
  > With underlying cardiac diseases such as congestive heart failure
  > Receiving other medications known to prolong QT interval(e.g. erythromycin, ketoconazole) or which are potent CYP3A4 inhibitors
  > With severe hepatic impairment
- This risk may be higher with daily doses greater than 30 mg. Use at lowest effective dose.

- Not licensed for use in gastro-intestinal stasis; not licensed for use in children for gastro-oesophageal reflux disease.
- Reduced ability to cross blood brain barrier, so less likely to cause extrapyramidal side effects compared with metoclopramide.
- Promotes gastrointestinal motility so diarrhoea can be an unwanted (or useful) side effect.
- Not to be used in patients with hepatic impairment.
- For administration via an enteral feeding tube: Use the suspension formulation, although the total daily dose of sorbitol should be considered. If administering into the jejunum, dilute the suspension with at least an equal volume of water immediately prior to administration.
- Available as: tablets (10 mg), oral suspension (5 mg/5 mL).

Evidence: [2, 3, 6, 10, 153-158]

**Entonox (nitrous oxide)**

Use:
- As self-regulated analgesia without loss of consciousness.
- Particularly useful for painful dressing changes.

Dose and routes
By inhalation:
- Child: Up to 50% to be administered using suitable anaesthetic apparatus in oxygen adjusted according to the patient's needs. Self-regulated usually over 5 years of age.

Notes:
- Is normally used as a light anaesthesic.
- Rapid onset and then offset.
- Should only be used as self-administration using a demand valve; all other situations require a specialist paediatric anaesthetist.
- Use is dangerous in the presence of pneumothorax or intracranial air after head injury.
- Hypoxia can occur immediately after administration so additional oxygen should always be given for several minutes following administration.
- Avoid concomitant use with methotrexate as can increase antifolate effect.
- Risk of enhanced hypotensive effect with a number of medications.
- Prolonged use can cause megaloblastic anaemia. Consider assessment of plasma vitamin B12 concentration in children at risk of deficiency.
- Nitrous oxide 1ml per 1ml various sizes of cylinders available from medical gas suppliers Linde GasUK and BOC Ltd. See BNFC for additional information.
- May be difficult to make available in hospice settings especially if needed infrequently, due to training, governance and supply implications.

Evidence: [2, 159-161]

**Erythromycin**
Use:
• Gastrointestinal stasis (motilin receptor agonist).

Dose and routes
By mouth or by intravenous infusion:
• **Neonate:** 3 mg/kg 4 times daily
• **Child 1 month–17 years:** 3 mg/kg 4 times daily
• **Adult:** 250-500 mg 3 times daily

Notes:
• Not licensed for use in children with gastrointestinal stasis.
• Erythromycin is excreted principally by the liver, so caution should be exercised in administering the antibiotic to patients with impaired hepatic function or concomitantly receiving potentially hepatotoxic agents.
• Erythromycin is a known inhibitor of the cytochrome P450 system and may increase the serum concentration of drugs which are metabolised by this system. Appropriate monitoring should be undertaken and dosage should be adjusted as necessary. Particular care should be taken with medications known to prolong the QT interval of the electrocardiogram.
• For administration via enteral feeding tube use the suspension. Dilute the suspension with an equal volume of water before administration.
• Absorbed in small intestine so no concerns with jejunal administration.
• Available as: tablets (250 mg, 500 mg) and oral suspension (125 mg/5 mL,
• 250 mg/5 mL, 500 mg/5 mL).

Evidence: [2, 162, 163] WRE

**Etoricoxib**
Uses:
- Anti-inflammatory analgesic; adjuvant for musculoskeletal pain

Dose and route:
Oral:
- **Child 12-15 years:** Initial dose of 30 mg once daily. Dose may be increased as necessary and as tolerated to a maximum of 60 mg once daily
- **Child 16 years and older:** Usual dose of 30-60 mg once daily.Doses of 90 mg daily may be used on a short term basis until symptoms controlled then attempt to reduce back to 60 mg daily. Doses up to 120 mg have been used on a short term basis in acute gouty arthritis in adults.

Notes:
- Oral selective cyclo-oxygenase (COX-2) inhibitor.
- Etoricoxib is not licensed for use in children less than 16 years of age. The pharmacokinetics of etoricoxib in children less than 12 years of age has not been studied.
- Etoricoxib may mask fever and other signs of inflammation.
- All NSAIDs should be used with caution in children with a history of hypersensitivity to any NSAID or in those with a coagulation disorder. However, etoricoxib may be better tolerated than other NSAIDs in patients with known hypersensitivity.
- Etoricoxib is contraindicated in those with: active peptic ulceration or active GI bleeding; severe hepatic or renal dysfunction; inflammatory bowel disease or congestive heart failure.
- The risk of cardiovascular events secondary to NSAID use is undetermined in children. All NSAIDs are associated with GI toxicity. In adults evidence on the relative safety of NSAIDs indicates differences in the risks of serious upper GI side-effects with piroxicam and ketorolac associated with the highest risk and ibuprofen at low to medium dose with the lowest risk. Children appear to tolerate NSAIDs better than adults and GI side-effects are less common although they do still occur.
- Common adverse events (1-10% patients): alveolar osteitis; oedema/fluid retention; dizziness, headache; palpitations, arrhythmia; hypertension; bronchospasm; abdominal pain; constipation, flatulence, gastritis, heartburn/acid reflux, diarrhoea, dyspepsia/epigastric discomfort, nausea, vomiting, oesophagitis, oral ulcer; ALT increased, AST increased; ecchymosis; asthenia/fatigue, flu-like disease.
- Potential drug interactions include warfarin (increase in INR); diuretics, ACE inhibitors and angiotensin II antagonists (increased risk of compromised renal function). Etoricoxib does NOT appear to inhibit or induce CYP isoenzymes. However, the main pathway of etoricoxib metabolism is dependent on CYP enzymes (primarily CYP3A4) so co-administration with drugs that are inducers or inhibitors of this pathway may affect the metabolism of etoricoxib.
- Etoricoxib tablets may be dispersed in 10ml water and will disintegrate to give fine granules that settle quickly but disperse easily and flush down an 8Fr NG or gastrostomy tube without blockage. There are no specific data relating to the jejunal administration of etoricoxib. Administer as above and monitor for lack of efficacy or increased side-effects.
- Available as: film coated tablets 30 mg, 60 mg, 90 mg, 120 mg. Tablets contain lactose.

Evidence: [1, 164, 165] SR EA

**Fentanyl**
Use:
• Step 2 WHO pain ladder (moderate to severe pain).

Dose and routes
Normally convert using oral morphine equivalent (OME) from previous analgesia.
Use the following starting doses in the opioid naive patient. The maximum dose stated applies to starting dose only.

MHRA/CHM advice: Transdermal fentanyl patches: life-threatening and fatal opioid toxicity from accidental exposure, particularly in children (October 2018)

Accidental exposure to transdermal fentanyl can occur if a patch is swallowed or transferred to another individual. Always fully inform patients and their carers about directions for safe use of fentanyl patches, including the importance of:

- not exceeding the prescribed dose;
- following the correct frequency of patch application, avoiding touching the adhesive side of patches, and washing hands after application;
- not cutting patches and avoiding exposure of patches to heat including via hot water;
- ensuring that old patches are removed before applying a new one;
- following instructions for safe storage and properly disposing of used patches or those which are not needed.

Patients and carers should be advised to seek immediate medical attention if overdose is suspected—see Side-effects and Patient and carer advice for further information.

***By transdermal patch or continuous infusion:***
• Based on oral morphine dose equivalent (given as 24 hour totals).

**72 hour Fentanyl patches are approximately equivalent to the following 24 hour doses of oral morphine**

| | | |
|---|---|---|
| morphine salt 30 mg daily | ≡ | fentanyl '12' patch |
| morphine salt 60 mg daily | ≡ | fentanyl '25' patch |
| morphine salt 120 mg daily | ≡ | fentanyl '50' patch |
| morphine salt 180 mg daily | ≡ | fentanyl '75' patch |
| morphine salt 240 mg daily | ≡ | fentanyl '100' patch |

***By oromucosal application (lozenge with oromucosal applicator)***

- **Child 2-18 years and greater than 10 kg:** 15 micrograms/kg as a single dose, titrated to a maximum dose 400micrograms (higher doses under specialist supervision).

***By intranasal (starting doses for opioid naïve patients and acute pain)***
- **Neonate - Child<2 years:** 1 microgram/kg as a single dose
- **Child 2-18 years:** 1-2 micrograms/kg as a single dose, with initial maximum single dose of 50 micrograms

***By continuous intravenous/subcutaneous infusion***
- **Neonate or infant:** 0.15-0.5 micrograms/kg/ hour
- **Child:** 0.25-1 microgram/kg/hour

***By intravenous/subcutaneous injection (lower doses are required in non-ventilated neonatesand opioid naïve patients)***
- **Neonate or infant:**
  > **Non-ventilated:** 0.15-0.25 micrograms/kg per dose slowly over 3-5 minutes; repeated 30-60 minutes
  > **Ventilated:** 0.25-0.5 micrograms/kg per dose slowly over 3-5 minutes; repeated every 30-60 minutes
- **Child over 1 year:** 0.25–0.5 micrograms/kg per dose, slowly over 3-5 minutes, repeated every 30-60 minutes.

Notes:
- Injection not licensed for use in children less than 2 years of age. Lozenges and nasal sprays are not licensed for use in children.
- In neonatology there is no lower CorGA as fentanyl is used for endotracheal intubation at all gestations.
- Can be safely used in poor, deteriorating or absent renal function.
- Avoid or reduce dose in hepatic impairment.
- Synthetic opioid, very different in structure from morphine, and therefore ideal for opioid switching.
- Evidence that it is less constipating than morphine has not been confirmed in more recent studies[166].
- Consider reducing starting doses in obese children – to use ideal body weight rather than actual body weight.
- Fentanyl products for the treatment of breakthrough pain are not interchangeable. If patients are switched from another fentanyl containing product a new dose titration is required.
- For break through pain, fentanyl effect is idiosyncratic: start at significantly lower doses than the equivalent for oral morphine. Always start at lower doses then titrate up.

**Intranasal**

- Intranasal route works more quickly and is shorter lasting than oromucosal.
- Pharmacokinetics of fentanyl intranasally arefavourable but it isnot always practical and/or well tolerated in children.
- Intranasal route has also been used for management of respiratory distress in paediatric palliative care.
- Injection solution can be administered by the intranasal route for doses less than 50micrograms which is the lowest strength of nasal spray available.

- Injection solution can be administered drop wise via nasal route (may be unpleasant) or using an atomiser device such as that used by A+E units for intranasal diamorphine.

**Lozenges**

- The usefulness of lozenges and buccal/sublingual tablets in children is limited by the dose availability andno reliable conversion factor. In practice this also varies between preparations and between individuals.
- Another caution is that oral morphine approximateequivalence of the smallest lozenge(200 micrograms) is 30 mg, meaning it is probably suitable to treat breakthrough pain only for children receiving a total daily dose equivalent of 180mg morphine or more.
- Older children will often choose to remove the lozenge before it is completely dissolved, giving them some much-valued control over their analgesia.
- The lozenge must be rotated in buccal pouch, not sucked.

**Fentanyl transdermal patches**

- The patch formulation is not usually suitable for the initiation or titration phases of opioid management in palliative care since the patches represent large dose incrementsand because of the time lag to achieve steady state.
- Fentanyl patches takes up to 17 hours to reach steady state. Commence fentanyl patch with last dose of slow release morphine.
- Fentanyl patches should be changed every 72 hours and the site of application rotated. In some children who are rapid metabolisers the patch may not last for 72 hours and the patches may need to be changed every 36-48 hours.
- Conversion ratio is 1:1 for transdermal fentanyl to intravenous/ subcutaneous routes.
- A reservoir of fentanyl accumulates in the body, and significant blood concentrations persist for at least 24 hours after discontinuing transdermal fentanyl. It takes 17 hours or more for the plasma-fentanyl concentration to decrease by 50%; replacement opioid therapy should therefore be initiated at a low dose and increased gradually.
- For rapidly escalating symptoms in the last few hours and days of life, continue transdermal fentanyl and give additional SC morphine PRN. If >2 PRN doses are required in 24 hours, give morphine by continuous subcutaneous infusion, while continuing transdermal fentanyl, starting with a dose equal to the sum of the PRN doses over the preceding 24 hours. If necessary, adjust the PRN dose taking into account the total opioid dose (i.e. transdermal fentanyl + continuous subcutaneous morphine).

**Formulations**

- **Intranasal spray** InstanylR (50 micrograms/metered spray, 100micrograms/ metered spray and 200 micrograms/metered spray). PecFentR (100 micrograms/ metered spray and 400 micrograms/metered spray).
  **Lozenge** with oromucosal applicator ActiqR (200 micrograms, 400 micrograms,600 micrograms, 800 micrograms, 1.2 mg and 1.6 mg).
  **Sublingual/buccal tablets** Abstral(R (100, 200, 300, 400, 600 and 800 micrograms) Recivit® (133, 267, 400 and 800 micrograms) and buccal tablets Effentora(R) (100, 200, 400, 600 and 800 micrograms); Breakyl(R) (200, 400, 600, 800 and 1200 micrograms).

**Patches:** various manufacturers (12 micrograms/hour, 25 micrograms/hour, 50 micrograms/hour, 75 micrograms/hour, 100 micrograms/hour); Ionys® transdermal system (40 microgram/dose)
**Injection:** 50 microgram per mL

- Schedule 2 CD

Evidence: [2, 4, 5, 13, 144, 167-190]

**Fluconazole**
Use:
- Mucosal candidiasis infection, invasive candidal infections or prevention of fungal infections in immunocompromised patients.

Dose and routes
Mucosal candidal infection
By mouth or intravenous infusion:
- **Neonate up to 13 days:** 3-6 mg/kg on first day then 3 mg/kg every 72 hours
- **Neonate 14-28 days-:** 3-6 mg/kg on first day then 3 mg/kg every 48 hours
- **Child 1 month–11 years:** 3-6 mg/kg on first day then 3 mg/kg (maximum 100 mg) daily
- **Child 12–17 years:** 50 mg/day. Increase to 100 mg/day in difficult infections.

Invasive candidal infections and cryptococcal infections
By mouth or intravenous infusion:
- **Neonate up to 13 days:** 6-12 mg/kg every 72 hours
- **Neonate 14-28 days:** 6-12 mg/kg every 48 hours
- **Child 1 month–17 years:** 6-12 mg/kg (max.800mg) every 24 hours

Prevention of fungal infections in immunocompromised patients
By mouth or intravenous infusion
- **Neonate up to 13 days:** 3-12 mg/kg every 72 hours
- **Neonate 14-28 days:** 3-12 mg/kg every 48 hours
- **Child 1 month–17 years:** 3-12 mg/kg (max.400 mg) every 24 hours

Notes:
- Use for 7-14 days in oropharyngeal candidiasis.
- Usefor14-30 days in other mucosal infections.
- Different duration of use in severely immunocompromised patients.
- Fluconazole is a potent CYP2C9 inhibitor and a moderate CYP3A4 inhibitor. Fluconazole is also an inhibitor of CYP2C19. Fluconazole treated patients who are concomitantly treated with medicinal products with a narrow therapeutic window metabolised through CYP2C9, CYP2C19 and CYP3A4, should be monitored.
- The most frequently (>1/10) reported adverse reactions are headache, abdominal pain, diarrhoea, nausea, vomiting, alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased and rash.
- For intravenous infusion, give over 10–30 minutes; do not exceed an infusion rate of 5–10mL/minute.
- Oral suspension may be administered via NG tube gastrostomy or jejunostomy. Bioavailability is unaffected by jejunal administration. Flush tube well after suspension is administered.
- Available as: capsules (50 mg, 150 mg, 200 mg); oral suspension (50 mg/5 mL, 200 mg/5 mL) and IV infusion (2 mg/mL in 50 mL, 100 mL or 200 mL infusion bags).

Evidence: [2, 10, 191, 192]

**Fluoxetine**
Use:
• Major depression.

Dose and routes
By mouth:
• **Child 8–17 years:** Initial dose 10 mg once a day. May be increased after 1-2 weeks if necessary to a maximum of 20 mg once daily.

Notes:
• Licensed for use in children from 8 years of age.
• Use with caution in children, ideally with specialist psychiatric advice.
• Increased risk of anxiety for first 2 weeks.
• Onset of benefit 3-4 weeks.
• Consider long half-life when adjusting dosage. Do not discontinue abruptly.
• May also help for neuropathic pain and intractable cough.
• Suicide related behaviours have been more frequently observed in clinical trials among children and adolescents treated with antidepressants compared with placebo. Mania and hypomania have been commonly reported in paediatric trials.
• The most commonly reported adverse reactions in patients treated with fluoxetine were headache, nausea, insomnia, fatigue and diarrhoea. Undesirable effects may decrease in intensity and frequency with continued treatment and do not generally lead to cessation of therapy.
• Because the metabolism of fluoxetine, (like tricyclic antidepressants and other selective serotonin re-uptake inhibitors), involves the hepatic cytochrome CYP2D6 isoenzyme system, concomitant therapy with drugs also metabolised by this enzyme system may lead to drug interactions.
• Must not be used in combination with a MAOI.
• Oral liquid may be administered via NG tube or gastrostomy. There are no specific reports of jejunal administration of fluoxetine. Monitor for loss of efficacy or increased side-effects.
• Available as: capsules (20 mg, 60 mg), dispersible tablets (20 mg) and oral liquid (20 mg/5 mL).

Evidence: [1, 2, 193-200]

**Gabapentin**
**Important safety information**

The levels of propylene glycol, acesulfame K and saccharin sodium may exceed the recommended WHO daily intake limits if high doses of gabapentin oral solution (Rosemont brand) are given to adolescents or adults with low body-weight (39–50 kg)—consult product literature.

MHRA/CHM advice: Gabapentin (Neurontin®): risk of severe respiratory depression (October 2017)

Gabapentin has been associated with a rare risk of severe respiratory depression even without concomitant opioid medicines. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment, and concomitant use of central nervous system (CNS) depressants might be at higher risk of experiencing severe respiratory depression and dose adjustments may be necessary in these patients.

Use:
- Adjuvant in neuropathic pain
- Neuroirritability
- Visceral hyperalgesia
- Third line management of abnormal tone and movement disorders in cerebral palsy
- Epilepsy

Dose and routes

Epilepsy
Consult BNFc or local neurology protocols

Neuropathic pain
By mouth:
- Neonate-Child 1 year: 5 mg/kg given as below
- Child 2 -11 years: 5-10 mg/kg given as below
  > Day 1 – give 5-10 mg/kg as a single dose (maximum single dose 300 mg),
  > Day 2 – give 5-10 mg/kg twice daily (maximum single dose 300 mg),
  > Day 3 onwards, give 5-10 mg/kg three times daily (maximum single dose 300 mg),
  > Increase further if necessary to maximum of 20 mg/kg/dose (maximum single dose 600 mg). See notes for day 3 onward titration regimes.
- From 12 years: Initially 300 mg once daily for day 1, then 300 mg twice daily for day 2, then 300 mg 3 times a day for day 3, then increase in steps of 300 mg every 3-7 days given in 3 divided doses daily.The maximum daily dose can be increased according to response to a maximum of 3600 mg/day.

Gabapentin to Pregabalin Switch for neuropathic pain
Consult appendix 3

Notes:

- Not licensed for neuropathic pain in children. Although does have a license as an adjunct for the treatment of focal seizures for those >6 years (maximum licensed dose 50 mg/kg/day if < 12 years) and as a monotherapy for the treatment of focal seizures in those >12 years.
- Patient Information; Medicines for Children Leaflets are available for gabapentin used for both neuropatheic pain and seizures: www.medicinesforchildren.org.uk/gabapentin-for-neuropathic-pain

www.medicinesforchildren.org.uk/gabapentin-for-preventing-seizures

- Speed of titration after first 3 days of initiation varies between:
  > fast regime, increase every 3 days;
  > slow regime (for debilitated children or when taking other CNS depressants),to increase every one to two weeks.
- No consensus on dose for neuropathic pain. Doses shown are based on doses for partial seizures and authors' experience.
- Gabapentin and pregabalin are a similar class of drug. Evidence from pre-clinical studies in animals suggest that both the anti-seizure and analgesic activity of gabapentin as with pregabalin is mediated via binding to the alpha-2 subunit of voltage gated calcium channels in the CNS with subsequent inhibition of excitatory neurotransmitter release and/or inhibition of descending inhibitory pain pathways.
- Absolute bioavailability of a 300 mg gabapentin capsule is approximately 60%. However, unlike pregabalin which shows linear pharmacokinetics, gabapentin absorption is saturable, leading to a non-linearpharmacokinetic profile accounting for the decrease in bioavailability seen with increasing gabapentin dose and variations in bioavailability in patient populations. Careful titration of dose is required.
- Peak plasma concentrations occur 2-3 hours after oral dosing.
- Food does not affect gabapentin bioavailability. However co-administration with antacids containing aluminium and magnesium can reduce bioavailability by up to 24%. Manufacturers recommend giving gabapentin two hours after antacids.
- Patients who use gabapentin and morphine concomitantly may experience increases in gabapentin concentrations. The dose of gabapentin or opioids should be reduced as clinically appropriate.
- Gabapentin is solely excreted unchanged by the kidneys. Therefore dose reduction is required in renal impairment (consult manufacturer's literature), but not in hepatic impairment.
- Very common (>1 in 10) side-effects: somnolence, dizziness, ataxia, viral infection, fatigue, fever.
- NICE Guidance CG173 (Neuropathic pain in adults) recommends:'offer a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment of neuropathic pain. If the initial treatment is not effective or is not tolerated, offer one of the remaining 3 drugs and consider switching again if the second and third drugs tried are also not effective or not tolerated'.
- Public Health England issued a warning to prescribers in December 2013, stating that pregabalin and gabapentin had potential for creating dependence and that they may be misused in certain situations. From April 2019 gabapentin has been reclassified as a Schedule 3 controlled drug.
- Adult evidence for use in pruritis in anaemia, anxiety, hot flushes, sweating,

  refractory hiccups, restless legs syndrome and refractory cough.
- Capsules can be opened but have a bitter taste.
- Absorbed in proximal small bowel. The oral solution or the capsule contents

(dispersed in water) can be given via a NG tube or gastrostomy. Flush tube well after administration. There are no specific data relating to jejunal administration of gabapentin. Administer using the above method. Monitor for loss of efficacy or increased side-effects.

- Available as: capsules (100 mg, 300 mg, 400 mg); tablets (600 mg, 800 mg), oral solution 250 mg/5 mL (Neurontin, United States import).
- Schedule 3 controlled drug but exempt from safe custody requirements.

Evidence: [1, 2, 10, 63, 65, 201-221] NoRE, WRE

**Gaviscon®**
Use:
• Gastro-oesophageal reflux, dyspepsia and heartburn.

Dose and routes
By mouth:
• **Neonate–2 years, body weight < 4.5 kg:** 1 dose (half dual sachet) when required mixed with feeds or with water for breast fed babies, maximum 6 doses in 24hours
• **Neonate–2 years, body weight > 4.5 kg:** 2 doses (1 dual sachet) when requiredmixed with feeds or with water for breast fed babies or older infants, maximum 6 doses in 24hours

Gaviscon Liquid and Tablets
• **Child 2-11 years:** 1 tablet or 5-10 mL liquid after meals and at bedtime
• **Child 12-17 years:** 1-2 tablets or 10-20mL liquid after meals and at bedtime

Gaviscon Advance
• **Child 2-11 years:** 1 tablet or 2.5-5mL suspension after meals and at bedtime (under medical advice only)
• **Child 12-17 years:** 1-2 tablets or 5-10mL suspension after meals and at bedtime

Notes:
• Gaviscon Infant Sachets licensed for infants and young children up to 2 years of age but use <1 year only under medical supervision. Gaviscon liquid and tablets are licensed for use from 2 years of age but age 2-6 years only on medical advice. Gaviscon Advance suspension and tablets are licensed for use from 12 years of age; use under 12 years on medical advice only.
• Gaviscon Infant should not to be used with feed thickeners, nor in patients with excessive fluid losses, (e.g. fever, diarrhoea, vomiting).
• Gaviscon Liquid contains 3.1 mmol sodium per 5mL; Gaviscon tablets contain 2.65 mmol sodium and also contain aspartame. Gaviscon Infant Sachets contain 0.92 mmol sodium per dose (half dual sachet).
• Available as: Gaviscon liquid and tablets; Gaviscon Advance suspension and tablets; Infant Sachets (comes as dual sachets, each half of dual sachet is considered one dose).
• Can be administed via nasogastric tube or gastrostomy. Not appropriate for administration via jejunostomy.

Evidence: [1-3]

**Glycerol (glycerin)**
Use:
• Constipation.

Dose and routes
By rectum:
• **Neonate of >34 weeks CorGA:** Tip of a glycerol suppository (slice a small chip off a 1 g suppository with a blade)
• **Child 1 month–11 months:** 1 g infant suppository as required
• **Child 1–11 years:** 2 g child suppository as required
• **Child 12–17 years:** 4 g adult suppository as required

Notes:
• Moisten with water before insertion.
• Hygroscopic and lubricant actions. May also be a rectal stimulant.
• Response usually in 20 minutes to 3 hours.
• Associated with NEC in <34 week babies.
• Available as: suppositories (1 g, 2 g, and 4 g).

Evidence: [1, 2, 89] NoRE

**Glycopyrronium bromide**

Use:

- Control of upper airways secretion and hypersalivation.

Dose and routes

By mouth:

- **Child 1 month-17 years:** Initial dose of 40 micrograms/kg 3–4 times daily. The dose may be increased as necessary to 100 micrograms/kg 3-4 times daily. Maximum 2 mg/dose given 3-4 times daily

Subcutaneous / Intravenous injection:

- **Child 1 month-11 years:** Initial dose of 4 micrograms/kg 3 to 4 times daily. The dose may be increased as necessary to 10 micrograms/kg 3-4 times daily, Maximum 200 micrograms/dose given 4 times daily
- **Child 12-17 years:** 200 micrograms every 4 hours when required

Continuous subcutaneous / intravenous infusion:

- **Child 1 month-11 years:** Initial dose of 12 micrograms/kg/24 hours. The dose may be increased as necessary to 40 micrograms/kg/24 hours (maximum 1.2 mg/24 hours)
- **Child 12-17 years:** Initial dose of 600 micrograms /24 hours. The dose may be increased as necessary to 1.2 mg/24 hours. Maximum recommended dose is 2.4 mg/24 hours.

Notes:

- Licensed oral solutions (Sialanar®K, Colonis Pharma generic) are licensed for use in children from 3 years of age with a chronic neurological disorder, for chronic pathological drooling. Not licensed for use in children for control of upper airways secretion and hypersalivation.
- Excessive secretions can cause distress to the child, but more often cause distress to those around him/her.
- Treatment is more effective if started before secretions become too much of a problem.
- Glycopyrronium does not cross the blood brain barrier and therefore has fewer side effects than hyoscine hydrobromide, which is also used for this purpose. Also fewer cardiac side effects.
- Slower onset response than with hyoscine hydrobromide or butylbromide.
- Oral absorption of glycopyrronium is very poor with wide inter-individual variation.
- Adult evidence for use in smooth muscle spasm (e.g. intestine, bladder), inoperable intestinal obstruction, para-neoplastic pyrexia and sweating and hyperhidrosis.
- Administration by CSCI: good compatibility data available for mixing with other commonly used palliative agents.
- Oral solution: Co-administration with food results in a marked decrease in systemic medicinal product exposure. Dosing should be at least one hour before or at least two hours after meals, or at consistent times with respect to food intake. High fat food should be avoided. Where the child's specific needs determine that co-

administration with food is required, dosing of the medicinal product should be consistently performed during food intake.

- For administration via an enteral feeding tube, tablets may be dispersed in water immediately prior to administration, or use the oral solution. Flush tube immediately with 10-20 mL water. There is no specific data on jejunal administration of glycopyrronium. Administer using the above method. Monitor for loss of efficacy or increased side-effects.
- Available as: tablets (1 mg, 2 mg), oral solution (200 micrograms/mL as glycopyrronium bromide (various) and 400 micrograms/mL as glycopyrronium bromide (Sialanar®), injection (200 micrograms/mL 1 mL and 3 ml ampoules).

Evidence: [2, 30, 206, 222, 223]

**Haloperidol**

Use:

- Nausea and vomiting where cause is metabolic, or in difficult to manage cases such as end stage renal failure.
- Restlessness and confusion / terminal agitation.
- Persistent severe aggression in autism or pervasive developmental disorders.
- Intractable hiccups.
- Psychosis (including steroid induced), hallucinations.

Dose and routes

By mouth for nausea and vomiting:

- **Child 1 month–11 years:** 10-20 micrograms/dose every 8-12 hours increased as necessary to a maximum of 50-60 micrograms/kg/dose every 8-12 hours
- **Child 12–17 years:** 1.5 mg once daily at night, increased as necessary to 1.5 mg twice a day; maximum 5 mg twice a day.

By mouth for restlessness and confusion:

- **Child 1 month–17 years:** 10–20 micrograms/kg every 8–12 hours; maximum 5 mg twice a day.

By mouth for intractable hiccups:

- **Child 1 month–11 years:** Initial dose of 50 micrograms/kg/24 hours (initial maximum 3 mg/24 hrs) in divided doses. The dose may be increased as necessary to a maximum of 170 micrograms/kg/24 hours in divided doses
- **Child 12–17 years:** 1.5 mg 3 times daily.

By continuous IV or SC infusion (for any indication):

- **Child 1 month–11 years:** Initial dose of 25 micrograms/kg/24 hours (initial maximum 1.5 mg/24hrs). The dose may be increased as necessary to a maximum of 85 microgram/kg/24 hours
- **Child 12–17 years:** Initial dose of 1.5 mg/24 hours. The dose may be increased as necessary to a suggested maximum of 5 mg/24 hours although higher doses may be used under specialist advice.

Notes:

- D2 receptor antagonist and typical antipsychotic.
- For dosage in psychosis please discuss with child psychiatrist.
- Not licensed for use in children with nausea and vomiting, restlessness and confusion or intractable hiccups. Injection is licensed only for IM administration in adults; IV and SC administration off-label (all ages).
- Haloperidol can cause potentially fatal prolongation of the QT interval and Torsades de Pointes, particularly if given IV (off-label route) or at higher than recommended doses. Caution is required if any formulation of haloperidol is given to patients with an underlying predisposition e.g. those with cardiac abnormalities, hypothyroidism, familial long QT syndrome, electrolyte imbalance or taking other drugs known to prolong the QT interval. If IV haloperidol is essential, ECG monitoring during drug administration is recommended.

- Side effects vary between age groups, with behavioural problems being common in children.
- Dosages for restlessness and confusion are often higher.

- Adult dosages can exceed 15 mg/24 hours in severe agitation.
- Oral doses are based on an oral bioavailability of ~50% of the parenteral route i.e. oral doses ~2x parenteral.
- Useful as long acting: – once daily dosing is often adequate.
- Oral solutions may be administered via NG tube or gastrostomy without further dilution. Flush tube well following administration. There is no specific data relating to jejunal administration of haloperidol. Administer using the above method. Monitor for increased side-effects or loss of efficacy.
- Available as: tablets (500 micrograms, 1.5 mg, 5 mg, 10 mg), capsules (500 micrograms), oral liquid (200 micrograms/mL, 1 mg/mL, 2 mg/mL), and injection (5 mg/mL).

Evidence: [1, 2, 5, 6, 10, 142, 224-233]

**Hydromorphone**
Use:
- Alternative opioid analgesic for severe pain especially if intolerant to other strong opioids.
- Antitussive.

Dose and routes
Normally convert using oral morphine equivalent (OME) from previous analgesia.
Use the following starting doses in opioid naive patient. The maximum dose stated applies to starting dose only.

By mouth:
- **Child 1–17 years:** 30 micrograms/ kg per dosemaximum 2 mg per dose every 3-4 hours increasing as required. Modified release capsules with an initial dose of 4 mg every 12 hours may be used from 12 years of age.

By IV or SC injection:
- **Child 1-17 years:** Initially 12 micrograms/kg per dose, slowly over at least 2-3 minutes every 3-6 hours.

Notes:
- Hydromorphone injection is licensed for the relief of severe pain in cancer in adults and adolescents aged >12 years. It can be administered by intravenous or subcutaneous injection or infusion.
- Oral form licensed for use in children from 12 years of age with cancer pain.
- Oral bioavailability 37-62% (wide inter-individual variation).
- 1mg of IV hydromorphone is equivalent to 2.5mg of oral hydromorphone.
- Onset of action 15 min for SC, 30 min for oral. Peak plasma concentration 1hour orally.
- Plasma half life 2.5 hours early phase, with a prolonged late phase. Duration of action 4-5 hours.
- Potency ratios seem to vary more than for other opioids. This may be due to inter-individual variation in metabolism or bioavailability.
- An osmotic-release oral delivery system (OROS®) for once daily administration has been developed, but as yet is unauthorized in the UK and Ireland.
- Conversion of oral morphine to oral hydromorphone: divide morphine dose by 7.5
- Conversion of IV morphine to IV hydromorphone: divide morphine dose by 7.5
- Dosage discontinuation: after short-term therapy (7–14 days), the original dose can be decreased by 10–20% of the original dose every 8 hours, gradually increasing the time interval between doses. After long-term therapy, the dose should be reduced by not more than 10–20% per week.
- Caution in hepatic impairment, use at reduced starting doses.
- Modified release capsules are given 12 hourly.
- Capsules (both types) can be opened and contents sprinkled on soft food. Capsule contents must not however be administered via an enteral feeding tube as likely to cause blockage.
- Available as: capsules (1.3 mg, 2.6 mg) and modified release capsules (2 mg, 4 mg, 8 mg, 16 mg, 24 mg).Injection (2 mg/mL, 10 mg/mL, 20 mg/mL and 50 mg/mL ). Oral solution available as a manufacturer's special.

Evidence: [1, 2, 4, 5, 48, 65, 171, 172, 234-239] No RE, ARE

**Hyoscine butylbromide**

Use:

- Adjuvant where pain is caused by spasm of the gastrointestinal or genitourinary tract (smooth muscle spasm)
- Antisecretory effect in bowel obstruction
- Management of secretions, especially where drug crossing the blood brain barrier is an issue
- Management of noisy breathing at the end of life (may be more effective if started early)

Dose and routes

By mouthor IM or IV injection:

- **Child 1 month-4 years:** 300–500 micrograms/kg (maximum 5 mg/dose) 3–4 times daily
- **Child 5-11 years:** 5-10 mg 3–4 times daily
- **Child 12-17 years:** 10–20 mg 3–4 times daily

By continuous subcutaneous infusion:

- **Child 1 month-4 years:** 1.5 mg/kg/24 hours (max 15 mg/24 hours)
- **Child 5-11 years:** 30 mg/24 hours
- **Child 12-17 years:** Up to 60-80 mg/24 hours
- Higher doses may be needed; doses used in adults range from 20-120 mg/24 hours (maximum dose 300 mg/24 hours).

Notes:

- Does not cross blood brain barrier (unlike hyoscine hydrobromide), hence no central antiemetic effect and doesn't cause drowsiness.
- Increased risk of cardiac arrhythmiaand anaphylaxis in patients with underlying cardiac disease.
- Hyoscine butylbromide injection is contraindicated in patients with tachycardia and should be used with caution in patients with cardiac disease. The MHRA recommends that these patients are monitored and that resuscitation equipment and trained personnel are readily available.
- Onset of action <10 min for SC/IV; 1–2 hours for PO. Time to peak plasma concentration 15 min–2 hours PO. Plasma half-life 1–5 hours. Duration of action <2 hours in adult volunteers but possibly longer in moribund patients.
- Oral bioavailability, based on urinary excretion, is <1%. Thus, any antispasmodic effect reported after PO administration probably relates to a local contact effect on the GI mucosa.
- Likely to exacerbate acid reflux.
- Tablets are not licensed for use in children <6 years old.
- Injection is not licensed for use in children.
- The injection solution may be given orally or via an enteral feeding tube. If the tube exits in the jejunum, consider using parenteral therapy. Injection solution can be stored for 24hours in the refrigerator.
- IV injection should be given slowly over 1minute and can be diluted with glucose 5% or sodium chloride 0.9%.
- Available as: tablets (10 mg) and injection (20 mg/mL).

Evidence: [1, 2, 10, 30, 223, 240-245]

**Hyoscine hydrobromide**
Use:
- Control of upper airways secretions and hypersalivation
- Bowel colic pain
- Paraneoplastic sweating or pyrexia

Dose and routes
By mouth or sublingual:
- **Child 2–11 years:** 10 micrograms/kg (maximum 300 micrograms single dose) 4 times daily
- **Child 12–17 years:** 300 micrograms 4 times daily

By transdermal route:
- **Neonate >32weeks CorGA - Child 2 years:** Quarter of a patch every every72 hours
- **Child 3–9 years:** Half of a patch every 72 hours
- **Child 10–17 years:** One patch every 72 hours

By SC or IV injection or infusion:
- **Child 1 month–17 years:** 10 micrograms/kg (maximum 600 micrograms) every 4–8 hours or CSCI/IV infusion 40-60 micrograms/kg/24 hours. Maximum suggested dose is 2.4 mg in 24 hours although higher doses are often used by specialist units.

Notes:
- Not licensed for use in children for control of upper airways secretion and hypersalivation.
- Higher doses often used under specialist advice.
- Can cause delirium or sedation (sometimes paradoxical stimulation) with repeated dosing.
- Constipating. May exacerbate acid reflux.
- Apply patch to hairless area of skin behind ear.
- The patch can cause alteration of the pupil size on the side it is placed.
- Transdermal patches contain metal in the backing, and must be removed before MRI scanning to avoid burns.
- Some specialists advise that transdermal patches should not be cut – however, the manufacturers of Scopoderm TTS patch have confirmed that it is safe to do this although outside of the product licence.
- Injection solution may be administered orally.
- Available as: tablets (150 micrograms, 300 micrograms), patches (releasing 1 mg/72 hours), and injection (400 microgram/mL, 600 microgram/mL). An oral solution is available via a 'specials' manufacturer.

Evidence: [1, 2, 30, 89, 222, 223, 243]

**Ibuprofen**
Use:
• Simple analgesic
• Pyrexia
• Adjuvant for musculoskeletal pain.

Dose and routes
By mouth:
• **Neonate:** 5 mg/kg/dose every 12 hours
• **Child 1–2 months:** 5 mg/kg 3–4 times daily preferably after food
• **Child 3–5 months:** 50 mg 3 times daily preferably after food; in severe conditions up to 30mg/kg daily in 3–4 divided doses
• **Child 6 months–11 months:** 50 mg 3–4 times daily preferably after food; in severe conditions up to 30 mg/kg daily in 3–4 divided doses
• **Child 1-3 years:** 100 mg 3 times daily preferably after food. In severe conditions up to 30 mg/kg daily in 3–4 divided doses
• **Child 4–6 years:** 150 mg 3 times daily, preferably after food. In severe conditions, up to 30 mg/kg daily in 3–4 divided doses
• **Child 7–9 years:** 200 mg 3 times daily, preferably after food. In severe conditions, up to 30 mg/kg daily in 3–4 divided doses. Maximum daily dose 2.4 g
• **Child 10–11 years:** 300 mg 3 times daily, preferably after food. In severe conditions, up to 30 mg/kg daily in 3–4 divided doses. Maximum daily dose 2.4 g
• **Child 12-17 years:** 300-400 mg 3-4 times daily preferably after food. In severe conditions the dose may be increased to a maximum of 2.4 g/day

Pain and Inflammation (by mouth using modified release preparation)
• **For Child 12–17 years:** 1.6 g once daily, dose preferably taken in the early evening, increased to 2.4 g daily in 2 divided doses, dose to be increased only in severe cases.

Pain and inflammation in rheumatic diseases, including idiopathic juvenile arthritis:
• **Child aged 3 months–8 years and body weight > 5kg:** 30–40 mg/kg daily in 3–4 divided doses preferably after food. Maximum 2.4 g daily.

In systemic juvenile idiopathic arthritis:
• Up to 60 mg/kg daily in 4–6 divided doses up to a maximum of 2.4 g daily (off-label ).

Notes:
• **Will cause closure of ductus arteriosus; contraindicated in duct dependent congenital heart disease.**
• Orphan drug licence for closure of ductus arteriosus in preterm neonate.
• Not licensed for use in children less than 3 months of age or weight less than 5kg, except for up to two doses for post immunisation pyrexia. (50mg/dose given a minimum of 6 hours apart).
• Topical preparations and granules are not licensed for use in children.
• Ibuprofen combines anti-inflammatory, analgesic, and antipyretic properties. It has fewer side-effects than other NSAIDs but its anti-inflammatory properties are weaker.

• Ibuprofen is a non-opioid analgesic, NSAID and non-selective COX inhibitor.
• Its analgesic effect can be as potent as low dose morphine.
• The risk of cardiovascular events secondary to NSAID use is undetermined in

children. In adults, all NSAID use (including cyclo-oxygenase-2 selective inhibitors) can, to varying degrees, be associated with a small increased risk of thrombotic events (e.g. myocardial infarction and stroke) independent of baseline cardiovascular risk factors or duration of NSAID use; however, the greatest risk may be in those patients receiving high doses long term. A small increased thrombotic risk cannot be excluded in children.

- All NSAIDs are associated with gastro-intestinal toxicity. In adults, evidence on the relative safety of NSAIDs indicates differences in the risks of serious upper gastro-intestinal side-effects—piroxicam and ketorolac are associated with the highest risk; indometacin, diclofenac, and naproxen are associated with intermediate risk, and ibuprofen with the lowest risk (although high doses of ibuprofen have been associated with intermediate risk).
- Caution in asthma and during chemotherapy, and look out for symptoms and signs of gastritis.
- Consider use of a proton pump inhibitor with prolonged use of ibuprofen.
- For administration via an enteral feeding tube, use a liquid preparation; dilute with an equal volume of water immediately prior to administration where possible. No specific information for jejunal administration. Administer as above and monitor for any signs of loss of efficacy or increased side-effects.
- Ibuprofen can be used topically particularly for sprains, strains and arthritis.
- Available as: tablets (200 mg, 400 mg, 600 mg), modified release tablet (800 mg), orodispersible tablets (200 mg), chewable capsules (100 mg), capsules (200 mg, 400 mg ), modified release capsules (200 mg, 300 mg), oral syrup (100 mg/5 mL), granules (600 mg/sachet), and spray, foam (50 mg per 1 g) creams and gels (5%).

Evidence: [1-3, 10, 246-250]

**Ipratropium Bromide**
Use:
- Wheezing/ Breathlessness caused by bronchospasm
- Localised management of sialorrhoea (with less systemic side effects)
- Rhinorrhoea associated with allergic and non-allergic rhinitis

Dose and routes:
Nebulised solution
- **Child 1 month-5 years:** 125-250 micrograms as required maximum 1 mg per day
- **Child 6-11 years:** 250 micrograms as required maximum 1 mg per day
- **Child 12-17 years:** 500 micrograms as required maximum 2 mg per day

Aerosol inhalation
- **Child 1 month-5 years:** 20 micrograms 3 times daily
- **Child 6-11 years:** 20-40 micrograms 3 times daily
- **Child 12-17 years:** 20-40 micrograms 3-4 times daily

Rhinorrhoea associated with allergic and non-allergic rhinitis
By intranasal administration
- **Child 12–17 years:** 2 sprays 2–3 times a day, dose to be sprayed into each nostril.

Notes
- Inhaled product should be used with a suitable spacer device, and the child/carer should be given appropriate training.
- In acute asthma, use via an oxygen driven nebuliser.
- Maximum effects 30-60 minutes after use.
- Duration of action 3-6 hours.
- Bronchodilation can usually be maintained with treatment 3 times a day.
- In severe acute asthma, dose can be repeated every 20-30 minutes in first two hours, then every 4-6 hours as necessary.
- Anti-muscarinic side effects occur with systemic absorption, including constipation, urinary retention, tachycardia, blurred vision.
- Available as: nebuliser solution (250 micrograms in 1 mL, 500 micrograms in 2 mL), aerosol inhaler (20 microgram per metered dose), nasal spray 21 microgram per metered dose.

Evidence: [2, 6, 251, 252] SRE

**Ketamine**

Use:

- Adjuvant to a strong opioid for neuropathic pain.
- Severe visceral pain / visceral hyeralgesia[5].
- Ischaemic pain.
- To reduce N-methyl-D-aspartate (NMDA) receptor wind-up pain and opioid tolerance.
- Emerging use in refractory status epilepticus.
- In neonates: for induction and maintenance of anaesthesia during procedures.
- Psychiatric use for treatment resistant depression in adolescents (secondary effect that this may offer, rather than because we advocate starting drugs for psychiatric diagnoses).

Dose and routes

By mouth or buccal or sublingual:

- **Neonate (>37 weeks CorGA) – Child 11 years:** Starting dose 100 microgram/kg, as required or regularly 6–8 hourly: increasein increments of 100 microgram/kg up to 400 microgram/kg as required. Doses equivalent to 3 mg/kg have been reported in adults
- **Over 12 years and adult:** 5-10 mg as required or regularly 6–8 hourly; increase in steps of 5-10 mg up to 50 mg as required. Doses up to 200 mg 4 times daily reported in adults

By continuous SC or IV infusion:

- **Child 1 month–adult:** Starting dose 20-40 micrograms/kg/hour. Increase according to response; usual maximum 100 micrograms/kg/hour. Doses up to 1.5 mg/kg/hour in children and 2.5 mg/kg/hour in adults have been reported.

By intravenous administrationfor anaesthesia.

- **Neonates:**

  > **Short procedures:** 1–2 mg/kg produces 5–10 minutes of surgical anaesthesia, adjusted according to response.By intravenous injection over at least 60 seconds

  > **Longer procedures:** Initially 0.5–2 mg/kg by intravenous injection, followed by a continuous intravenous infusion of 8micrograms/kg/minute adjusted according to response; up to 30 micrograms/kg/minute may be used to produce deep anaesthesia

Notes:

- NMDA antagonist.
- Specialist use only.
- Not licensed for use in children with neuropathic pain.
- Ketamine is a racemic mixture: The S(+) and R(–) stereoisomers of ketamine bind to the dizocilpine site of the NMDA receptor with different affinities, the former showing approximately 2 to 3 fold greater affinity for the receptor than the latter.
- In many countries s-ketamine is licensed. For s-ketamine usually you divide the ketamine dose by 2.
- Higher doses (bolus injection 1–2 mg/kg, infusions 0.6-2.7 mg/kg/hour) used as an anaesthetic e.g. for short procedures.
- Sublingual doses should be prepared in a maximum volume of 2 mL. The bitter taste may make this route unpalatable. Special preparations for sublingual use are

available in UK.

- Enteral dose equivalents may be as high as 3 times the IV or SC dose because ketamine is potentiated by hepatic first pass metabolism.Some papers quote a 1:1 SC to oral conversion ratio and other1:6 IV to oral conversion.
- Agitation, hallucinations, anxiety, dysphoria, diploplia, nystagmus, vomiting and sleep disturbance are recognised side effects. These may be less common in children and when sub-anaesthetic doses are used.
- Ketamine can cause urinary tract symptoms- frequency, urgency, dysuria and haematuria. Consider discontinuing ketamine if these symptoms occur.
- Caution in severe hepatic impairment, consider dose reduction.
- In view of ketamine's side-effect profile including cognitive impairment and also renal tract damage, long-term use should be avoided if possible.
- Do not stop suddenly as hyperalgesia or allodynia may occur. Withdraw over 2-3 weeks.
- Animal studies indicate that it can induce neuronal cell death in the immature brain. No real preterm outcome data, so only for use in babies over 37weeks CorGA.
- Dilute in 0.9% saline for subcutaneous or intravenous infusion.
- Can be administered as a separate infusion or by adding to opioid infusion/ PCA/ NCA.
- Can also be used intranasally and as a topical gel.
- Intranasal esketamine is licensed in the USA to treat refractory depression.
- Oral solution may be administered via an enteral feeding tube. No specific information on jejunal administration.
- Available as: Injection (10 mg/mL, 50 mg/mL, 100 mg/mL) and oral solution 50 mg in 5 mL (from a 'specials' manufacturer). Injection solution may be given orally. Mix with a flavoured soft drink to mask the bitter taste. Schedule 2 CD.

Evidence: [2, 172, 237, 253-272] WRE, ARE

**Ketorolac**

Use:

- Short-term management of moderate to severe acute postoperative pain; limited evidence of extended use in chronic pain.

Doses and routes:

Short-term management of moderate to severe acute postoperative pain (NB Licensed duration is a maximum of 2 days; not licensed for use in adolescents and children less than 16 years of age).

IV bolus (over at least 15 seconds) or IM bolus:

- **Child 1-15years:** Initially 0.5–1 mg/kg (max. 10mg), then 500 micrograms/kg (max. 15 mg) every 6 hours as required; max. 60 mg daily
- **Child >16 years:** Initially 10mg, then 10–30 mg every 4–6 hours as required (up to every 2 hours during initial postoperative period); max. 90 mg daily (those weighing less than 50 kg max. 60 mg daily).

Chronic pain in palliative care (unlicensed indication; data limited and of poor quality. Anecdotal reports of effectiveness for patients with bone pain unresponsive to oral NSAIDs).

Sublingual

- **Child 4-18 years:** 0.5 mg/kg up to three times a day (usinginjection solution)

SC bolus

- **Child>16 years:** 15-30 mg/dose, three times daily

CSCI

- **Child >16 years:** Initial dose of 60 mg/24 hours. Increase if necessary by 15 mg/24 hours to a maximum of 90 mg/24 hours

Notes:

- Ketorolac is a non-opioid, NSAID and preferential COX-1 inhibitor which has potent analgesic effects with only moderate anti-inflammatory action.
- Licensed only for the short-term management (maximum of 2 days) of moderate to severe acute postoperative pain in adults and adolescents from 16 years of age.
- SC administration is an unlicensed route of administration.
- Contraindications: previous hypersensitivity to ketorolac or other NSAIDs; history of asthma; active peptic ulcer or history of GI bleeding; severe heart, hepatic or renal failure; suspected or confirmed cerebrovascular bleeding or coagulation disorders. Do not use in combination with any other NSAID.
- Dose in adults with mild renal impairment should not exceed 60mg/day.
- All NSAIDs are associated with GI toxicity. In adults, evidence on the relative safety of NSAIDs indicates ketorolac and piroxicam are associated with the highest risk. Use the lowest effective dose for the shortest time. In addition, consider use in combination with a gastro-protective drug especially if ketorolac is used for a prolonged period (outside the licensed indication). Use of ketorolac in adults carries a 15 times increased risk of upper gastrointestinal complications, and a 3 times increased risk compared with other nonselective NSAIDs.
- In adults all NSAID use can, to varying degrees, be associated with a small increased

risk of thrombotic effects. The risk of cardiovascular effects secondary to NSAID use is undetermined in children, but in adults, ketorolac is associated with the highest myocardial infarction risk of all NSAIDs.

- Other potential adverse effects;
  > Very common (>10% patients): headache, dyspepsia, nausea, abdominal pain;
  > Common (1-10% patients): dizziness, tinnitus, oedema, hypertension, anaemia, stomatitis, abnormal renal function, pruritus, purpura, rash, bleeding and pain at injection site. Risk of adverse effects likely to increase with prolonged use.
- Drug interactions include: anticoagulants (contraindicated as the combination may cause an enhanced anticoagulant effect); corticosteroids (increased risk of GI ulceration of bleeding); diuretics (risk of reduced diuretic effect and increase the risk of nephrotoxicity of NSAIDs); other potential nephrotoxic drugs.
- Onset of action 10-30mins when IV/IM; maximal analgesia achieved within 1-2 hours and median duration of effect 4-6 hours.
- Potent NSAID equivalent to twice the strength of naproxen.
- SC injection can be irritant therefore dilute to the largest volume possible (0.9% NaCl suggested). Alkaline in solution so high risk of incompatibility if mixed with acidic drugs. Some data of compatibility in 0.9% sodium chloride with diamorphine or oxycodone. Incompatibilities include with cyclizine, glycopyrronium, haloperidol, levomepromazine, midazolam and morphine.
- Available as: Injection 30 mg/mL (injection contains ethanol as an excipient) and eye drops (5 mg per 1mL) for use in inflammation after eye surgery.
- Oral 10 mg tablets and injection 10 mg/mL no longer available in the UK (discontinued early 2013 due to lack of demand).

Evidence: [1, 237, 273-285]

**Lactulose**
Use:
- Constipation, faecal incontinence related to constipation.
- Hepatic encephalopathy (portal systemic encephalopathy) and coma.

Dose:
Constipation:
By mouth: initial dose twice daily then adjusted to suit patient
- **Neonate:** 2.5 mL/dose twice a day
- **Child 1 month-11 months:** 2.5 mL/dose 1-3 times daily
- **Child 1year-4 years:** 5 mL/dose 1-3 times daily
- **Child 5-9 years:** 10 mL/dose 1-3 times daily
- **Child 10-17 years:** 15 mL/dose 1-3 times daily.

Hepatic encephalopathy:
- **Child 12-17 years:** use 30-50mL three times daily as initial dose. Adjust dose to produce 2-3 soft stools per day.

Notes:
- Licensed for constipation in all age groups. Not licensed for hepatic encephalopathy in children.
- Increases colonic bacterial flora (macrogols do not).
- Side effects may cause nausea and flatus, with colic especially at high doses. Initial flatulence usually settles after a few days.
- Precautions and contraindications; Galactosaemia, intestinal obstruction. Caution in lactose intolerance.
- Use is limited as macrogols are often better in palliative care. However the volume per dose of macrogols is 5-10 times greater than lactulose and may not be tolerated in some patients.
- Lactulose is less effective than macrogols, or sodium picosulfate for opioid induced constipation in ambulatory palliative care patients.
- Sickly taste.
- Onset of action can take 36-48 hours.
- May be taken with water and other drinks.
- May be administered via NG tube or gastrostomy. Dilution with 2-3x the volume of water will reduce the viscosity of the solution and aid administration. As the site of action is the colon, lactulose will have a therapeutic effect if it is delivered directly into the stomach or jejunum. Administer using the above method.
- 15 mL/day is 14 kcal so unlikely to affect diabetic or ketogenic diets.
- Does not irritate or directly interfere with gut mucosa.
- Available as oral solution 10 g/15 mL or 680 mg/1 mL. Cheaper than Movicol (macrogol).

Evidence: [1, 2, 5, 6, 89, 286-290]

**Lansoprazole**

Uses:

- Gastro-oesophageal reflux disease; erosive oesophagitis; prevention and treatment of NSAID induced gastric and oesophageal irritation; treatment of duodenal and gastric ulcer.
- Fat malabsorption despite pancreatic enzyme therapy in cystic fibrosis

Dose and routes:

Oral

- **Child body weight <30 kg:** 0.5-1 mg/kg with maximum 15 mg once daily in the morning
- **Child body weight>30 kg:** 15-30 mg once daily in the morning

Notes:

- Lansoprazole is not licensed in the UK for infants, children or adolescents. Lansoprazole is however licensed in the US for use from 1 year of age. Exact doses limited by available formulations.
- Lansoprazole is a gastric proton pump inhibitor. It inhibits the final stage of gastric acid formation by inhibiting the activity of H+/K+ ATPase of the parietal cells in the stomach. The inhibition is dose dependent and reversible, and the effect applies to both basal and stimulated secretion of gastric acid.
- For optimal effect, the single daily dose is best taken in the morning.
- Lansoprazole should be taken at least 30 minutes before food, as intake with food slows down the absorption and decreases the bioavailability.
- The dose may be increased if symptoms do not fully resolve (consider increasing the single daily dose or BD dosing).
- Studies in infants and children indicate they appear to need a higher mg/kg dose than adults to achieve therapeutic acid suppression.
- Oral bioavailability is good at 80-90% compared to 60% for omeproazole.
- There is some anecdotal experience that Lansoprazole FasTabs may be halved to give a 7.5 mg dose.
- No dose adjustment is needed in patients with renal impairment. Reduction of dose (50%) is recommended in patients with moderate to severe hepatic impairment.
- Hypomagnesaemia may develop with prolonged use.
- Common adverse effects (>1 in 100 to <1 in 10): headache, dizziness; nausea, diarrhoea, stomach pain, constipation, vomiting, flatulence, dry mouth, pharyngitis, increase in liver enzyme levels, urticaria, itching, rash.
- Lansoprazole may interfere with absorption of drugs where gastric pH is critical to its bioavailability (e.g. atazanavir, itraconazole); may cause increase in digoxin levels and increase in plasma concentration of drugs metabolised by CYP3A4 (e.g. theophylline and tacrolimus). Drugs which inhibit or induce CYP2C19 or CYP3A4 may affect the plasma concentration of lansoprazole. Sucralfate and antacids may decrease the bioavailability of lansoprazole.
- PPIs are an independant risk factor for Clostridium Difficile infection.
- MHRA safety warning 2015: there is a very low risk of subacute cutaneous lupus erythematosus associated with use of PPIs.
- Capsules: Capsules should be swallowed whole with liquid. For patients with difficulty swallowing; studies and clinical practice suggest that the capsules may be opened and the granules mixed with a small amount of water, apple/tomato juice or sprinkled onto a small amount of soft food (e.g. yoghurt, apple puree) to ease administration.

- FasTabs: Place on the tongue and gently suck. The FasTab rapidly disperses in the mouth releasing gastro-resistant microgranules which are then swallowed. FasTabs can be swallowed whole with water or mixed with a small amount of water if preferred. FasTabs contain lactose and aspartame and should be used with caution in known PKU patients.
- For administration via a NG or gastrostomy tube, lansoprazole FasTabs can be dispersed in 10 mL water and administered via an 8Fr NG tube without blockage. For smaller bore tubes, dissolve the contents of a lansoprazole capsule in 8.4% sodium bicarbonate before administration. If the tube becomes blocked, use sodium bicarbonate to dissolve any enteric coated granules lodged in the tube. Lansoprazole less likely than omeprazole MUPS to cause blockage of small bore tubes.Lansoprazole is absorbed in the small bowel; therefore, jejunal administration is not expected to reduce bioavailability. Administer as above.
- Available as 15 mg and 30 mg capsules and 15 mg and 30 mg orodispersible tablets.

Evidence: [1, 2, 5, 10, 291-305]

**Levetiracetam**
Use:
• Epileptic seizures

Dose and route:

**Background seizure management**

By mouth.
• **Child 1-5 months:** Initially 7 mg/kg once daily then increase in steps of up to 7 mg/kg twice daily (maximum per dose 21 mg/kg twice daily). Dose to be increased every 2 weeks
• **Child 6 months–17 years (body weight up to 50 kg):** Initially 10 mg/kg once daily, then increase in steps of up to 10 mg/kg twice daily (maximum per dose 30 mg/kg twice daily). Dose to be increased every 2 weeks
• **18 years and over or body weight 50 kg and above:** 250 mg twice daily then increase in steps of 500 mg twice daily (maximum per dose 1.5 g twice daily). Dose to be increased every 2-4 weeks

By intravenous route
• **Body weight up to 50 kg:**10 mg/kg once daily then increase in steps of up to 10mg/kg twice daily (maximum per dose 30mg/kg twice daily). Dose to be increased every 2 weeks
• **Body weight 50 kg and above:** 250 mg twice daily then increase in steps of 500 mg twice daily (maximum per dose 1.5 g twice daily). Dose to be increased every 2-4 weeks

By Continuous Subcutaneous or Intravenous Infusion.
• **Dose conversion for oral:** intravenous:subcutaneous is 1:1:1
• **Take total daily oral or intravenous dose and give as subcutaneous or intravenous infusion over 24hours**

**Management of breakthrough seizures**
Can be used for breakthrough seizure management in prolonged seizures, usually after other first line medications have been tried (e.g. midazolam, paraldehyde).

No need to measure levels
By enteral, subcutaneous or intravenous route
• **Neonate:** 10-20 mg/kg, then top up after 2-12 hours if required, with 10–20mg/kg, aiming not to give more than 40mg/kg/day (including any routine dose in this calculation)
• **Child over 1 month:** 20 mg/kg then top up after 2-12 hours if required, with 10–20 mg/kg, aiming not to give more than 60 mg/kg/day (including any routine dose in this calculation)

Notes:
• Benefits of levetiracetam over phenobarbitone or phenytoin for breakthrough seizure management include fewer side effects and lower volume enteral dose availability.
• Can be combined in syringe driver with midazolam, morphine, hyoscine butylbromide, hydromorphone, methotrimeprazine, metoclopramide,

dexamethasone, haloperidol, glycopyrrolate and clonidine.

- Dilute in 0.9% NaCl. IV doses should be given over at least 15 minutes.
- Dilute to largest volume possible to minimise pain and irritation on administration. Dose for intravenous infusion should be diluted to a suggested concentration of around 15 mg/mL with a compatible diluent and administered as a 15 minute intravenous infusion. For subcutaneous administration need to dilute to a concentration of 15 mg/mL or less as high osmolarity may cause tissue damage. It is therefore preferable to use the intravenous or enteral route.
- Can be given as twice daily bolus subcutaneously subject to volume consideration.
- Available as: Tablets 250 mg, 500 mg, 750 mg and 1 g; Oral solution 100 mg/mL; Solution for Infusion 100 mg/mL.

Evidence: [1, 2, 306-309] NoRE

**Levomepromazine**

Use

- Broad spectrum antiemetic where cause is unclear, or where probably multifactorial.
- Second line if a specific antiemetic fails.
- Antipsychotic and anxiolytic
- Sedation for terminal agitation

Dose and routes

Used as antiemetic

By mouth:

- **Child 2–11 years:** Initial dose 50-100 micrograms/kg given once or twice daily. This dose may be increased as necessary and as tolerated. Not to exceed 1mg/kg/dose (or maximum of 25 mg/dose) given once or twice daily
- **Child 12-17 years:** Initial dose 3 mg once or twice daily. This dose may be increased as necessary and as tolerated to a maximum of 25 mg once or twice daily.

By continuous IV or SC infusion over 24hours:

- **Child 1 month–11 years:** Initial dose of 100micrograms/kg/24 hours increasing as necessary to a maximum of 400micrograms/kg/24 hours.Maximum 25mg/24 hours
- **Child 12–17 years:** Initial dose of 5 mg/24 hours increasing as necessary to a maximum of 25 mg/24 hours

By SC or IV injection:

- **Child 12–17 years:** Initial as required dose 2.5 mg given once or twice daily.

Used for sedation and confusion

By continuous subcutaneous or intravenous infusion over 24hours:

- **Child 1 year–11 years:** Initial dose of 350 micrograms/kg/24 hours (maximum initial dose 12.5 mg), increasing as necessary up to 3 mg/kg/24 hours
- **Child 12–17 years:** Initial dose of 12.5mg/24 hours increasing as necessary up to 200 mg/24 hours.

By SC or IV injection:

**Child 12–17 years:** Initial dose of

Child <35 kg as required dose 2.5 mg given once or twice daily.

Child >35 kg as required dose 5 mg given once or twice daily.

Notes:

- Licensed for use in children with terminal illness for the relief of pain and accompanying anxiety and distress.
- A low dose is often effective as antiemetic. Titrate up as necessary. Higher doses are very sedative and this may limit dose increases.
- If the child is not stable on high dosage for nausea and vomiting, reconsider cause and combine with other agents e.g. dexamethasone.
- Some experience in adults withbuccal use at low dose as antiemetic (e.g. 1.5 mg three times daily as needed).
- Can cause hypotension, particularly with higher doses. Somnolence and asthenia are frequent side effects.
- Levomepromazine and its non-hydroxylated metabolites are reported to be potent inhibitors of cytochrome P450 2D6. Co-administration of levomepromazine and

drugs primarily metabolised by the cytochrome P450 2D6 enzyme system may result in increased plasma concentrations of these drugs.

- May lower seizure threshold.
- Avoid, or use with caution, in patients with liver dysfunction or cardiac disease. Start at low dose in patients with severe renal impairment and give once daily, titrating according to response.
- Tablets may be halved or quartered to obtain smaller doses. Tablets/segments may be dispersed in water for administration via a NG or gastrostomy tube. Flush tube well after administration.There is no specific information relating to jejunal administration of levomepromazine. Administer using the above method. Monitor for loss of efficacy or increased side-effects.
- For SC infusion dilute with sodium chloride 0.9%. Water for injection may also be used. The SC dose is considered to be twice as potent as that administered orally.
- Available as: tablets (25 mg) and injection (25 mg/mL). A 6 mg tablet is also available via specialist importation companies. An extemporaneous oral solution may be prepared.

Evidence: [1, 2, 5, 10, 310-313] CC, EA

**Lidocaine (Lignocaine) patch**
Use
- Localised neuropathic pain

Dose and routes
Topical:
- **Child 3–17 years:** Apply 1-2 plasters to affected area(s). Apply plaster once daily for 12 hours followed by 12 hours plaster free period (to help reduce risk of skin reactions)
- **Adult 18 years or above:** Up to 3 plasters to affected area(s). Apply plaster once daily for 12 hours followed by 12 hours plaster free period (to help reduce the risk of skin reactions).

Notes:
- Not licensed for use in children or adolescents under 18 years.
- The lidocaine in the plaster diffuses continuously into the skin, providing a local analgesic effect. The mechanism by which this occurs is through stabilisation of neuronal membranes, thought to cause down-regulation of sodium channels resulting in pain reduction.
- Cut plaster to size and shape of painful area. Do NOT use on broken or damaged skin or near the eyes.
- When lidocaine 5% medicated plaster is used according to the maximum recommended dose (3 plasters applied simultaneously for 12 hours) about 3± 2% of the total applied lidocaine dose is systemically available and is similar for single and multiple administrations.
- Maximum recommended number of patches in adults currently is 3 per application.
- The plaster contains propylene glycol which may cause skin irritation. It also contains methyl parahydroxybenzoate and propyl parahydroxybenzoate which may cause allergic reactions (possibly delayed). Approximately 16% of patients can be expected to experience adverse reactions. These are localised reactions due to the nature of the medicinal product.
- The plaster should be used with caution in patients with severe cardiac impairment, severe renal impairment or severe hepatic impairment.
- An adequate treatment period is a minimum of 4 weeks in duration. Consider discontinuation if no response.
- For long-term use, treatment should be reviewed regularly to assess whether the number of plasters required can be reduced or the plaster-free period extended.
- The plasters must be used within 14 days of opening the sachets.
- A recent analysis by anatomic site of patch placement suggests that application to the head was tolerated less well compared with the trunk and extremities.
- Doses extrapolated from BNF on line Aug 2019.
- Available as 700 mg/medicated plaster (5% w/v lidocaine).

Evidence: [1, 5, 314-321] NoRE, ARE

**Lomotil® (co-phenotrope)**

Use:
- Diarrhoea from non-infectious cause.
- Control of faecal consistency after colostomy or ileostomy.

Dose and routes
Tablets: diphenoxylate hydrochloride 2.5mg, atropine 25micrograms

By mouth:
- **Child 2–3 years:** Half tablet 3 times daily
- **Child 4–8 years:** 1 tablet 3 times daily
- **Child 9–11 years:** 1 tablet 4 times daily
- **Child 12–15 years:** 2 tablets 3 times daily
- **Child 16–17 years:** Initially 4 tablets then 2 tablets 4 times daily.

Notes:
- A mixture of diphenoxylate hydrochloride and atropine sulfate in proportions of 100:1.
- Not licensed for use in children < 4 years.
- Tablets may be crushed. For administration via a NG tube or gastrostomy, tablets may be crushed and dispersed in water immediately before use. There is no specific information on jejunal administration – suggest administered as above.
- Young children are particularly susceptible to overdosage, which is primarily an opioid intoxication (central nervous system and respiratory depression with miosis), occasionally associated with atropine toxicity (central nervous system excitement, hypertension, fever, flushed dry skin). Atropine effects occur before, during, or after opioid effects. Symptoms may be delayed and observation is needed for at least 48 hours after ingestion. Overdose can be difficult to manage with a mixed picture of opioid and atropine poisoning. Furthermore, the presence of subclinical doses of atropine may give rise to atropine side-effects in susceptible individuals.
- Available only as tablets Co-Phenotrope (2.5 mg diphenoxylate hydrochloride and
- 25 micrograms atropine sulphate).

Evidence: [1, 2, 322-325]

**Loperamide**
Use:
- Diarrhoea from non-infectious cause
- Faecal incontinence
- Management of high ileostomy output

Dose and routes for management of chronic diarrhoea
By mouth:
- **Child 1–11 months:** Initial dose of 100 micrograms/kg twice daily given 30 minutes before feeds. Increase as necessary up to a maximum of 2 mg/kg/day given in divided doses
- **Child 1–11years:** Initial dose of 100 micrograms/kg (maximum single dose 2 mg) 3-4 times daily. Increase as necessary up to a maximum of 1.25 mg/kg/day given in divided doses (maximum 16 mg/day)
- **Child 12–17years:** Initial dose of 2 mg 2-4 times daily. Increase as necessary up to a maximum of 16 mg/day given in divided doses.

Notes:
- Not licensed for use in children with chronic diarrhoea.
- Capsules not licensed for use in children < 8 years.
- Syrup not licensed for use in children < 4 years.
- Common side effects: constipation, nausea, flatulence.
- As an antidiarrhoeal, loperamide is about 50x more potent than codeine. It is longer acting; maximum therapeutic impact may not be seen for 16-24 hours.
- For NG or gastrostomy administration: Use the liquid preparation undiluted. Flush well after dosing. Alternatively, the tablets can be used without risk of blockage, although efficacy is unknown. Jejunal administration will not affect the therapeutic response to loperamide. However, owing to the potential osmotic effect of the liquid preparation, it may be appropriate to further dilute the dose with water immediately prior to administration.
- Available as tablets (2 mg), capsules (2 mg), orodispersible tablets (2 mg) and oral syrup (1 mg/5 mL).

Evidence: [1, 2, 10, 326-328]

**Lorazepam**
Use
- Background anxiety.
- Agitation and distress.
- Adjuvant in cerebral irritation.
- Background management of dyspnoea.
- Muscle spasm.
- Status epilepticus.

Dose and routes for all indications except status epilepticus:
By mouth:
- **Child < 2 years:** 25 micrograms/kg 2–3 times daily
- **Child 2–5 years:** 500 micrograms 2–3 times daily
- **Child 6–10 years:** 750 micrograms 3 times daily
- **Child 11–14 years:** 1 mg 3 times daily
- **Child 15–18 years:** 1–2 mg 3 times daily.

Sublingual:
- **Children of all ages:** 25 micrograms/kg as a single dose. Increase to 50 micrograms/kg (maximum 1 mg/dose) if necessary
- **Usual adult dose:** 500 micrograms–1mg as a single dose, repeat as required.

For status epilepticus
By Slow IV injection:
- **Neonate:** 100 micrograms/kg for a single dose then 100microgram/kg after 10 minutes if required
- **Child 1 month–11 years:** As above with a maximum single dose of 4mg
- **Child 12-17years:** 4 mg for a single dose then a further 4 mg after 10 minutes if required.

Notes
- Not licensed for use in children for these indications other than status epilepticus.
- Tablets licensed in children over 5 years for premedication, injection not licensed in children less than 12 years except for treatment of status epilepticus.
- Potency in the order of 10 times that of diazepam per mg as anxiolytic/sedative.
- Well absorbed sublingually with rapid onset of effect. There may however be variable absorption by this route with further variation possible depending on the formulation used.
- Specific sublingual tablets are not available in the UK but generic lorazepam tablets (specifically Genus, PVL or TEVA brands) do dissolve in the mouth so can be given sublingually.
- Tablets may be dispersed in water for administration via an enteral feeding tube. There is no specific information on jejunal administration. Monitor for increased side-effects or loss of efficacy.
- May cause drowsiness and respiratory depression if given in large doses.
- Caution in renal and hepatic failure.
- Available as tablets (1 mg, 2.5 mg) and injection (2 mg/mL and 4 mg/mL).

Evidence: [2, 5, 10, 225, 329] NoRE, ARE

**Macrogols**
Use
- Constipation.
- Faecal impaction.
- Suitable for opioid-induced constipation.

Dose and routes paediatric sachets for those less than 12 years of age);

By mouth for constipation or prevention of faecal impaction:
- **Child under 1 year:** ½-1 paediatric sachet daily
- **Child 1–5 years:** 1 paediatric sachet daily (adjust dose according to response; maximum 4 sachets daily)
- **Child 6–11 years:** 2 paediatric sachets daily (adjust dose according to response; maximum 4 sachets daily)
- **Child 12–17 years:** 1–3 adultsachets daily.

By mouth for faecal impaction:
- **Child under 1 year:** ½-1 paediatric sachet daily
- **Child 1–4 years:** 2 paediatric sachets on first day and increase by 2 sachets every 2 days (maximum 8 sachets daily). Treat until impaction resolved then switch to maintenance laxative therapy
- **Child 5–11 years:** 4 paediatric sachets on first day and increase by 2 sachets every 2 days (maximum 12 sachets daily). Treat until impaction resolved then switch to maintenance laxative therapy
- **Child 12–17 years:** 4 sachets daily of adult preparation, then increase by 2 sachets daily to a maximum of 8 adult sachets daily. Total daily dose should be drunk within a 6 hour period. After disimpaction switch to maintenance laxative therapy.

Notes
- Not licensed for use in children < 5 years with faecal impaction and < 2 years with chronic constipation.
- Need to maintain hydration. Caution if fluid or electrolyte disturbance.
- Caution with high doses (volumes) in those with impaired gag reflex, reflux oesophagitis or impaired consciousness.
- Do not use adult sachets in children. Risk of electrolyte imbalance.
- Mix powder with water: follow manufacturers' instructions.
- For administration via a feeding tube: dissolve the powder (or liquid concentrate) in water as directed and flush down the feeding tube. Flush well after dosing. As the mechanism of action is local within the bowel, jejunal administration should not affect efficacy. Administer as above.
- Macrogol oral powder is available as Movicol and Movicol Paediatric Sachets, CosmoColand CosmoCol Paediatric Sachets, Laxido and Laxido Paediatric Sachets, Macilax and Macilax Paediatric Sachets. Movicol is also available as a liquid concentrate (dilute with water before administration).

Evidence: [1, 2, 10, 287, 330, 331]

**Melatonin**

Use:

- Sleep disturbance due to disruption of circadian rhythm (not anxiolytic).

Dose and routes

By mouth:

- **Child 1 month-17 years:** Initial dose 2–3 mg, increasing every 1–2 weeks dependent on effectiveness up to maximum 10mg daily.

Notes:

- 1 mg and 5 mg m/r tablets (Slenyto®) licensed in children for insomnia with ASD and Smith-Magenis syndrome. All other formulations of melatonin are not licensed for use in children or are unlicensed 'special' formulations.
- Specialist use only.
- Reduced clearance in hepatic impairment.
- Some prescribers use a combination of immediate release and m/r tablets to optimise sleep patterns.
- Immediate release capsules may be opened and the contents sprinkled on cold food if preferred. If available, sustained release capsules may also be opened but the contents should not be chewed. If administration via an enteral feeding tube is required, use of an unlicensed liquid special is preferred.
- Licensed UK formulations: 1 mg and 5 mg m/r tablets (Slenyto®) and 2 mg m/r tablets (Circadin®) and 1 mg/mL oral solution (Colonis®)). Various unlicensed formulations, including immediate release capsules and oral liquid may be available from 'specials' manufacturers or specialist importing companies.

Evidence: [1, 2, 332-349] NoRE

**Methadone**
**(WARNING: requires specialist advice)**
Use:
- Major opioid used for moderate to severe pain, particularly neuropathic pain and pain poorly responsive to other opioids.
- Not normally used as first line analgesia in the UK.

**Caution:**
**Methadone should only be commenced by practitioners experienced in its use.**
This is due to wide inter-individual variation in response, very variable conversion ratios with other opioids, complex pharmacokinetics and a long half life.
Initial close monitoring is particularly important.

Dose and routes

**In opioid naïve children**
By mouth:
- **Child 1-12 years:** 30-100 micrograms/kg (maximum 5mg/dose initially) 1-3 times daily
- **Child >12 years:**100-200 micrograms/kg every 8-12 hours (maximum 5 mg/dose initially)
- Methadone has a long and variable half-life with potential to cause sedation, respiratory depression and even death from secondary peak phenomenon.
- Titration of methadone dosing must be done under close clinical observation of the patient particularly in the first few days. Due to large volume of distribution, higher doses may berequired for the first few days whilst body tissues become saturated. Once saturation is complete, a smaller dose may be sufficient. To prevent adverse effects, increments in enteral dosing should be very cautious and usually by no more than 25% approximately at weekly intervals with a maximum increase of 50% (experienced practitioners may increase more frequently).
- Continued clinical reassessment is required to avoid toxicity as the time to reach steady state concentration following a change in dosing may be up to 12 days.

- For breakthrough pain, we would recommend using a short half-life opioid.

**In opioid substitution/ rotation or switch**
Caution:

Substitution, rotation or switch to methadone is a specialist skill and should only be undertaken in close collaboration with practitioners experienced in its use. There is a risk of unexpected death through overdose.

- It can be difficult to convert a short or long acting opioid to an equivalent dose of methadone. Current practice is usually to admit to a specialist inpatient unit for 5-6 days or titrate orally at home with very close supervision.
- Other opioids should be considered first, if switching from morphine due to unacceptable effects or inadequate analgesia.

**Consultation with a pain clinic or specialist palliativecare service is advised**

**Equianalgesic doses:**

Dose conversion ratios from other opioids are not static but are a function of previous opioid exposure, and are highly variable.

Published tables of equianalgesic doses of opioids, established in healthy non-opioid tolerant individuals, indicate that methadone is 1–2 times as potent as morphine in single dose studies, but in individuals on long-term (and high dose) morphine, methadone is closer to 10 times as potent as morphine; it can be 30 times more potent or occasionally even more. The potency ratio tends to increase as the dose of morphine increases.

Ref [4]

In adults there are several protocols for opioid rotation to methadone which are not evidence based in paediatrics.

- One approach incorporates a transition period where the dose of the former opioid is reduced and partially replaced by methadone which is then titrated upwards [350]. This approach is considered safer.
- In another approach, previous opioid therapy is completely stopped before starting a fixed dose of methadone at variable dose intervals [351]. This approach carries more risks.

**<u>To switch smoothly to methadone</u>**

Day1: 30% reduction of former opioid and substitute with oral methadone divided in 3 doses

Conversion rate: (Morphine in mg: Methadone in mg)
OME 30-90 mg/day = 4:1[352]
OME 90-300 mg/day = 6:1[352]
OME 301-600 mg/day = 8:1[352]
OME 601-800 mg/day = 12:1 [353]
OME 801-1000 mg/day = 15:1[353]

That means; if the OME dose is 900 mg/day; 1/3 is 300 mg/day and the equianalgesic methadone dose is 20 mg, add to the remaining 600 mg OME the 3 x 6.5 mg methadone

Next day reduce according to result of first reduction; i.e. by further 300 mg OME

After 3-5 days you should have completed the opioid switch to methadone. Methadone is 2.5 to 15 times more potent than morphine.

**To make a complete switch to methadone**

1. Calculate the total oral morphine requirement (or oral morphine equivalent (OME), if using a different opioid) over the previous 48 hours and calculate the average 24 hour requirement. Do not include breakthrough doses for incident pain. When calculating OME always use the lowest conversion dose.
2. Reduce the total oral daily dose OME by 30-50% to account for incomplete cross tolerance.
3. Convert the final calculated oral morphine daily dose to oral methadone daily dose by dividing by 15 (most guides say 10 so this is a cautious approach).
4. Divide this into three daily doses. (As a rule, the initial dose should not usually exceed 10 mg 3x per day in an adult/patient over 50 kg, 5 mg 3x per day in child/ patient under 50 kg). Initially give either 2 or 3 doses/24 hours.
5. If converting from a long acting opioid, give the first methadone dose 6 hours after the last long acting opioid dose or 10- 12 hours after opioid patch removal. Consider using an alternative short acting opioid (such as Oramorph) for breakthrough pain management and consider reduction of the previous breakthrough dose to 50%.

**Monitor closely for at least the first 72 hours and be cautious with any dose increments during this period.** Generally, dose increments should not exceed 20% of previous dose.

If excess sedation occursreduce dose by 25-50% or omit dose. Sudden good analgesia can also indicate overdose and should trigger consideration of dose reduction or omission.

**Converting oral methadone to SC/IV or CSCI/CIVI methadone**

- Approximate dose ratios for switching between oral dosage and parenteral intravenous/ subcutaneous form 2:1 (oral:parenteral).
- Calculate the total daily dose of oral methadone and halve it (50%). This will be the 24hour parenteral/subcutaneous methadone dose.
- Seek specialist guidance if mixing with any other drug.
- If CSCI methadone causes a skin reaction, consider doubling the dilution and changing the syringe every 12 hours.
- Administer IV methadone slowly over 3-5 minutes.

Notes:
- Not licensed for use in children.
- Methadone is a racemic mixture: L-isomer, analgesic active (levomethadone; L-polamidon®); R-isomerunknown action.
- In some countries levomethadone is available. It has a different strength to methadone.
- Data on methadone in paediatric patients is limited; known to have wide inter-individual pharmacokinetic variation.
- Use methadone with caution, as methadone's effect on respiration lasts longer than analgesic effects.
- Side effects are the same as for all strong opioids.
- Following concerns regarding methadone and sudden death from prolongation of QT interval or torsade de pointes (especially at high doses) it is recommended that patients have an ECG prior to initiation of treatment and regularly whilst on methadone, particularly if they have any risk factors or are having intravenous treatmentwith methadone.
- Opioid antagonists naloxone and naltrexone will precipitate an acute withdrawal

syndrome in methadone dependent individuals. Naloxone will also antagonise the analgesic, CNS and respiratory depressant effects of methadone.

- Methadone has the potential for a number of significant drug interactions. Drugs that induce cytochrome P450 3A4 enzymes (e.g. carbamazepine, phenobarbital, phenytoin, rifampicin and some HIV drugs) will increase the rate of metabolism of methadone and potentially lead to reduced serum levels. Drugs that inhibit the system (e.g. amitriptyline, ciprofloxacin, fluconazole) may lead to increased serum levels of methadone.
- Renal impairment: if severe (i.e.GFR <10 ml/min or serum creatinine >700 mmol/l) –reduce methadone dose by 50% and titrate according to response. Significant accumulation is not likely in renal failure, as elimination is primarily via the liver.
- As methadone has a long half-life, infusion of naloxone may be required to treat opioid overdose.
- Available as: linctus (2 mg/5 mL), mixture (1 mg/mL), oral solution (1 mg/mL, 5 mg/mL, 10 mg/mL, and 20 mg/mL), tablets (5 mg), and injection (10 mg/mL, 50 mg/mL, 50 mg/2 mL).
- Schedule 2 CD.

Evidence: [1, 2, 4, 5, 11, 48, 89, 354-369]

**Methylnaltrexone**
Use:
- Opioid-induced constipation when the response to other laxatives alone is inadequate and other relevant factors have been / are being addressed.

Dose and routes
SC (usual route) or IV bolus:
- **Child 1month– 12 years:** 0.15 mg/kg (maximum 8 mg) as a single dose
- **Child >12 years:** with weight 38-61 kg: 8 mg as a single dose
- **Child >12 years:** with weight 62-114 kg: 12 mg as a single dose
- **Child >12 years:** but with body weight less than 38 kg, use 0.15 mg/kg.

A single dose may be sufficient. However repeat doses may be given with a usual administration schedule of a single dose every other day. Doses may be given with longer intervals, as per clinical need. Patients may receive 2 consecutive doses (24 hours apart) only when there has been no response (no bowel movement) to the dose on the preceding day. (30 50% of patients given methylnaltrexone have a bowel movement within 4 hours, without loss of analgesia).

Notes:
- μ-opioid receptor antagonist that acts exclusively in the peripheral tissues including the GI tract (increasing bowel movement and gastric emptying) and does not affect the central analgesic effects of opioids.
- Not licensed for use in children or adolescents less than 18 years.
- Not licensed for IV administration – usual route is SC.
- Methylnaltrexone is contraindicated in cases of known or suspected bowel obstruction other than that caused by opiate-induced constipation.
- The onset of effect may be within 15-60 minutes.
- Common side-effects include abdominal pain/colic, diarrhoea, flatulence and nausea.
- If administered by SC injection rotate the site of injection. Do not inject into areas where the skin is tender, bruised, red or hard.
- Constipation in palliative care is usually multifactorial and other laxatives are often required in addition.
- Reduce dose by 50% in severe renal impairment.
- Does not cross blood brain barrier.
- Available as single use vial 12 mg/0.6 ml solution for SC injection (Relistor(R))

Evidence: [1, 206, 370-375]

**Metoclopramide**
To minimise the risk of neurological side effects associated with metoclopramide, the EMA in 2013 issued the following recommendations:**(NB use of metoclopramide in palliative care was excluded from these recommendations HOWEVER caution should be exercised nevertheless).**

Use of metoclopramide is contraindicated in children younger than 1 year.

In children aged 1-18 years, metoclopramide should only be used as a second-line option for prevention of delayed chemotherapy-induced nausea and vomiting, and for treatment of established postoperative nausea and vomiting, and only when other treatments do not work or cannot be used.

Metoclopramide should only be prescribed for short term use (up to 5 days).

Use
- Antiemetic if vomiting caused by gastric compression or hepatic disease.
- Prokinetic for slow transit time (not in complete obstruction or with anticholinergics).
- Hiccups.

Dose and routes
By mouth, IM injection, SC injection or IV injection (over at least 3 minutes):
- **Neonate:** 100 microgram/kg every 6–8hours (by mouth or IV only).
- **Child 1 month–11 months and body weight up to 10 kg:** 100 microgram/kg (maximum 1 mg/dose) twice daily.
- **Child 1–18 years:** 100-150 microgram/kg repeated up to 3 times daily. The maximum dose in 24 hours is 500 microgram/kg (maximum 10 mg/dose; 30 mg per day).

If preferred the appropriate total daily dose may be administered as a continuous SC or IV infusion over 24 hours.

Notes:
- Not licensed for use in infants less than 1 year of age.Tablets not licensed for use in <15 years (<61 kg).
- Not licensed for continuous IV or SC infusion.
- Metoclopramide can induce acute dystonic reactions such as facial and skeletal muscle spasms and oculogyric crises; children (especially girls, young women, and those under 10 kg) are particularly susceptible. With metoclopramide, dystonic effects usually occur shortly after starting treatment and subside within 24 hours of stopping it.
- Intravenous doses should be administered as a slow bolus over at least 3 minutes to reduce the risk of adverse effects.
- Oral liquid formulations should be given via a graduated oral syringe to ensure dose accuracy in children. The oral liquid may be administered via an enteral feeding tube.There is no specific information on jejunal administration. Administer using the above method and monitor for efficacy.
- Available as: tablets (10 mg), oral solution (5 mg/5 mL) and injection (5 mg/mL).

Evidence: [1-3, 10, 89, 91, 93, 96, 153, 155, 376-380]

**Metronidazole topically**
Use:
• Odour caused by anaerobic bacteria associated with wounds or lesions.

Dose and routes
By topical application:
• Apply to clean wound 1–2 times daily and cover with non-adherent dressing.
• Cavities: smear gel on paraffin gauze and pack loosely.

Notes:
• Off label use.
• Anabact® not licensed for use in children < 12 years.
• Metrogel® not licensed for use with children.
• Available as: cream and gel (Anabact® 0.75%, Metrogel® 0.75%) or liquid.

Evidence: [1, 2, 381, 382]

**Miconazole oral gel**
Use:
• Oral and intestinal fungal infection.

Dose and routes
By mouth:
Prevention and treatment of oral candidiasis
• **Neonate:** 1mL 2-4 times a day smeared around inside of mouth after feeds.
• **Child 1 month–1 year:** 1.25 mL 4 times daily smeared around inside of mouth after food.
• **Child 2–17 years:** 2.5 mL 4 times daily after meals; retain near lesions before swallowing (orthodontic appliances should be removed at night and brushed with gel).

Prevention and treatment of intestinal candidiasis
• **Child 4 months – 17 years:** 5 mg/kg 4 times daily; max. 250 mg (~10 mL) 4 times daily.

Notes:
• Use after food and retain near lesions before swallowing.
• Treatment should be continued for 7 days after lesions have healed.
• Not licensed for use in children under 4 months or during the first 5-6 months of life of an infant born preterm.
• Infants and babies: The gel should not be applied to the back of the throat due to possible choking. The gel should not be swallowed immediately, but kept in the mouth as long as possible.
• Contraindicated in infants with impaired swallow.
• Available as: oral gel (20 mg per gram or 124 mg per 5 mL~ 24 mg/mL) in 15 g and 80g tube.
• A buccal tablet of miconazole is now available. Indicated for the treatment of oropharyngeal candidiasis in immunocompromised adults, Loramyc(R) 50 mg muco-adhesive buccal tablets should be applied to the upper gum just above the incisor tooth once daily for 7-14 days. Currently no experience in children, but licensed in USA for child >16 years. May be an option for adolescents.
• Note increased INR/ bleeding has been reported with concomitant use of buccal miconazole and oral anticoagulants.

Evidence: [2, 383-385]

**Midazolam**
Use:
- Status epilepticus and terminal seizure control.
- Management of anxiety/agitation associated with symptoms at the end of life.
- Anxiety associated with dyspnoea.
- Adjuvant for pain of cerebral irritation.

Dose and routes
**Drug doses are quite different depending on underlying disease (i.e. children with cancer or organ failure) and children with severe neurological impairment (SNI). Use lower doses for children with cancer or organ failure and higher doses for children with SNI.**

By SC or IV infusion over 24 hours for seizure control at end of life:
- **Neonate - Child 18 years:** Initial dose 1-3 mg/kg/24 hours increasing up to 7 mg/kg/24 hours (maximum 60 mg/24 hoursor 150 mg/24 hours in specialist units for patients with refractory epilepsy).

Seek specialist advice, and consider addition of other agents such as phenobarbital if midazolam is not effective.

Buccal or Intranasal doses for status epilepticus:
- **Neonate:** 300microgram/kg as a single dose, repeated once if necessary.
- **Child 1–2 months:** 300microgram/kg (maximum initial dose 2.5mg), repeated once if necessary.
- **Child 3 months–11 months:** 2.5mg, repeated once if necessary.
- **Child 1–4 years:** 5mg, repeated once if necessary.
- **Child 5–9 years:** 7.5mg, repeated once if necessary.
- **Child 10–17 years:** 10mg, repeated once if necessary.

By buccal or intranasal administration for status epilepticus, wait 10minutes before repeating dose.
NB -In single dose for seizures, midazolam is twice as potent as rectal diazepam. For patients who usually receive rectal diazepam for management of status, consider an initial dose of buccal midazolam that is 50% of their usual rectal diazepam dose to minimise the risk of respiratory depression

Conscious sedation (to be administered 30-60 minutes before a procedure; or to be administered for terminal haemorrhage in conjunction with an opiate):
By oral administration
- **Child:** 500 micrograms/kg (maximum 20 mg) as a single dose

By buccal or intranasal administration
- **Child 6 months-9years:** 200-300micrograms/kg (maximum 5 mg) as a single dose
- **Child 10-17years:** 6-7 mg as a single dose

By rectum
- **Child 6 months–11 years:** 300–500 micrograms/kg(maximum 20 mg) as a single dose

By intravenous or subcutaneous injection

**The dosages below are based on the BNFc [2]. However research**

**evidence and adult formularies [5] suggests that buccal/intranasal and subcutaneous injections have very similar bioavailability. Many units therefore will use doses of 100 micrograms/kg.**

- **Child 1 month–5 years:** Initially 25–50 micrograms/kg, to be administered over 2–3 minutes, 5–10 minutes before procedure, dose can be increased if necessary in small steps to maximum total dose per course; maximum 6 mg per course.
- **Child 6–11 years:** Initially 25–50 micrograms/kg, to be administered over 2–3 minutes, 5–10 minutes before procedure, dose can be increased if necessary in small steps to maximum total dose per course; maximum 7.5 mg per course.
- **Child 12–17 years:** Initially 25–50 micrograms/kg, to be administered over 2–3 minutes, 5–10 minutes before procedure, dose can be increased if necessary in small steps to maximum total dose per course; maximum 10 mg per course.

For anxiety/ agitation/ dyspnoea:
Use 25-50% of the conscious sedation dose.

Notes

- Buccal (Buccolam oromucosal solution) midazolam is not licensed for use in infants less than 3 months of age. Midazolam injection is not licensed for use in seizure control or anxiety.Not licensed for use in children less than 6 months for premedication and conscious sedation.
- The range of potential indications for midazolam in paediatric palliative care is very wide, but most are not licensed in infants in children. Please see product literature.
- Recommended SC/IV doses vary enormously in the literature. If in doubt, start at the lowest recommended dose and titrate rapidly.
- Onset of action by buccal and intranasal route 5-15 minutes. Time to peak concentration 30 mins.Half life 2-5 hours. For buccal administration, if possible, divide the dose so half is given into one cheek and the remaining half into the other cheek.
- Onset of action by oral or gastrostomy route 10-30 minutes. If enteral tube administration is indicated, the oral liquid or injection can be used.
- Onset of action by IV route 2-3 minutes; SC route 5-10 minutes.
- Both high and low doses can lead to paradoxical agitation.
- Caution in known hypersensitivity; renal failure; hepatic or cardiac impairment; neuromuscular respiratory weakness; pulmonary insufficiency.
- Important drug interactions:Midazolam is a major substrate of CYP3A4. Please refer to current edition of BNF for significant drug interactions. Fatalities have occurred after concurrent administration with higher than approved doses of olanzapine
- Available as: oral solution (2 mg/mL special import USA, unlicensed), buccal liquid (pre-filled oral syringes 10 mg in 2 mls; 7.5 mg in 1.5 mls; 5 mg in 1 mL; 2.5 mg in 0.5 mlsBuccolam(R)), and injection 1mg/mL, 2mg/mL, 5mg/mL). Other oral and buccal liquids (e.g.Epistatus(R) 10 mg/ml) are also available from 'specials' manufacturers or specialist importing companies (unlicensed).
- The buccal and oral formulations available may differ in strength – take care with prescribing.

Schedule 3 CD (CD No Register Exempt Safe Custody)

Evidence: [2, 6, 145, 147, 149, 385-392]

**Morphine**
Use:
- Major opioid.
- First line opioid for pain.
- Dyspnoea.
- Cough suppressant

Dose and routes:
Opioid naive patient: Use the following starting doses. (The maximum dose stated applies to starting dose only).
Opioid conversion: Convert using OME (Oral Morphine Equivalent) from previous opioid.

By mouth or by rectum
- **Neonate:** Initially 25-50 micrograms/kg every 6-8 hours adjusted to response
- **Child 1–2 months:** Iinitially 50 micrograms/kg every 4 hours, adjusted according to response
- **Child 3–5 months:** Initially 50-100micrograms/kg every 4 hours, adjusted according to response
- **Child 6–11 months:** Initially 100-200 micrograms/kg every 4 hours, adjusted according to response
- **Child 1–11 years:** Iinitially 200–300 micrograms/kg (initial maximum 5-10 mg) every 4 hours, adjusted according to response
- **Child 12–17 years:** Iinitially 5–10 mg every 4 hours, adjusted according to response

By single SC injection or IV injection (over at least 5 minutes):
- **Neonate:** Initially 25 micrograms/kg every 6-8 hours adjusted according to response.
- **Child 1-5months:** Initially 50-100micrograms/kg every 6 hours adjustedaccording to response.
- **Child 6 months-1 years:** Initially 50-100micrograms/kg every 4 hours adjusted according to response.
- **Child 2-11 years:** Initially 100 micrograms/kg every 4 hours adjusted according to response, maximum initial dose of 2.5 mg.
- **Child 12-17 years:** Initially 2.5-5 mg every 4 hours adjusted according to response(maximum initial dose of 20 mg/24 hours).

By continuous SC or IV infusion:
- **Neonate:** 120 micrograms/kg/24hours adjusted according to response,
- **Child 1-2 months:** 240 micrograms/kg/24hours adjusted according to response,
- **Child 3 months–17 years:** 480 micrograms/kg/24hours (maximum initial dose of 20 mg/24 hours)adjusted according to response.

Breakthrough pain
- For breakthrough pain use 10-16% of total daily morphine dose every 1-4 hours as needed.
- Contact the medical palliative team if someone has needed three doses consecutively as they will need a review of their pain control.

Dyspnoea
30-50% of the dose used for pain.

Notes:
- Oramorph® solution not licensed for use in children under 1 year; Oramorph® unit dose vials not licensed for use in children under 6 years; Sevredol® tablets not licensed for use in children under 3 years; Filnarine® SR tablets not licensed for use in children under 6 years; MST Continus® preparations licensed to treat children with cancer pain (age-range not specified by manufacturer); MXL® capsules not licensed for use in children under 1 year; suppositories not licensed for use in children.
- Caution in renal or hepatic impairment.Reduce dose and/or interval frequency.
- Where opioid substitution or rotation is to morphine: use oral morphine equivalency (OME).
- Particular side effects include urinary retention and pruritus in paediatric setting, in addition to the well recognised constipation, nausea and vomiting.
- Morphine toxicity often presents as myoclonic twitching.
- Rectal route should be avoided if possible, and usually contraindicated in children with low platelets and/or neutropenia.
- In an emergency, when oral intake not appropriate, MST tablets can be administered rectally.
- Administration via enteral feeding tubes: For immediate pain relief use oral solution; no further dilution is necessary for intragastric administration. For administration via a jejunostomy the oral solution should be diluted with an equal volume of water. The tube must be flushed well following dosing to ensure that the total dose is delivered. For sustained pain relief, use MST Continus sachets (via gastrostomy only), dispersed in at least 10 mL of water. Flush the tube well following dosing to ensure that the total dose is delivered. Note that any granules left in the tube will break down over a period of time and a bolus of morphine will be delivered when the tube is next flushed; this has resulted in a reported fatality. Ensure that dose prescribed can be administered using whole sachets when possible. Use of Zomorph capsules opened to release the granules should be done with caution in children due to issues with dose accuracy and the granules should only be administered via an adult size gastrostomy.

Available as: (all Schedule 2 CD except oral solution of strength 10 mg in 5 ml)
- Tablets (10 mg, 20 mg, 50 mg).
  - Oral solution (10 mg/5 mL (POM), 100 mg/5 mL).
  - Modified release tablets and capsules 12 hourly (5 mg, 10 mg, 15 mg, 30 mg, 60 mg, 100 mg, 200 mg).
  - Modified release suspension 12 hourly (20 mg, 30 mg, 60 mg, 100 mg, 200 mg).
- Modified release capsules 24hourly (30 mg, 60 mg, 90 mg, 120 mg, 150 mg, 200 mg).
  - Suppositories (10 mg) – 0ther strengths may be available from specials manufacturers.
  - Injection (1 mg/mL, 10 mg/mL, 15 mg/mL, 20 mg/mL and 30 mg/mL).

Evidence: [1-3, 6, 10, 46, 48, 144, 171, 253, 393-412]

**Nabilone**

Use:

- Nausea and vomiting caused by cytotoxic chemotherapy (not first or second line therapy).
- For nausea and vomiting unresponsive to conventional antiemetics.

Dose and routes

By mouth:

- **Child <18 kg:** 0.5 mg twice a day
- **Child 18-30 g:** 1 mg twice a day
- **Child >30 kg:** 1 mg three times a day
- **Adult dose:** 1–2 mg twice a day (maximum dose 6 mg/day in 2-3 divided doses)

Notes:

- Not licensed for use in children.
- Nabilone is a synthetic cannabinoid.
- Individual variation requiring close medical supervision on commencement and dose adjustments.
- The effects of Nabilone may persist for a variable and unpredictable period of time following its oral administration.
- Side effects include somnolence and dizziness
- Adverse psychiatric reactions can persist for 48 to 72 hours following cessation of treatment.
- For specialist use only.
- Available as: capsules (250 microgram, 1 mg). Schedule 2 controlled drug.

Evidence: [1, 2, 5, 413-415] ARE

**Naloxone**
Use:
- Emergency use for reversal of opioid-induced respiratory depression or acute opioid overdose.

Dose and routes
Complete reversal of respiratory depression due to acute opioid overdose

By intravenous injection:
**(review diagnosis; further doses may be required if respiratory depression deteriorates)**
- **Neonate – Child 11 years:** 100 micrograms/kg; if no response repeat at intervals of 1 minute until a maximum of 2 mg administered.
- **Child 12-17 years:** Initially 400 micrograms, then 800 micrograms for up to 2 doses at 1 minute intervals if no response to preceding dose, then increased to 2 mg for 1 dose if still no response (4 mg dose may be required in seriously compromised patients).

By continuous intravenous infusion, adjusted according to response
- **Neonate – Child 17 years:** Rate adjusted according to response (initially, rate may be set at 60% of the initial resuscitative intravenous injection dose per hour),
- ***The initial resuscitative intravenous injection dose is that which maintained satisfactory self ventilation for at least 15 minutes.***

Notes
- Potent opioid antagonist.
- Naloxone has a short duration of action; repeated doses or infusion may be necessary to reverse effects of opioids with longer duration of action.
- Important: Only give by subcutaneous or intramuscular routes if intravenous route is not feasible; intravenous administration has more rapid onset of action.
- Also see methylnaltrexone.
- Naloxone acts within 2 minutes of IV injection and within 3-5 minutes of SC or IM injection.
- Although oral availability of naloxone is relatively low, be alert for opioid withdrawal symptoms, including recurrence of pain, at higher doses.
- Available as: injection (20 microgram/mL, 400 microgram/mL, 1 mg/mL).

Evidence: [2, 416, 417] ARE

**Naproxen**

Uses:

- Non-steroidal anti-inflammatory agent analgesic; relief of symptoms in inflammatory arthritis and treatment of acute musculoskeletal syndromes.

Dose and route:

By mouth

- **Child 1 month-17 years:** 5.0-7.5 mg/kg/dose twice daily (maximum 1 g/ day)

Doses up to 10 mg/kg twice daily (not exceeding 1 g daily) have been used in severe conditions. High doses should ideally be used only for a short period. In general, use the lowest effective dose for the shortest treatmentduration possible.

Notes:

- Naproxen is licensed for use from 5 years of age for juvenile idiopathic arthritis; not licensed for use in children less than 16 years for other conditions.
- Naproxen is contraindicated in patients with a history of hypersensitivity to any NSAID or in those with a coagulation disorder.
- Use with caution in renal, cardiac or hepatic failure as this may cause a deterioration in renal function; the dose should be kept as low as possible and renal function monitored. Avoid use if GFR <20ml/min/1.73m2 and in those with severe hepatic or cardiac failure.
- Generally naproxen is regarded as combining good efficacy with a low incidence of side-effects.
- The risk of cardiovascular events secondary to NSAID use is undetermined in children. In adults COX-2 selective inhibitors, diclofenac (150mg daily) and ibuprofen (2.4g daily) are associated with an increased risk of thrombotic events (e.g. myocardial infarction and stroke). Naproxen (in adults 1g daily) is associated with a lower thrombotic risk. The greatest risk may increase with dose and duration of exposure so the lowest effective dose should be used for the shortest possible duration of time.
- All NSAIDs are associated with GI toxicity. In adults, evidence on the relative safety of NSAIDs indicates differences in the risks of serious upper GI side-effects – piroxicam and ketorolac are associated with the highest risk; indometacin, diclofenac and naproxen are associated with intermediate risk and ibuprofen with the lowest risk. Children appear to tolerate NSAIDs better than adults and GI side-effects are less common although they do still occur and can be significant.
- Other potential side-effects include headache, dizziness, vertigo, fluid retention and hypersensitivity reactions.
- The anti-pyretic and anti-inflammatory actions of naproxen may reduce fever and inflammation therefore reducing their utility as diagnostic signs.
- Potential drug interactions include warfarin (increase in INR); diuretics, ACE inhibitors and angiotensin II antagonists (increased risk of compromised renal function). Naproxen is a substrate of CYP1A2 and CYP2C8/9 and can increase the plasma concentrations of methotrexate and lithium.
- For administration via an enteral feeding tube, use the oral suspension if available. Naproxen tablets may be crushed before administration and can be mixed with water for administration via a feeding tube. However,

  naproxen is poorly soluble in water and the tablet must be crushed to a fine powder before mixing with water to avoid tube blockage. There may be better choices of

NSAID if administration via a feeding tube is necessary and oral suspension is not available. Enteric coated naproxen tablets should be swallowed whole and NOT be crushed or chewed. Naproxen should be taken with or after food.
- Available as: tablets 250 mg and 500 mg; enteric coated tablets 250 mg, 375 mg and 500 mg; oral suspension 25 mg/mL .

Evidence: [1, 2, 5, 10]

**Nystatin**

Use:
- Oral and perioral fungal infection.

Dose and routes

By mouth:
- **Neonate:** 100 000units 4 times a day.
- **Child 1 month-1 year:** 200 000 units 4 times a day.
- **Child 2-17 years:** 400-600 000 units 4 times a day.

Notes:
- Licensed for use in all ages. Neonates – nystatin is licensed for prophylaxis against oral candidosis at a dose of 1ml daily.
- Retain near lesions before swallowing.
- Administerafter food or feeds. If possible divide the dose between both sides of the mouth.
- Treatment for 7 days and should be continued for 48 hours after lesions have healed.
- Available as: oral suspension 100 000 units/mL, 30 mL with pipette.

Evidence: [2, 191, 418]

**Octreotide**

Use:
- Bleeding from oesophageal or gastric varices.
- Nausea and vomiting.
- Intestinal obstruction.
- Intractable diarrhoea.
- Hormone secreting tumours, ascites, bronchorrhoea.

Dose and routes

By subcutaneous injection
- **Neonate:** Initially 2–5 micrograms/kg every 6–8 hours, adjusted according to response; increased if necessary up to 7 micrograms/kg every 4 hours, dosing up to 7 micrograms/kg may rarely be required.
- **Child 1 month-17 years:** Initially 1–2 micrograms/kg every 4–6 hours, adjusted according to response; increased if necessary up to 7 micrograms/kg every 4 hours, dosing up to 7 micrograms/kg may rarely be required.

By continuous intravenous or subcutaneous infusion
- **Child 1 month-17 years:** 1 microgram/kg/hour. Higher doses may be required initially. When there is no active bleeding reduce dose over 24 hours. Usual maximum dose is 50 micrograms/hour.

Notes:
- Not licensed for use in children.
- Octreotide is a synthetic analogue of somatostatin with a longer duration of action which acts as an inhibitory hormone throughout the body but particularly the gastro-enterohepatic system, increasing water and electrolyte absorption.
- Monitor glucose levels if used in a non end of life condition.
- Administration: for IV injection or infusion, dilute with sodium chloride 0.9% prior to administration. Check the manufacturer's recommendations regarding dilution. For SC bolus injections, may be administered undiluted but this can be painful (this can be reduced if the ampoule is warmed in the hand to body temperature before injection). For SC infusion dilute with 0.9% NaCl.
- Avoid abrupt withdrawal (associated with biliary colic and pancreatitis).
- Available as: injection for SC or IV administration (50 micrograms/mL, 100 micrograms/mL, 200 micrograms/mL, 500 micrograms/mL).
  Also available as depot injection for IM administration every 28 days (10 mg, 20 mg and 30 mg SandostatinLarR). Recommend specialist palliative care advice.

Evidence: [2, 89, 419]

**Olanzapine**
Uses:
- Psychoses; delirium; agitation; anorexia when all other treatments have failed.
- Nausea and vomiting.

Dose and route:
Oral:

Psychoses / mania
**Child <12 years and <25 kg:** Initial dose 2.5 mg at night
**Child <12 years and >25 kg:** Initial dose 2.5-5 mg at night.
**Child 12-17 years:** initial dose 5 mg at bedtime.

Increase gradually as necessary and as tolerated to a maximum of 20mg day given usually as a single dose at night.Can be given as twice daily dose if needed.

Agitation/delirium
**Child <12 years:** Initial dose 1.25 mg at night and as required,
**Child 12-17 years:** Initial dose 2.5 mg at night and as required.

Increase gradually as necessary and as tolerated tomaximum 10mg/day.

Nausea and vomiting; anorexia
**Child <12 years:** Initial dose 1.25 mg (or 0.625 mg if 2.5 mg tablets can be cut into quarters) at night and PRN,
**Child 12-17 years:** Initial dose 1.25-2.5 mg at night and as required.

Dose may be increased as necessary and as tolerated to a suggested maximum of 7.5 mg/day.

Notes:
- Olanzapine is not licensed for use in children and adolescents less than 18 years of age although there is general acknowledgement of 'off-label' use in adolescents for the treatment of psychosis and schizophrenia and mania associated with bipolar disorder.
- Use in the treatment of agitation/delirium, nausea and vomiting and anorexia in palliative care are all 'off-label' indications.
- Olanzapine is an atypical (second generation) antipsychotic agent and antagonist of dopamine D1, D2, D4, 5-HT2, histamine- 1-, and muscarinic-receptors.
- Olanzapine has 5x the affinity for 5HT2 receptors than for D2 receptors resulting in fewer extrapyramidal sideeffects.
- Activity of olanzapine at multiple receptors is similar to levomepromazineand therefore it has a potential role in the treatment of nausea and vomiting refractory to standard medication.
- Use with caution in those with cardiovascular disease or epilepsy (and conditions predisposing to seizures as lowers seizure threshold).
- Very common (> 10% patients) adverse effects: weight gain; elevated triglyceride levels; increased appetite; sedation; increased ALT and AST levels; decreased bilirubin; increased GGT and plasma prolactin levels.

  Common (1-10% patients) adverse effects: elevated cholesterol levels; dry mouth.

- Rare but potentially serious adverse effects include neuroleptic malignant syndrome, cardiovascular disease, severe respiratory disease and bone marrow depression, hepatitis, pancreatitis. Hyperglycaemia and sometimes diabetes can occur.
- Dose titration should be slow to minimise sedation.
- A greater magnitude of weight gain and lipid and prolactin alterations have been reported in adolescents compared to adults. If prolonged use is likely, consider the monitoring of blood lipids, weight, fasting blood glucose and prolactin. Consider an ECG and BP measurement before initiation.
- Consider lower starting dose (maximum 5mg in adults) in patients with renal and/or hepatic impairment.
- Olanzapine has good oral bioavailability with peak plasma concentrations occurring within 5-8 hours. Absorption is not affected by food. Long elimination half-life of ~33 hours. Onset of actions is hours-days in delirium; days-weeks in psychoses.
- Olanzapine does not inhibit or induce the main CYP450 isoenzymes. Olanzapine is metabolised by CYP1A2 therefore drugs/substances that specifically induce or inhibit this isoenzyme may affect the pharmacokinetics of olanzapine e.g. carbamazepine, fluvoxamine, nicotine.
- Orodispersible tablets: place in mouth where the tablet will rapidly disperse in saliva or disperse in a full glass of water (or other drink) immediately before administration. May be dispersed in water for administration via a NG or gastrostomy feeding tube. There are no specific reports of jejunal administration of olanzapine. Administer using the above method. Monitor for loss of efficacy or increased side-effects. Some anecdotal experience that 5mg orodispersible tablets may be halved to give a 2.5 mg dose. Halve immediately before administration and do not save the remaining half for a future dose
- Coated tablets: swallow whole with liquid or crushed and mixed with soft food.
- Orodispersible tablets contain aspartame and may be harmful for people with PKU.
- Coated tablets contain lactose.
- Available as: tablets 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg; orodispersible tablets / lyophilisate 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg.

Evidence: [1, 2, 420-436]

**Omeprazole**

Use:

- Gastro-oesophageal reflux.
- Acid related dyspepsia.
- Gastrointestinal prophylaxis (e.g. with combination NSAID/steroids).
- Treatment of duodenal and gastric ulcers.

Dose and routes

By mouth:

- **Neonate:** 700 microgram/kg once daily; increase if necessary to a maximum of1.4 mg/kg once daily (max dose: 2.8 mg/kg once daily).
- **Child 1 month–1 year:** 700 microgram/kg once daily; increase if necessary to a maximum of 3 mg/kg once daily (max dose: 20 mg once daily).
- **Child body weight 10–19 kg:** 10 mg once daily; increase if necessary to a maximum of 20 mg once daily.
- **Child body weight 20 kg and above:** 20 mg once daily; increase if necessary to a maximum of 40 mg once daily.

Intravenous (by infusion over 20-30 minutes)

- **Child 1 month -11 years:** initially 500 micrograms/kg (max:20 mg) once daily, increased, if necessary to 2 mg/kg (max: 40 mg) once daily.
- **Child 12-17 years:** 40 mg once daily.

Notes:

- Oral formulations are not licensed for use in children except for severe ulcerating reflux oesophagitis in children > 1 year.
- Infusion not licensed for use in children under 12years.
- Many children with life limiting conditions have gastro-oesophageal reflux disease and may need to continue with treatment long term.
- Can cause agitation.
- Occasionally associated with electrolyte disturbance.
- MHRA safety warning 2015: there is a very low risk of subacute cutaneous lupus erythematosus associated with use of PPIs.
- For oral administration tablets can be dispersed in water or with fruit juice or yoghurt. Capsules can be opened and mixed with fruit juice or yoghurt.
- Administer with care via enteral feeding tubes to minimise risk of blockage. Capsules may be opened and contents dispersed in 8.4% sodium bicarbonate for administration. Dispersible tablets disintegrate to give a dispersion of small granules. The granules settle quickly and may block fine-bore feeding tubes (less than 8Fr).For administration via small bore tubes use of an oral suspension (unlicensed) is recommended. Omeprazole is absorbed when administered into the jejunum with no reduction in bioavailability. Choice of formulation depends on the size of tube.
- Available as: gastoresistant tablets (MUPS) tablets (10 mg, 20 mg, 40 mg), capsules (10 mg, 20 mg, 40 mg),intravenous infusion (40 mg) and oral suspension available as an unlicensed special (10 mg in 5ml but other strengths may be available so be careful).

Evidence: [1-3, 10, 304, 437-443]

**Ondansetron**

Use:

- Antiemetic, if vomiting caused by damage to gastrointestinal mucosa (eg chemotherapy or radiotherapy).
- Pure 5HT3 antagonist, so receptor profile is complementary to levomepromazine – consider for N&V that breaks through despite regular levomepromazine.
- Has been used inmanaging opioid induced pruritus.
- For severe gastroenteritis.

Dose and routes

Prevention and treatment of chemotherapy- and radiotherapy-induced nausea and vomiting.

Terminal half life is 3 hours. Cleareance reduced in younger infants -75% in neonates and 50% at 3 months. Children <4 months must be closely monitored.

By intravenous infusion over at least 15 minutes

- **Child 6 months–17 years:** either 5 mg/m2 immediately before chemotherapy (max. single dose 8 mg), then give by mouth, or 150 micrograms/kg immediately before chemotherapy (max. single dose 8 mg) repeated every 4 hours for 2 further doses, then give by mouth; max. total daily dose 32 mg

By mouth following intravenous administration

**Note:**
Oral dosing can start 12 hours after intravenous administration

- **Child 6 months–17 years:**
- Body surface area less than 0.6 m2or body-weight 10 kg or less: 2 mg every 12 hours for up to 5 days (max. total daily dose 32 mg)
- Body surface area 0.6 m2 – 1.2 m2 or greater or body-weight over 10 kg: 4 mg every 12 hours for up to 5 days (max. total daily dose 32 mg)
- Body surface area greater than 1.2 m2or body-weight over 40 kg: 8mg every 12 hours for up to 5 days (max. total daily dose 32 mg)

Nausea and vomiting

By mouth or slowintravenous injection over 2-5 minutesor by intravenous infusion over 15 minutes

- **Child 1-17 years:** 100 microgram/kg/dose every 8-12 hours. Maximum single dose 4 mg.

Notes:

- Ondansetron injection is licensed for the management of chemotherapy-induced nausea and vomiting (CINV) in children aged ≥6 months, and for the prevention and treatment of post operative nausea and vomiting (PONV) in children (as a single dose) aged ≥1 month. Oral ondansetron is licensed from 6 months of age for the management of CINV but the oral formulation is not recommended for PONV in children due to a lack of data.
- Onset of action PO <30 mins, IV <5 mins and duration 12 hours.
- Contraindicated in congenital long QT syndrome. Ondansetron prolongs the QT

interval in a dose-dependent manner. In addition, post-marketing cases of Torsade de Pointes have been reported in patients using ondansetron. Ondansetron should be administered with caution to patients who have or may develop prolongation of QTc, including patients with electrolyte abnormalities, congestive heart failure, bradyarrhythmias or patients taking other medicinal products that lead to QT prolongation or electrolyte abnormalities.

- Hypokalaemia and hypomagnesaemia should be corrected prior to ondansetron administration.
- Powerfully constipating.
- Headache is a common adverse effect.
- Repeat IV doses of ondansetron should be given no less than 4 hours apart.
- For intravenous infusion, dilute to a concentration of 320–640 micrograms/mL with Glucose 5% or Sodium Chloride 0.9% or Ringer's Solution; give over at least 15 minutes.
- Oral solution may be administered via an enteral feeding tube. However be aware of the large sorbitol content of high doses. There is no specific data on jejunal administration. Administer using the above method. Monitor for loss of efficacy or increased side-effects.
- Can be give via subcutaneous infusion via syringe driver.
- Available as: tablets (4 mg, 8 mg, orodispersible films/tablets (4 mg, 8 mg), oral syrup (4 mg/5 mL), injection (2 mg/mL, 2 mL and 4 mL amps). 16mg suppositories also available.

Source: [2, 3, 6, 90, 142, 377, 444-447]

**Oxycodone**
Use:
- Alternative opioid for severe pain
- Pain of all types unless opioid insensitive

Dose and routes

Opioid switch: Convert using OME (Oral Morphine Equivalent) from previous opioid.

Use the following starting doses in the opioid naive patient. The maximum dose stated applies to the starting dose only.

By mouth:
Conversion
- Oral Morphine 1.5: Oral Oxycodone 1
- i.e. 15 mg Morphine: 10 mg Oxycodone

- **Child 1 month–11 years:** Initial dose 200 micrograms/kg (maximum single dose 5 mg) every 4 -6 hours.
- Child 12-17 years: Initial dose 5 mg every 4-6 hours.

- Titrate as for morphine: Increase dose if necessary according to severity of pain.

- **m/r tablets Child 8-11 years:** Initial dose 5 mg every 12 hours, increased if necessary
- **m/r tablets Child 12-17 years:** Initial dose 10 mg every 12 hours, increased if necessary.

By intravenous injection, subcutaneous injection or continuous subcutaneous infusion:
Conversion:
- Oral to IV or SC Oxycodone single bolus doseinjection: Divide the oral Oxycodone dose by 1.5(some texts suggest divide by 2 but clinically 1.5 used).
- Oral to a continuous subcutaneous infusion of Oxycodone over 24 hours: Divide the total daily dose of oral Oxycodone by 1.5 (some texts suggest divide by 2 but clinically 1.5 used).
- SC/IV Morphine to SC/IV Oxycodone ratio is approximately1:1. i.e. use same dose.
- Reason behind odd conversion ratio is bioavailability and rounding factors for safety.

Notes:
- Not licensed for use in children less than 12 years of age.
- No neonatal dose available.
- No evidence of any benefit over morphine and significantly more expensive.
- Associated with dose dependant QTc prolongation.
- Available in combination with naloxone as alternative to laxative therapy in opioid-induced constipation Targinact® (Napp) – not licensed in children.
- It is important to prescribe breakthrough analgesia which is 5-10% of the total 24 hour dose, given every 1 to 4 hours.
- It is moderately different from morphine in its structure, making it a hypothetical candidate for opioid substitution.

- Caution in hepatic or renal impairment.
- Oxycodone injection may be given IV or SC as a bolus or by infusion. For CSCI, dilute with WFI, 0.9% sodium chloride or 5% glucose.
- Oxycodone liquid may be administered via an enteral feeding tube.There is no specific data relating to jejunal administration. Monitor for lack of efficacy or side-effects.
- Safety Information: oxycodone modified release tablets are available as 12-hourly and 24-hourly preparations. Care with prescribing and do not confuse brands.
- Controlled drug schedule 2.
- Available as: capsules (5 mg, 10 mg, 20 mg), oral solution (5 mg/5 mL, 10 mg/mlL and m/r tablets (5 mg, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg, 120 mg), injection (10 mg/mL and 50 mg/mL).

Evidence: [1, 2, 5, 10, 54, 168, 448-455]

**Oxygen**

Use

- Breathlessness caused by hypoxaemia.
- Placebo effect, especially where family feels need to intervene promptly.
- Alternative to air blowing on face.

Dose and routes:

By inhalation through nasal cannula

- Flow rates of 1– 2.5L/min adjusted according to response. This will deliver between 24–35% oxygen depending on the patient's breathing pattern and other factors. Lower flow rates may be appropriate particularly for preterm neonates.

By inhalation through facemask

- Percentage inhaled oxygen is determined by the oxygen flow rateand/or type of mask. 28% oxygen is usually recommended for continuous oxygen delivery.

Notes:

- The evidence to support the use of O2 in non-hypoxemic patients is scant at best, which is why it best to use it in an N of 1 fashion. The patient will say if it works or not. General experience is that response to O2 for the treatment of breathlessness is just as likely/unlikely regardless of the patient's PaO2, so try it and if it doesn't help stop.
- Oxygen saturations do not necessarily correlate with the severity of breathlessness. Where self-report is not possible observation of the work of breathing is a more reliable indicator of breathlessness.
- Frequent or continuous measurement of oxygen saturations may lead to an over-reliance on technical data and distract from evaluation of the child's overall comfort, symptom relief and wellbeing.
- Target oxygen saturations of 92 – 96% may be appropriate in acute illness but are not necessarily appropriate for palliative care. More usual target oxygen saturations are above 92% in long-term oxygen therapy and 88-92% in children at risk of hypercapnic respiratory failure. Lower saturation levels may be tolerated in children with cyanotic congenital heart disease.
- It is important to be clear about the overall aims of oxygen treatment and realistic saturation levels for an individual child, as this will affect decisions about target oxygenation.
- In cyanotic congenital heart disease, oxygen has little effect in raising SaO2 and is not generally indicated. Pulmonary hypertension, in the early stages, may respond to oxygen, so it may be appropriate in the palliative care setting.
- Moving air e.g. from a fan maybe equally effective in reducing the sensation of breathlessness when the child is not hypoxaemic.
- Nasal cannulae are generally preferable as they allow the child to talk and eat with minimum restrictions. However continuous nasal oxygen can cause drying of the nasal mucosa and dermatitis.
- Oxygen administration via a maskor via NIPPV can be claustrophobic and/or damage facial skin. This can be reduced by using a nasal mask.The duration of supply from an oxygen cylinder will depend on the size of the cylinder and the flow rate.

- An oxygen concentrator is recommended for patients requiring more than 8 hours oxygen therapy per day.
- Liquid oxygen is more expensive but provides a longer duration of portable oxygen

supply. Portable oxygen concentrators are now also available.
- If necessary, two concentrators can be Y-connected to supply very high oxygen concentrations.
- Higher concentrations of oxygen are required during air travel.
- Home oxygen order forms (HOOF) and further information available from www.bprs.co.uk/oxygen.html
- A secondary supply of oxygen for children spending a prolonged time away from home requires a second HOOF available from the above website e.g. short breaks, holiday or extended periods with other relatives.

Evidence: [1, 2, 5, 456-461]

**Pamidronate (Disodium)**

Use:

- Adjuvant for bone pain caused by metastatic disease.
- Adjuvant for bone pain due to osteopenia or osteoporosis associated with neuromuscular conditions.
- Tumour-induced hypercalcaemia.
- Treatment of secondary osteoporosis to reduce fracture risk.
- Osteogenesis imperfecta.

**NB Seek specialist advice before use.**

Dose and routes

For bone pain (metastatic bone disease or osteopenia); secondary osteoporosis:

An effect on pain can be seen within 2 weeks, but may need a year before definitive assessment. Continue dosing for as long as effective and tolerated or until substantial decline in performance status.

By IV infusion

- 1 mg/kg as a single dose infused over 4-6 hours repeated monthly as required; concentration not exceeding 90 mg in 250 mL.

OR

- 1 mg/kg infused over 4-6 hours on 3 consecutive days and repeated every 3 months as required; concentration not exceeding 90 mg in 250 mL.

Formalignant hypercalcaemia: **(Seek specialist advice)**

By IV infusion

- 1 mg/kg infused over 6 hours; concentration not exceeding 90 mg in 250 mL. Then repeated as indicated by corrected serum calcium.

For osteogenesis imperfecta

By IV infusion

- In total all patients receive 12 mg/kg over the course of 1 year as:
- 1 day regimen: 1 mg/kg/day on a single day repeated monthly
- 2 day regimen: 1.5 mg/kg/day on 2 consecutive days, repeated every 3 months
- 3 day regimen: 1mg /kg/day on 3 consecutive days, repeated every 3 months
- Usual maximum single dose 90 mg (although occasionally higher doses are seen)
- If there is any concern about the starting dose, 0.5 mg/kg may be considered as the first dose for the first cycle.

Notes:

- Not licensed for use in children.Well tolerated by children, but long term effects unknown.
- Local guidelines vary. Some centres advise DEXA scan and investigations into calcium metabolism before and after treatment. Effectiveness of Pamidronate in bone pain does not necessarily depend on demonstrating osteoporosis, but demonstration that iatrogenic osteopetrosis has not developed afterwards can be reassuring.Flu-like symptoms often accompany first infusion, though typically do not recur with subsequent doses.

- Bisphosphonates have been used for some years in adults with bone metastases. It is becoming clear that they have a role in the wider causes of bone pain seen in children, particularly with neurological conditions.
- Current guidelines suggest initial dose be given as an inpatient. Subsequent doses could be given at home, if the necessary medical and nursing support is available. May have worsening of pain at first.
- IV zoledronic acid can also be used 25-50 microgram/kg/ dose (maximum 4-5 mg) repeated if necessary every 6-12 months. Under specialist advice only.
- Oral risedronate and oral alendronate limited use for these indications due to poor and variable bioavailability.
- If the IV route is unavailable, bisphosphonates can be administered by CSCI over 12-24 hours, together with SC hydration.
- Many bisphosphonates are available in different formulations, including oral, although absorption tends to be poor by the oral route and further reduced by food or fluids other than plain water.
- Caution: monitor renal function and electrolytes; ensure adequate hydration.
- Prolonged hypocalcaemia and hypomagnesaemia may occur with concurrent use of aminoglycoside and a bisphosphonate. Consider calcium and vitamin D oral supplements to minimise potential risk of hypocalcaemia for those with mainly lytic bone metastases and at risk of calcium or vitamin D deficiency (e.g. through malabsorption or lack of exposure to sunlight).
- Risk of renal impairment is increased by concurrent use with other nephrotoxic drugs.
- Risk in adults of atypical femoral fractures, and of osteonecrosis especially of the jaw and the external auditory canal. Not widely reported in children but suggest dental treatment before treatment and good dental hygiene advised. Patient/ family education.
- Available as: injection vials for infusion of various volumes, at 3 mg/mL, 6 mg/mL, 9 mg/mL, 15 mg/mL.

Evidence: [1, 5, 462-471]

**Paracetamol**
**(US: Acetaminophen)**

Use:
- Mild to moderate pain (step 1 of WHO pain ladder).
- Pyrexia.

Dose:
The recommended indications and doses of paracetamol have been revised to take account of MHRA and Toxbase advice that paracetamol toxicity may occur with doses between 75-150 mg/kg/day (ingestion of over 150 mg/kg/day is regarded as a definite risk of toxicity).

Oral:
- **Neonate 28–32 weeks corrected gestational age:** 20 mg/kg as a single dose then 10-15 mg/kg every 8 - 12 hours as necessary (maximum 30 mg/kg/day in divided doses).
- **Neonates over 32 weeks corrected gestational age:** 20 mg/kg as a singledose then 10-15 mg/kg every 6 - 8 hours as necessary (maximum 60 mg/kg/day in divided doses).
- **Child 1 month–5 years:** 20-30 mg/kg as a single dose then 15-20 mg/kg every 4-6 hours as necessary (maximum75 mg/kg/day in divided doses).
- **Child 6-11 years:** 20-30 mg/kg (max 1 g) as a single dose then 15-20 mg/kg every 4-6 hours as necessary (maximum 75 mg/kg/day or 4 g/day in divided doses).
- **Over 12 years:** 15-20 mg/kg (maximum 500 mg -1 g) every 4-6 hours as necessary (maximum 4 g /day in divided doses).

Rectal:
- Neonate 28–32 weeks corrected gestational age: 20 mg/kg as a single dose then 10-15 mg/kg every 12 hours as necessary (maximum 30 mg/kg/day in divided doses).
- Neonates over 32 weeks corrected gestational age: 30 mg/kg as a single dose then15-20 mg/kg every 8 hours as necessary (maximum 60 mg/kg/day in divided doses).
- Child1–2 months: 30 mg/kg as a single dose, then 15-20 mg/kg every 4-6 hours as necessary (maximum 75 mg/kg/day in divided doses).
- Child 3 months-11years: 30 mg/kg as a single dose (maximum 1 g) then 15-20 mg/kg every 4-6 hours as necessary (maximum75 mg/kg/day or 4 g/day in divided doses).
- Over 12 years: 15-20 mg/kg (maximum 500 mg -1 g) every 4-6 hours as necessary (maximum 4 g/day in divided doses).

IV: as infusion over 15 minutes
- Preterm neonate over 32 weeks corrected gestational age: 7.5 mg/kg every 8 hours, maximum 25 mg/kg/day.
- Neonate: 10 mg/kg every 4-6 hours (maximum 30 mg/kg/day).
- Infant and child bodyweight <10 kg: 10 mg/kg every 4-6 hours (maximum 30 mg/kg/day)
- Child bodyweight 10-50 kg: 15 mg/kg every 4-6 hours (maximum 60 mg/kg/day).
- Bodyweight over 50 kg: 1 g every 4-6 hours (maximum 4 g/day).

Notes:

- Many children and young people with life limiting illness have low weight for their age. The doses above are therefore quoted mainly by weight rather than age (unlike most of the entries in the BNF and BNFc), in order to minimise risk of over-dosing in this patient group.
- Not licensed for use in children under 2 months by mouth; not licensed for use in preterm neonates by intravenous infusion; not licensed for use in children under 3 months by rectum; doses for severe symptoms not licensed; paracetamol oral suspension 500 mg/5 mL not licensed for use in children under 16 years.
- Oral and licensed rectal preparations are licensed for use in infants from 2 months for post immunisation pyrexia (single dose of 60 mg which may be repeated once after 4-6 hours if necessary), and from 3 months as antipyretic and analgesic.
- IV paracetamol is licensed for short term treatment of moderate pain, and of fever when other routes not possible.
- Consider use of non pharmacological measures to relieve pain, as alternative or in addition to analgesics.
- Hepatotoxic in overdose or prolonged high doses.
- In moderate renal impairment use maximum frequency of 6 hourly; in severe renal impairment maximum frequency 8 hourly.
- Onset of action 15-30 minutes orally, 5-10 minutes IV (analgesia), 30 minutes IV (antipyretic). Duration of action 4-6 hours orally and IV. Oral bioavailability 60-90%. Rectal bioavailability about 2/3 of oral. However, rectal absorption is now known to be erratic and incomplete, and results in slower absorption than oral administration, (except in babies when the oral preparation used rectally speeds absorption compared with suppositories). Elimination is slower in babies under 3 months.
- Dispersible tablets have high sodium content (over 14mmol per tablet), so caution with regular dosing (consider using the liquid preparation instead).
- For administration via an enteral feeding tube: Use tablets dispersed in water for intragastric or intrajejunal administration. If the sodium content is problematic, use the liquid formulation. This can be used undiluted for intragastric administration; however, the viscosity of the paediatric liquid preparations is very high; it is difficult to administer these suspensions via a fine bore tube without dilution. If administering intrajejunally, dilute with at least an equal quantity of water to reduce osmolarity and viscosity.
- For management of feverish illness in children, see updated NICE clinical Guideline CG160. (Consider using either paracetamol or ibuprofen in children with fever who appear distressed, and consider changing to the other agent if distress is not alleviated. But do not use antipyretic agents with the sole aim of reducing body temperature).However, a recent Cochrane systematic review states “there is some evidence that both alternating and combined antipyretic therapy may be more effective at reducing temperatures than monotherapy alone”.
- Available as: tablets and caplets (500 mg), capsules (500 mg), soluble tablets (120 mg, 500 mg), oral suspension (120 mg/5 mL, 250 mg/5 mL), Fastabs 250 mg, suppositories (60 mg, 125 mg, 250 mg, 500 mg and other strengths available from ‘specials’ manufacturers or specialist importing companies) and intravenous infusion (10 mg/mL in 50 mL and 100 mL vials).

Evidence: [1-3, 6, 10, 247, 472-475]WRE

**Paraldehyde (rectal)**
Use:
• Treatment of prolonged seizures and status epilepticus.

Dose and route:
By rectal administration (dose shown is forpremixed enema 50:50 with olive oil)
• **Neonate:** 0.8 mL/kg as a single dose.
• **I month-17 years:** 0.8 mL/kg (maximum 20mL) as a single dose.

Notes:
• Rectal administration may cause skin irritation.
• Contra-indicated in gastric disorders and in colitis.
• Paraldehyde enema for rectal use is an unlicensed formulation and route of administration.
• Available as paraldehyde enema: premixed solution of paraldehyde in olive oil in equal volumes from 'special-order' manufacturers or specialist importing companies.

Evidence: [2, 6, 476-482] WRE

**Phenobarbital**

Use:

- Adjuvant in pain of cerebral irritation.
- Control of terminal seizures.
- Sedation (soporific and anxiolytic).
- Epilepsy including status epilepticus. Commonly used first line for seizures in neonates (phenytoin or benzodiazepine are the main alternatives).
- Agitation refractory to midazolam in end of life care.

Dose and routes

Status epilepticus / terminal seizures / agitation

***Loading doses are not usally necessary unless it is for rapid control of terminal seizures in someone not already on anticonvulsants This is because in paediatric palliative care it is not often used for emergency seizure control, but for cerebral irritation. Where it is for seizures, it is normally used for prophylaxis or adding it to other anticonvulsants. In those cases there is usually no hurry to get to an effective serum concentration***

**Loading dose if required**

Oral, intravenous or subcutaneous injection:

All ages: 20 mg/kg/dose (maximum 1 g) administered over 20 minutes if by IV or SC injection (but see notes below).

Subcutaneous or intravenous injection or infusion:

- **Neonates for control of ongoing seizures:** 2.5-5 mg/kg once or twice daily as maintenance.
- **Child 1 month-11 years:** 2.5-5 mg/kg (maximum single dose 300 mg) once or twice daily or may be given as a continuous infusion over 24 hours.
- **Child 12-17 years:** 300 mg twice daily or may be given as a continuous infusion over 24 hours.

Epilepsy:

By mouth:

- **Neonates for control of ongoing seizures:** 2.5-5 mg/kg once or twice daily as maintenance.
- **Child 1 month–11 years:** 1–1.5 mg/kg twice a day, increased by 2 mg/kg daily as required (usual maintenance dose 2.5–4 mg/kg once or twice a day).
- **Child 12–17 years:** 60–180 mg once a day.

Notes:

- Licence is only for seizures. Not licensed for agitation in end of life care.
- Single loading dose is required for initiation of therapy if immediate effect is needed; administer via enteral route if possible. Loading dose can be administered intravenously over 20 minutes or as a slow subcutaneous loading dose however the volume of resultant solution will limit the rate at which a subcutaneous bolus can be administered.
- Loading dose used to reach steady state quickly and avoid late toxicity due to accumulation.
- For patients already on oral phenobarbital but needing parenteral treatment, doses equivalent to the patient's usual total daily dose of oral phenobarbital can be used.

- Elimination half life of 2-6 days in adults, 1-3 days in children.
- Phenobarbital induces various enzymes of the CYP450 system and thus may reduce the plasma concentrations of concomitant drugs that are metabolised by this system.
- Consider vitamin D supplementation in patients who are immobilised for long periods or who have inadequate sun exposure or dietary intake of calcium.
- Tablets may be crushed for administration if preferred.
- The liquid preparations may be administered via an enteral feeding tube. For administration via a jejunostomy tube, dilution with water is recommended to reduce the liquid viscosity.
- Use a separate site to commence subcutaneous infusion. SC bolus injections should be avoided because they can cause tissue necrosis due to the high pH.
- It is essential to dilute the injection in 10 times the volume of water for injection before intravenous or subcutaneous injection (i.e. to maximum concentration of 20 mg/mL).
- Available as: tablets (15 mg, 30 mg, 60 mg), oral elixir (15 mg/5 mL) and injection (15 mg/mL, 30 mg/mL, 60 mg/mL and 200 mg/mL). The licensed oral elixir of 15 mg in 5 mL contains alcohol 38% and it is preferable to obtain an alcohol free oral liquid via one of the specials manufacturers. CD Schedule 3 (CD No Register Phenobarbital).

Evidence: [2, 3, 149, 206, 483]

**Phenytoin**

Use:

- Epilepsy (3rd or 4th line oral antiepileptic) including for status epilepticus.
- Neuropathic pain (effective, at least short term, but not used first line).

Dose

All forms of epilepsy (including tonic-clonic, focal and neonatal seizures) except absence seizures.Neuropathic pain.

Oral or slow IV injection:

- **Neonate:** Initial loading dose by slow IV injection 18 mg/kg **THEN by mouth** 2.5-5 mg/kg twice daily adjusted according to response and plasma phenytoin levels. Usual maximum 7.5 mg/kg twice daily.
- 1 month -11 years: Initial dose of 1.5-2.5 mg/kg twice daily then adjust according to response and plasma phenytoin levels to 2.5-5 mg/kg twice daily as a usual target maintenance dose. Usual maximum dose of 7.5 mg/kg twice daily or 300 mg daily.
- 12 -17 years: initial dose of 75-150 mg twice daily then adjusted according to response and plasma phenytoin levels to 150-200 mg twice daily as a usual target maintenance dose. Usual maximum dose of 300 mg twice daily.

Status epilepticus, acute symptomatic seizures:
Slow IVinjection or infusion:

- **Neonate:** 20 mg/kg loading dose over at least 20 minutes, then 2.5-5 mg/kg/ dose (over 30 minutes) every 12 hours as a usual maintenance dose in first week of life. Adjust according to response and older babies may need the higher doses. After the first dose, oral doses usually as effective as intravenous in babies over 2 weeks old.
- **1 month – 11 years:** 20 mg/kg loading dose over at least 20 minutes, then 2.5-5 mg/kg twice daily usual maintenance dose.
- **12 -17 years:** 20 mg/kg loading dose over at least 20 minutes, then up to 100 mg (over 30 minutes) 3 to 4 times daily usual maintenance dose.

Notes:

- Licensed status: suspension 90mg in 5mL is a 'special' and unlicensed. Other preparations are licensed for use in children as an anticonvulsant (age range not specified).
- Phenytoin acts as a membrane stabiliser.
- It has a narrow therapeutic index, unpredictable half life, and the relationship between dose and plasma-drug concentration is non-linear. The rate of elimination is also very variable, especially in the first few weeks and months of life. Co-treatment with commonly used drugs can significantly alter the half life.
- Phenytoin has numerous interactions with other drugs due to hepatic enzyme induction. Long term use is associated with significant side effects. It is no more effective than other anti-epileptics and hence not usually used first line, although it does enable rapid titration.
- Continuous ECG and BP monitoring required during IV administration.
- Oral bioavailability 90-95% is roughly equivalent to intravenous, plasma half-life 7-42 hours. Poor rectal absorption.

- Reduce dose in hepatic impairment. Monitor carefully if reduced albumin or protein binding e.g. in renal failure.
- Caution: cross-sensitivity is reported with carbamazepine.
- Avoid abrupt withdrawal.
- Consider vitamin D supplementation in patients who are immobilised for long periods or who have inadequate sun exposure or dietary intake of calcium.
- Before and after administration, flush intravenous line with Sodium Chloride 0.9%.
- For intravenous injection, give into a large vein at a rate not exceeding 1 mg/kg/minute (max. 50 mg/minute).
- For intravenous infusion, dilute to a concentration not exceeding 10 mg/mL with Sodium Chloride 0.9% and give into a large vein through an in-line filter (0.22–0.50 micron) at a rate not exceeding 1 mg/kg/minute (max. 50mg/minute); complete administration within 1 hour of preparation.
- Prescriptions for oral preparations should include brand name and be of consistent preparation type, to ensure consistency of drug delivery.
- Preparations containing phenytoin sodium are not bioequivalent to those containing phenytoin base (such as Epanutin Infatabs® and Epanutin® suspension); 100 mg of phenytoin sodium is approximately equivalent in therapeutic effect to 92 mg phenytoin base. The dose is the same for all phenytoin products when initiating therapy, however if switching between these products the difference in phenytoin content may be clinically significant. Care is needed when making changes between formulations and plasma phenytoin concentration monitoring is recommended.
- Bioavailability may be reduced unpredictably by enteral feeds and/or nasogastric tube feeds, so flush with water to enhance absorption, interrupt enteral feeding for at least 1-2 hours before and after giving phenytoin, and maintain similar timings and regimes from day to day. Use the oral suspension for enteral tube administration; dilution with an equal volume of water is recommended for gastrostomy administration. Absorption is exceptionally poor via the jejunal route; plasma concentration should be monitored closely if this route is used. Dilution of the suspension is important as phenytoin suspension is hyperosmolar and may cause diarrhoea when administered into the jejunum.
- Available as tablets (phenytoin sodium 100 mg, generic), capsules (phenytoin sodium 25 mg, 50 mg,100 mg, 300 mg), Epanutin R Infatabs (chewable tablets of phenytoin base 50 mg), oral suspension (EpanutinRphenytoin base 30 mg/5 mL, and 90 mg/5 mLphenytoin base available as an ‘unlicensed special’), and injection (phenytoin sodium 50 mg/mL generic)

Evidence: [2, 3, 5, 6, 10, 66, 451, 484-488], WRE

**Phosphate (rectal enema)**
Use:
• Constipation refractive to other treatments.

Dose and routes:
Phosphates enema BP Formula B (with standard or long rectal tube):
• **Child 3–6 years:** 45-65 mL once daily.
• **Child 7-11 years:** 65-100 mL once daily.
• **Child 12–17 years:** 100-128 mL once daily.

Fleet$^{R}$Ready to Use enema:
• **Child 3–6 years:** 40-60 mL once daily.
• **Child 7-11 years:** 60-90 mL once daily.
• **Child 12–17 years:** 90-118 mL once daily.

Notes
• Maintain good hydration and watch for electrolyte imbalance.
• Onset 30 minutes to 6 hours.
• Contraindicated in acute gastro-intestinal conditions (including gastro-intestinal obstruction, inflammatory bowel disease, and conditions associated with increased colonic absorption).
• There have been case reports of hyperphosphataemia and tetany in children following the use of phosphate enemas.
• NICE Guidance CG99 (Constipation in children & Young People) makes a 'Do Not Do Recommendation': 'Do not administer phosphate enemas for disimpaction unless under specialist supervision in hospital / health centre / clinic, and only if all oral medications and sodium citrate have failed'.
• Use only after specialist advice.

Evidence: [1, 2, 489-493], WRE

**Pregabalin**

Use:

- Epilepsy (focal seizures with or without secondary generalisation)
- Peripheral and central neuropathic pain
- Generalised anxiety disorder

Dose and route:

Epilepsy (adjunctive therapy for partial seizures)

- Child: suggested maintenance dose of 5-10 mg/kg/day. Start at low dose and increase gradually every 3-7 days as tolerated. Maximum 600 mg/day given in 2-3 divided doses. Younger children less than 6 years may need up to 15 mg/kg/day.

Neuropathic Pain

- Child:
  Day 1-3: 1 mg/kg once a day
  Day 4-6: 1 mg/kg 12 hourly
  Day 7: Increase every 3-7 days by 1 mg/kg until
  1. Effective analgesia reached, or
  2.Side effects experienced, or
  3. Max total daily dose of 6mg/kg/day (although higher dses of 12 mg/kg have been used).

Gabapentin to Pregabalin switch for neuropathic pain
Consult appendix 3

Notes:

- Not licensed for use in children or adolescents less than 18 years of age.
- Licensed in adults as adjunctive therapy for partial seizures; for the treatment of peripheral and central neuropathic pain and for the treatment of generalised anxiety disorder.
- NICE Guidance CG173 (Neuropathic pain in adults) recommends: 'offer a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment of neuropathic pain, if the initial treatment is not effective or is not tolerated, offer one of the remaining 3 drugs and consider switching again if the second and third drugs tried are also not effective or not tolerated'.
- MHRA/CHM issued a warning to prescribers in April 2019, advising on the risk of pregabalin abuse and dependence. Pregabalin re-classified as a Schedule 3 controlled drug. Be aware also of potential serious risks of interaction between pregabalin and other medicines that can cause CNS depression, particularly opioids.
- Pregabalin binds to the alpha-2 subunit of voltage gated calcium channels in the CNS thus inhibiting the release of excitatory neurotransmitters.
- Pregabalin has a binding affinity 6x greater than that of gabapentin.
- Oral bioavailability 90% or greater; can be taken with or without food. Peak plasma concentrations occur within 1.5 hours.
- Limited pharmacokinetic data in children suggests total exposure to pregabalin to be 30% lower in paediatric patients of weight <30kg (compared to those of weight 30kg or greater) due to increased drug clearance. Terminal half-life averaged 3-4 hours in children up to 6 years of age and 4-6 hours in those aged 7 years or older.
- Pregabalin does not bind to plasma proteins. It undergoes negligible liver metabolism nor does it affect the major CYP450 enzymes and therefore is unlikely to have significant drug interactions.

- Pregabalin is predominantly excreted unchanged by the kidneys and thus accumulates in renal impairment. Dose reduction is necessary in patients with renal impairment.
- No dosage adjustment is needed in hepatic impairment.
- Case reports of more profound psychological side effects with pregabalin than gabapentin.
- For administration via an enteral tube preferably use the oral solution. There are no specific data on the jejunal administration of pregabalin. Administer using the oral solution and monitor for loss of effect or increase in side-effects.
- Most commonly reported adverse effects are dizziness, somnolence and headache. These are generally transient and mild to moderate in nature and may be minimised by a gradual increase to the therapeutic dose.
- Available as: oral capsules 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, 300 mg and oral solution 20 mg/ml.
- Schedule 3 controlled drug although exempt from safe storage requirements.

Evidence: [1, 494-498] WRE

**Promethazine**
The MHRA / CHM issued advice in March 2008 and February 2009 recommending that children under the age of 6 years should not be given over the counter preparations containing promethazine. This was on the back of serious events including deaths.

Use:
- Sleep disturbance.
- Mild sedation (soporific).
- Antihistamine.
- Can also be used to treat nausea and vomiting (including motion and opioid-induced), and vertigo.
- Sedation in neonatal intensive care.

Dose and routes (for promethazine hydrochloride)
By mouth:

Symptomatic relief of allergy:
- **Child 2–4 years:** 5 mg twice daily or 5–15 mg at night.
- **Child 5–9 years:** 5–10 mg twice daily or 10–25 mg at night.
- **Child 10–17 years:** 10–20 mg 2–3 times daily or 25 mg at night increased to 25 mg twice daily if necessary.

Sedation (short term use):
- **Child 2–4 years:** 15-20 mg at night.
- **Child 5–9 years:** 20-25 mg at night.
- **Child 10–17 years:** 25-50 mg at night.

Nausea and vomiting (particularly in anticipation of motion sickness)
- **Child 2–4 years:** 5 mg twice daily.
- **Child 5–9 years:** 10 mg twice daily.
- **Child 10–17 years:** 20–25 mg twice daily.

Sedation in neonatal intensive care
By mouth or by slow intravenous injection
- **Neonate >37 CorGA:** 0.5–1 mg/kg 4 times daily, adjusted according to response

Notes:
- Phenothiazine antihistamine (anti H1) with moderatemuscarinic and D2 receptor antagonism. Has also been used orally for dyspnoea in adults.
- Not licensed for sedation in children under 2 years
- Used in neonatal units on bigger babies for oral sedation when usual IV sedationoptions not working. Note drug interactions, particularly causing increased antimuscarinic and sedative effects.
- Caution in epilepsy, asthma, renal and severe hepatic impairment. Risk of hypotension if co-prescribed with opioid.
- Note when prescribing, subcutaneous dose should be lower than corresponding oral dose due to significant first pass metabolism.
- Promethazine is not generally recommended for subcutaneous administration due to the risk of local necrosis, but diluted in an adequate volume of sodium chloride 0.9% can usually be administered by CSCI

over 24 hours. Do not give bolus SC injections.

- Oral preparation can be effective for up to 12 hours (peak plasma concentration 2-3 hours after administration). Drowsiness may wear off after a few days of treatment.
- For use by feeding tube: the elixir is slightly viscous. No further dilution is necessary, for intragastric administration, but dilute with an equal volume of water for intrajejunal administration, or to reduce viscosity and resistance to flushing. Tablets will disintegrate if shaken in water for 5 minutes.
- Available as: promethazine hydrochloride tablets (10 mg, 25 mg), oral elixir (5 mg/5 mL), and injection (25 mg/mL). (Promethazine teoclate tablets also available, 25 mg, licensed for nausea, vertigoand labyrinthine disorders. Slightly longer acting than promethazine hydrochloride and dosing slightly different).

Evidence: [2, 3, 10, 405, 499], NoRE, ARE

**Ranitidine**
Use:
- Gastro-oesophageal reflux oesophagitis, dyspepsia.
- Treatment of gastritis, benign gastric and duodenal ulcers.
- Gastro-protection (e.g. with combination NSAID/steroids or anticipating stress ulceration).
- Other conditions requiring reduction in gastric acid.

Dose and routes
By mouth:
- **Neonate:** 2 mg/kg 3 times daily, increasing if necessary to maximum 3 mg/kg 3 times daily (absorption unreliable).
- **Child 1–5 months:** 1 mg/kg 3 times daily increasing if necessary to maximum 3 mg/kg 3 times daily.
- **Child 6 months–2 years:** 2–4 mg/kg twice a day.
- **Child 3–11 years:** 2–4 mg/kg (maximum single dose 150 mg) twice a day. Dose may be increased up to 5 mg/kg (maximum 300 mg/dose) twice daily in severe gastro-oesophageal reflux disease,
- **Child 12–18 years:** 150 mg twice a day or 300 mg at night. May be increased if necessary in moderate to severe gastro-oesophageal reflux disease to 300 mg twice a day or 150 mg 4 times daily for up to 12 weeks.

By slow intravenous injection, diluted to 2.5 mg/ml and given over at least minutes (some adult centres give as subcutaneous injection (unlicensed route)):
- **Neonate:** 0.5–1 mg/kg every 6–8 hours (may need 2 mg/kg 8 hourly as variable first pass metabolism affects uptake).
- **Child 1 month–17 years:** 1 mg/kg (max. 50 mg) every 6–8 hours (may be given as an intermittent infusion at a rate of 25 mg/hour).

Notes:
- Oral formulations not licensed for use in children < 3 years; injection not licensed for children less than 6 months.
- Use gastric pH to judge best dose in early infancy.
- Ranitidine is an H2 antagonist.
- Proton pump inhibitors (PPIs), H2 antagonists and prokinetics all relieve symptoms of non-ulcer dyspepsia and acid reflux, PPIs being the most effective. PPIs and H2 antagonists are effective at preventing NSAID-related peptic ulcers. Adding a bedtime dose of H2 antagonist to high dose PPI may improve nocturnal acid reflux, but evidence is poor.
- Time to peak plasma concentration is 2-3 hours, half-life 2-3 hours (longer at birth and in pre-term babies), duration of action 8-12 hours.
- Ranitidine may increase plasma concentration of midazolam.
- May cause rebound hyperacidity at night.
- Via feeding tubes, use effervescent tablets as first choice, unless sodium content is a concern. Use oral liquid as alternative. (Standard tablets do not disperse readily in water).
- Can use IV if needed in severe nausea and vomiting. Some centres use subcutaneous doses BD – QDS.
- Available as: tablets and effervescent tablets (75 mg, 150 mg, 300 mg), oral solution (75 mg/5 mL NB contains ethanol) and injection (25 mg/ml).

Evidence: [1-3, 5, 10, 500-503]

**Risperidone**

Use:

- Severe neuro-irritability.
- Dystonia and dystonic spasms refractory to first and second line treatment.
- Psychotic tendency / crises in Battens disease.
- Has anti-emetic activity (some experience in refractory nausea and vomiting in adults; not evaluated in children).
- Delirium.
- Treatment of mania or psychosis under specialist supervision.
- Short term treatment of persistent aggression in conduct disorder in children and in autism or moderate to severe dementia.

Dose and routes

Oral:

- **Child 5–17 years (weight 20–50 kg):** 250 micrograms once daily; increasing, if necessary, in steps of 250 microgramson alternate days to maximum of 750 micrograms daily.
- **Child 5-17 years (>50 kg):** 500 micrograms once daily; increasing in steps of 500 microgram on alternate days to maximum of 1.5 mg daily.

**In Juvenile Battens Disease**, may need 500 micrograms dailyincreasingto 1.5 mg TDS during crises with hallucinations: this dose can be reduced or stopped as symptoms settle (episodes usually last 1-6 weeks).

**In Severe neuro-irritability**, increase as below until control achieved then hold.

| | |
|---|---|
| Day 1-2: | 10 microgram/kg/day |
| Day 3-7: | 20 microgram/kg/day |
| Day 8-14: | 40 microgram/kg/day |
| Day 15-42: | 60 microgram/kg/day |

Notes

- Risperidone is a dopamine D2, 5-HTA, alpha-1 adrenoceptor and histamine-1 receptor antagonist.
- Risperidone is licensed for the short-term symptomatic treatment (up to 6 weeks) of persistent aggression in conduct disorder in children from the age of 5 years, using the doses above. Not licensed for use in children for mania, psychosis or autism (use different doses under specialist supervision).
- 99% bioavailable. 1-2 hours to peak plasma concentration. Onset of action hours to days in delirium; days to weeks in psychosis. Plasma half-life 24 hours. Duration of action 12-48 hours.
- Caution in epilepsy (lowers seizure threshold) and cardiovascular disease; extrapyramidal symptoms less frequent than with older antipsychotic medications; can cause orthostatic hypotension; withdraw gradually after prolonged use.
- Risperidone can cause significant weight gain. Other common side effects include anxiety, depression, sleep disorders, hypertension, oedema, malaise.

- Initial and subsequent doses should be halved in renal or hepatic impairment.
- Oral liquid is the preferred preparation for administration via enteral feeding tubes. Tablets also disintegrate in water within 5 minutes for easy administration via enteral feeding tubes.There is no specific data relating to jejunal administration of risperidone. Administer using the above method. Monitor for loss of efficacy or increased side-effects.The oral liquid may be diluted in any non-alcoholic drink except tea.
- Available as: tablets (500 microgram, 1 mg, 2 mg, 3 mg, 4 mg, 6 mg), orodispersible tablets (500 microgram, 1 mg, 2 mg, 3 mg, 4 mg),oral solution 1 mg/mL.

Evidence: [2, 10, 224, 504-509] NoRE

**Salbutamol**

Use:

- Wheezing/breathlessness caused by bronchospasm including exacerbations associated with respiratory tract infection.
- Also used in hyperkalemia.
- Prevention and treatment of chronic lung disease in premature infants.
- Sometimes used in muscular disorders disorders were it is felt to have an effect on the degradation of motor neurone protein muscle weakness (seek specialist advice, not covered here).

Dose and routes for exacerbation of reversible airway obstruction, and prevention of allergen- or exercise-induced bronchospasm.

(NB see separate detailed guidance in standard texts for use in acute asthma,including for intravenous preparation, not covered here).

Aerosol inhalation:

- **Child 1 month-17 years:** 100-200 micrograms (1-2 puffs) for relief ofsymptoms up to four times a day. See separate dosing guidance for individual preparations.

Nebulised solution:

- **Neonate:** 1-2.5 mg up to four times daily,
- **Child 1 month-4 years:** 2.5 mg, then 2.5 mg every 20-30minutes, or when required, give by oxygen-driven nebuliser if avaliable.
- **Child 5-11 years:** 2.5-5 mg,then 2.5-5 mg every 20-30minutes, or when required, give by oxygen-driven nebuliser if avaliable.
- **Child 12-17 years:** 5 mg then 5 mg every 20-30minutes, or when required, give by oxygen-driven nebuliser if avaliable.

Oral liquid is available but salbutamol should generally only be admisnistered orally in the context of neuromuscular disease, where a systemic effect is felt to occur on the rate of degredation of motor neurone proteins.

Notes

- Salbutamol is a short acting beta 2 adrenergic receptor agonist.
- Salbutamol is not licensed for use in hyperkalaemia; injection is not licensed for use in children.
- In palliative care, if airflow obstruction is suspected, a pragmatic approach may be to give a trial (e.g. 1–2 weeks) of a bronchodilator and evaluate the impact on symptoms. Spirometry should normally be used to confirm a possible underlying asthma diagnosis.
- Clinical efficacy of salbutamol in infants <18 months is uncertain, presumably due to the immaturity of the receptors; ipratropium may be more helpful in those less than 1-2 years.
- For an acute episode, many paediatricians now advise multi-dosing of salbutamol 100microgram up to 10 times, via a spacer where practicable for the patient instead of a nebuliser.
- Onset of action 5 minutes inhaled, 3-5 minutes nebulised. Peak response 0.5-2 hours.Duration of action 4-6 hours. Only 10-20%of inhaled dose reaches lower airways.

- Side effects: increased heart rate; feeling “edgy” or agitated; tremor.
- The side effects listed above may prevent use, in which case ipratropium bromide is a good alternative.
- Advise family to seek advice if a previously effective dose fails to provide at least 3 hours relief, and warn of the dangers of exceeding prescribed inhaler and nebuliser doses.
- Caution: tachycardia and risk of QT prolongation at increasing doses.
- Interactions: increased risk of hypokalemia with corticosteroids, diuretics, theophylline.
- Inhaled product should be used with a suitable spacer device, and the child/ carer should be given appropriate training. Inhaler technique should be explained and checked. The HFA (hydrofluoroalkane) propellant now used in multi-dose inhalers tends to clog the nozzle, so weekly cleaning is recommended.
- Salbutamol nebules are intended to be used undiluted. However, if prolonged delivery time (more than 10 minutes) is required, the solution may be diluted with sterile 0.9% NaCl. Salbutamol can be mixed with nebulised solution of ipratropium bromide.
- Available as nebuliser solution (2.5 mg in 2.5 mL, 5 mg in 2.5 mL), respirator solution (5 mg in 1 mL), aerosol inhalation (100 micrograms/puff) by metered dose inhaler (MDI), with various spacer devices. Various types of dry powder inhaler are also available, 100 and 200 microgram per puff.
  Preparations for injection (500 micrograms/ml) and intravenous infusion (1 mg/ mL) are also available.

Evidence: [1-3, 510-515]

**Senna**
Use:
• Constipation

Dose and routes
By mouth:
Initial doses which can be adjusted according to response and tolerance.

**Syrup:**
• **Child 1 month–3 years:** 2.5-10 mL of syrup once a day.
• **Child 4-17 years:** 2.5-20 mL of syrup a day.

**Tablets:**
• **Child 2-3 years:** 0.5-2 tablets once daily.
• **Child 4-5 years:** 0.5-4 tablets once daily.
• **Child 6-17 years:** 1-4 tablets once daily.

Notes:
• Mainly stimulant laxative acting on large bowel. Improves intestinal motility and increases water secretion into bowel lumen. Senna passes unchanged into large bowel, (therefore still effective administered into the jejunum). It is hydrolysed by bacterial flora in the large bowel to yield the active compound.
• For opioid induced constipation in palliative care a reasonable approach is to start with a stimulant alone, optimise the dose and only add a second agent if not adequately effective.
• Syrup is not licensed for use in children < 2 years and tablets are not licensed for use in children <6 years.
• Onset of action 8-12 hours.
• Initial dose should be low then increased if necessary, often at 12-24 hour intervals.
• Doses can be exceeded on specialist advice: opioid induced constipation often requires higher doses than in manufacturer's Product Information.
• Oral liquid may be administered via an enteral feeding tube; flush well before and after the dose. Therapeutic effect will be unaffected by jejunal administration.
• Available as: tablets (7.5 mg sennoside B) and oral syrup (7.5 mg/5 mL sennoside B)
• NICE Guidance for Constipation in Children and young people advises the use of polyethylene glycol 3350 based laxatives before introducing stimulates such as senna.

Evidence: [1, 2, 6, 10, 155, 492, 516-519]

**Sodium Citrate**
Use:
- Constipation: Acts as osmotic laxative. Usually combined with faecal softener in micro-enemas.

Dose and routes

**Micolette Micro-enema**

**Enema**, sodium citrate 450 mg, sodium lauryl sulfoacetate 45 mg, glycerol 625 mg, together with citric acid, potassium sorbate, and sorbitol in a viscous solution, in 5-mL

- By rectum: **Child 3–17 years:** 5–10 mL as a single dose

**Micralax Micro-enema**

**Enema**, sodium citrate 450 mg, sodium alkylsulfoacetate 45 mg, sorbic acid 5 mg, together with glycerol and sorbitol in a viscous solution in 5-mL

- By rectum: **Child 3–17 years:** 5 mL as a single dose

**Relaxit Micro-enema**

**Enema**, sodium citrate 450 mg, sodium lauryl sulfate 75 mg, sorbic acid 5 mg, together with glycerol and sorbitol in a viscous solution in a 5mL ingle dose pack with nozzle.

- By rectum: **Child 1 month–17 years:** 5 mL as a single dose (insert only half nozzle length in child 2 years or under).

Notes
- Sodium citrate is an osmotic agent. Sodium lauryl sulfoacetate is a faecal softener.
- As micro-enema, often used in combination with oral laxatives, particularly in neuromuscular disorders, faecal loading and faecal impaction.
- Usually acts within 15 minutes of administration.
- Contraindicated in acute gastro-intestinal conditions.
- Caution: can cause harmful sodium and water retention in susceptible patients.
- Available as: micro-enema (5 mL). All currently marketed preparations include sodium citrate 90 mg/ml, but other constituents vary.
- NICE Guidance for the management of constipation in children and young people advocated the use of polyethylene glycol 3350 containing laxatives and stimulant laxatives before the use of rectal measures. Sodium Citrate is considered the first line rectal measure, in preference to phosphate enemas.

Evidence: [1, 2, 492, 517-519]

**Sodium Picosulfate**
Use:
• Constipation (stimulant laxative).

Dose and routes:
By mouth:
• **Child 1 month–3 years:** Initial dose of 2.5 mg once a day increasing if necessary according to response to a suggested maximum of 10 mg daily,
• **Child 4–17 years:** Initial dose of 2.5 mg once a day increasing if necessary according to response to a suggested maximum of 20 mg daily.

Notes
• Elixir is licensed for use in children; capsules are not licensed for use in children less than 4 years of age.
• Acts as a stimulant laxative.
• NICE Guidance CG99: Constipation in children and young people advocates the use of polyethylene glycol 3350 containing laxatives prior to a trial of a stimulant laxative.
• Onset of action 6-12 hours.
• Contraindicated in intestinal obstruction and dehydration.
• Effectiveness dependent upon breakdown by gut flora – previous effectiveness may therefore be lost during courses of antibiotics and ensuing altered gut flora.
• For administration via an enteral feeding tube: use the liquid preparation; dilute with an equal volume of water. Sodium picosulfate reaches the colon without any significant absorption; therefore, the therapeutic response will be unaffected by jejunal administration.
• Available as: elixir (5 mg/5 mL) and capsules (2.5 mg).

Evidence: [1, 2, 10, 492, 517-519]

**Sucralfate**
Use:
- Stress ulcer prophylaxis.
- Prophylaxis against bleeding from oesophageal or gastric varices; adjunct in the treatment of: oesophagitis with evidence of mucosal ulceration, gastric or duodenal ulceration, upper GI bleeding of unknown cause.
- Haemostasis (topical use).

Dose and route:
Oral
Stress ulcer prophylaxis.Prophylaxis against bleeding from oesophageal or gastric varices; adjunct in the treatment of: oesophagitis with evidence of mucosal ulceration, gastric or duodenal ulceration, upper GI bleeding of unknown cause.
- **Child 1 month-1 year:** 250 mg four to six times daily.
- **Child 2-11 years:** 500 mg four to six times daily.
- **Child 12-14 years:** 1 g four to six times daily.
- **Child 15-17 years:** 1 g six times daily (maximum 8g/day).

Topical
For haemostasis
- Sucralfate suspension 2 g in 10 mL can be applied twice daily topically, for example as mouth wash, orally for oesophageal lesions or rectally for rectal lesions.
- Sucralfate paste can be applied topically for other lesions, made with 2 x 1g tablets crushed in 5 mL aqueous jelly lubricant such as KY jellyor water.

Notes:
- Complex of aluminium hydroxide and sulphated sucrose. In the gut it seems to act by protecting mucosa from acid-pepsin attack. Minimal antacid properties.
- Sucralfate acts locally and is minimally absorbed.
- Not licensed for use in children less than 15 years; tablets are not licensed for prophylaxis of stress ulceration.
- Spread doses evenly throughout waking hours.
- Following reports of bezoar formation associated with sucralfate, the CSM has advised caution in seriously ill patients, especially those receiving concomitant enteral feeds or those with predisposing conditions such as delayed gastric emptying.
- Caution – absorption of aluminium from sucralfate may be significant in patients on dialysis or with renal impairment.
- Administration of sucralfate suspension and enteral feeds via a NG or gastrostomy tube should be separated by at least 1 hour to avoid formation of an insoluble complex that may block fine-bore feeding tubes. By mouth sucralfate should be given 1 hour before mealsto reduce chance of bezoar formation. Suggest diluting with water before administration. Not appropriate for jejunal administration as the site of action is gastric and duodenal.
- Tablets may be crushed and dispersed in 10-15 mL water.
- Available as: oral suspension (1 g in 5mL special order), tablets (1 g).Oral suspension, cream, powder and enema available as special order.

Evidence: [1, 2, 5, 6, 10, 520-525]

**Sucrose**
Use:
• Analgesia for procedural pain in babies.

Dose and routes:
By mouth:
• **Neonate >32 weeks:** 0.5-2mL of 24% sucrose orally 2 minutes before the procedure.Incremental doses 0.1mL can be used up to the maximum of 2mLs. A baby may be given multiple doses during a single procedure. Sucrose can be administered maximally up to 4 times per 24 hours in preterm infants, and up to 8 times in 24 hours in neonates and older babies.

Notes
• The effect of sucrose is enhanced when combined with other non-pharmacological techniques for providing analgesia including non-nutritive sucking and behavioural measures such as swaddling.
• Oral administration using vial dispenser directly onto the anterior portion of the tongue. If needed, the vial can be closed and laid flat after first opening, and be used again in the same infant within a period of 8 hours.
• Contraindicated in babies with oesophageal atresia, trache-oesophageal fistula, confirmed or suspected intra-abdominal pathology (eg. NEC), fructose intolerance.
• Use with caution in infants with altered gag or swallow reflex / swallowing problems, cardio-respiratory instability or any major GI pathology.
• With medical approval, infants who are nil by mouth (NBM) can have the dose of oral sucrose applied with a small swab directly onto the tongue.
• Hypoglycaemia or hyperglycaemia: sucrose given orally, for procedural pain management within the recommended dosing, does not alter blood glucose levels.
• Neonates and infants of mothers maintained on methadone may have altered endogenous opiate systems, resulting in a lack of analgesic effect of oral sucrose in the first days to weeks of life.
• Endotracheal tube in situ: the NBM dose of oral sucrose may be applied directly onto the infant's tongue using a mouth swab.
• Algopedol® is licensed for use in term and preterm infants less than 4 months of age.
• Preservative-free oral solution of sucrose 24% (Algopedol®) in 2 mL vials for single patient use.

Evidence:[3, 526-530]

**Tapentadol**
Use:
• Opioid analgesic

Dose and Route:

Opioid naïve patient: Use the following initial doses

By mouth;

Moderate to severe acute pain (using immediate release preparations)
• **Child 2-17 years (body-weight >16 kg):** 1.25 mg/kg/dose every 4 hours (maximum single dose 50 mg), the dose for children with a high BMI must not exceed the calculated dose for a body-weight at the 97.5 percentile for the given age.The maximum dose per day is 7.5mg per kg body weight ( 6 x single dose)(*see notes below) ≙
• **18 years and older:** Initially 50 mg every 4–6 hours, adjusted according to response, on the first day of treatment, an additional dose of 50 mg may be taken 1 hour after the initial dose; maximum 700 mg in the first 24 hours; maximum 600 mg per day.

Severe chronic pain (using modified-release preparations)

• **18 years and older:** Initially 50 mg every 12 hours, adjusted according to response; maximum 500 mg per day.

Tapentadol is ~3x LESS potent than morphine. Oral 50 mg tapentadol = 15 mg morphine

Notes:
• Dual action centrally acting opioid analgesic; agonist at the μ-opioid receptor and inhibitor of noradrenaline reuptake. The latter enhances the action of the descending pain inhibitory pathway contributing to a synergistic analgesic effect.
• *Tapentadol oral solution is licensed for the relief of moderate to severe acute pain in children from 2 years of age (>16 kg body weight) for a maximum of 72 hours. Use of tablet formulations or for treatment of chronic pain or for a duration >72 hours in children is off-label. Data on safety and efficacy of long-term use in children is not yet available and clinical trials are on-going.
• Tapentadol oral solution, immediate-release and modified-release tablets are licensed in adults for treatment of moderate to severe acute and chronic pain.
• Tapentadol can be taken with or without food.
• Tapentadol oral solution 20 mg/mL can be taken undiluted or diluted in water or any non-alcoholic drink. Use the dosing pipette (5ml subdivided in 0.1ml (2mg) intervals) provided to ensure the exact dose can be accurately measured.
• Tapentadol oral solution can be administered via an enteral feeding tube.
• Tapentadol oral solution contains 2 mg/mL propylene glycol.
• Modified-release tapentadol tablets should be swallowed whole; crushing or chewing will lead to a rapid release of an overdose of tapentadol.
• Dosage adjustment is not required in mild or moderate renal impairment. Use is not recommended in severe renal impairment.
• Dosage adjustment is not required in mild hepatic impairment. Reduce initial dose in moderate hepatic impairment. Use is not recommended in severe hepatic

impairment.

- Based on immediate release tablets – onset of action is less than 1 hour with time to peak serum concentrations around 75 minutes. Duration of action 4-6 hours. Duration of action of modified-release tablets is 12 hours.
- Tapentadol is rapidly and completely absorbed after oral administration. However mean absolute bioavailability after a single-dose administration is ~32% due to extensive first-pass metabolism.
- The major elimination pathway for tapentadol is glucuronide conjugation. Tapentadol does not have any active metabolites. The potential for drug-drug interactions is low. Plasma protein binding is low.
- Potential adverse effects as for other opioids. However GI side-effects are reportedly less than with oxycodone or morphine.
- MHRA/CHM advice: Tapentadol (Palexia): risk of seizures and reports of serotonin syndrome when co-administered with other medicines (January 2019). Tapentadol can induce seizures and should be prescribed with caution in patients with a history of seizure disorders or epilepsy. Seizure risk may be increased in patients taking other medicines that lower seizure threshold, for example, antidepressants such as selective serotonin reuptake inhibitors (SSRIs), serotonin-noradrenaline reuptake inhibitors (SNRIs), tricyclic antidepressants, and antipsychotics.
- Care needed if switching from another μ-agonist to tapentadol as this may cause low-grade opioid withdrawal. As required doses of the original opioid should be used to counter this (e.g. give an immediate release product at 25-50% of the original dose).
- Available as (all Schedule 2 CD)
- Oral solution 20 mg/mL (licensed from 2 years) Palexia®
- Immediate-release tablets 50 mg, 75 mg (licensed from 18 years only) Palexia®
- Modified-release tablets 50 mg, 100 mg, 150 mg, 200 mg, 250 mg (licensed from 18 years only) Palexia®

Evidence: [2, 5, 531-536]

**Temazepam**
Use:
- Sleep disturbance (short term use), especiallywhere anxiety is a cause.
- Premedication before surgery and investigations

Dose and routes
By mouth,
- **Child 12-17 years:** 10-20 mg 1hour before procedures.
- **Adult:** 10–20 mg at night. Dose may be increased to 40 mg at night in exceptional circumstances.

Notes:
- Tablets not licensed for use in children.
- Temazepam is a GABA mimetic, anxiolytic sedative.
- Oral bioavailability at least 90%; peak plasma concentration within 50 minutes of oral administration. Long plasma half life of 8-15 hours.
- Except in the imminently dying, contraindicated in respiratory depression, compromised airway and untreated sleep apnoea syndrome.
- Correct contributory factors to insomnia if possible. Use in association with non drug measures.
- Can cause paradoxical increased hostility and aggression requiring dose adjustment. Can also paradoxically increase anxiety. May impair judgement and reaction time.
- Oral solution may be administered via an enteral feeding tube. If administered via the jejunum monitor for loss of efficacy or increased side-effects.
- Available as: tablets (10 mg, 20 mg) and oral solution (10 mg/5 mL).
- Schedule 3 controlled drug (CD No register).

Evidence: [1, 2, 5, 10]

**Tizanidine**
Use:
- Skeletal muscle relaxant.
- Chronic severe muscle spasm or spasticity.

Dose and routes
Children doses based on WRE
- **Child 18 months–6 years:** 1 mg/day; increase if necessary according to response.
- **Child 7-11 years:** 2 mg/day; increase if necessary according to response.
- **Child >12 years:** as per adult dose [1]: Initially 2 mg increasing in increments of 2 mg at intervals of 3–4 days. Give total daily dose in divided doses up to 3–4 times daily. Usual total daily dose 24 mg. Maximum total daily dose 36 mg.

Children doses based on
- **Child 2-15 years:** 50 microgram/kg/day in divided doses.

Notes:
- Not licensed for use in children.
- Monitor liver function monthly for first 4 months.
- Usually prescribed and titrated by neurologists.
- Timing and frequency of dosing is individual to the specific patient as maximal effect is seen after 2–3 hours and is short-lived.
- Use with caution in liver disease, monitor liver function regularly.
- Use with caution with drugs known to prolong the QT interval.
- Avoid abrupt withdrawal – risk of rebound hypertension and tachycardia.
- Tizanidine plasma concentrations are increased by CYP1A2 inhibitors potentially leading to severe hypotension.
- Drowsiness, weakness, hypotension and dry mouth are common side-effects.
- Tablets may be crushed and administered in water if preferred. May be administered via an enteral feeding tube. Tablets do not disperse readily, but will disintegrate if shaken in 10 mL of water for 5 minutes. The resulting dispersion will flush via an 8Fr NG tube without blockage.There is no specific data for jejunal administration. Administer using the above method. Monitor for increased side-effects or loss of efficacy.
- Available as: tablets (2 mg, 4 mg).

Evidence: [1, 10, 37, 42, 537-542]

**Tramadol**
The WHO now advises there is insufficient evidence to make a recommendation for an alternative to codeine (tramadol) and recommends moving directly from non-opioids (Step 1) to low dose strong opioids for the management of moderate uncontrolled pain in children.

Use:
• Minor opioid with additional non-opioid analgesic actions.

Dose and routes
By mouth:
• **Child 5-11 years:** 1-2 mg/kg every 4-6 hours (maximum initial single dose of 50 mg; maximum of 4 doses in 24 hours). Increase if necessary to a maximum dose of 2 mg/kg (maximum single dose 100 mg) every 6 hours,
• **Child 12–17 years:** Initial dose of 50 mg every 4–6hours. Increase if necessary to a maximum of 400 mg/day given in divided doses every 4-6 hours.

By IM or IV injection or infusion:
• **Child 5-11 years:** 1-2 mg/kg every 4-6 hours (maximum initial single dose of 50 mg; maximum 4 doses in 24 hours). Increase if necessary to a maximum dose of 2 mg/kg (maximum single dose 100 mg) every 6 hours,
• **Child 12-17 years:** Initial dose of 50 mg every 4-6 hours. Dose may be increased if necessary to 100 mg every 4-6 hours. Maximum 600 mg/day in divided doses.

Notes:
• Not licensed for use in children < 12 years.
• By mouth tramadol is about 1/10 as potent as morphine.
• Onset of action after an oral dose is 30 to 60 minutes. Duration of action is 4-9hours.
• Causes less constipation and respiratory depression than the equivalent morphine dose.
• Side effects include diarrhoea, retching, fatigue and paraesthesia.
• Analgesic effect is reduced by ondansetron.
• Soluble or orodispersible tablets may be dissolved in water for administration via an enteral feeding tube or use the oral drops or disperse capsule contents.There are no specific data relating to jejunal administration, but as modified-release preparations are available it is likely that tramadol is absorbed throughout the small bowel. Administer using the above method and monitor for increased side-effects.
• Available as capsules (50 mg, 100 mg), soluble tablets (50 mg), orodispersible tablets (50 mg), m/r tablets and capsules (50 mg, 100 mg, 150 mg, 200 mg, 300 mg, 400 mg), oral drops (100 mg/mL) and injection (50 mg/mL). Care with prescribing as both 12-hourly and 24-hourly m/r preparations are available. Schedule 3 CD (No register Exempt Safe Custody)

Evidence: [1, 2, 10, 48, 65, 409, 543-546]

**Tranexamic acid**
Use:
- Oozing of blood (e.g. from mucous membranes / capillaries), particularly when due to low or dysfunctional platelets.
- Menorrhagia.

Dose and routes
By mouth:
Inhibition of fibrinolysis
- **Child 1 month–17 years:** 15–25 mg/kg (maximum 1.5 g) 2–3 times daily.

Menorrhagia
- **Child 12-17 years:** 1 g 3 times daily for up to 4 days. If very heavy bleeding a maximum daily dose of 4 g (in divided doses) may be used. Treatment should not be initiated until menstruation has started.

By intravenous injection over at least 10 minutes:

Inhibition of fibrinolysis
- **Child 1 month -17 years:** 10 mg/kg (maximum 1 g) 2-3 times a day.

By continuous intravenous infusion:

Inhibition of fibrinolysis
- **Child 1 month-17 years:** 45 mg/kg over 24 hours.

By other routes

Mouthwash 5% solution:
- **Child 6-17 years:** 5-10 mL 4 times a day for 2 days. Not to be swallowed.

Topical treatment:
- Apply gauze soaked in 100mg/mL injection solution to affected area.

Notes:
- Injection not licensed for use in children under 1 year or for administration by intravenous infusion.
- Can cause clot 'colic' if used in presence of haematuria.
- Reduce dose in mild to moderate renal impairment and avoid in severe renal impairment.
- For administration via an enteral feeding tube, the oral suspension (unlicensed) or injection solution is preferred. Tablets may be dispersed in water for tube administration but may not be appropriate for small bore tubes. No specific information for jejunal administration.
- Parenteral preparation can be used topically.
- Available as: tablets (500 mg), syrup (500 mg/5 mL available from 'specials' manufacturers) and injection (100 mg/mL 5 mL ampoules). Mouthwash only as extemporaneous preparation.

Evidence: [2, 6, 547-552]

**Trihexyphenidyl**
Uses:
- Dystonias; Sialorrhoea (drooling); Antispasmodic.

Dose and route:
By mouth
- **Child 3 months-17 years:** Initial dose of 1-2 mg daily in 1-2 divided doses, increased every 3-7 days by 1 mg daily; adjusted according to response and side-effects; maximum 2 mg/kg/daily (maximum 70 mg/daily).

Generally, the doses needed to control drooling are much lower than those needed for dystonias.

Notes:
- Anticholinergic agent thought to act through partially blocking central (striatal) cholinergic receptors.
- Not licensed for use in children.
- Use in conjunction with careful observation and a full non-drug management programme including positioning, massage, holding, distraction, checking for causes of exacerbations etc. Advisable to seek specialist neurological input before use of trihexyphenidyl.
- Side-effects are very common and it is important to start at a low dose and increase gradually to minimise the incidence and severity. Mouth dryness, GI disturbance, blurring of vision, dizziness and nausea can occur in 30-50% patients. Less common side-effects include urinary retention, tachycardia and with very high doses CNS disturbance.
- Use with caution in children with renal or hepatic impairment.
- Onset of action is usually within 1 hour, maximum effect occurs within 2-3 hours and duration of effect ~6-12 hours.
- May take several weeks for maximal effect on dystonic movements to be seen.
- Do not withdraw abruptly in children who have been on long-term treatment.
- Tablets may be crushed and mixed in soft food.
- For administration via a gastrostomy the liquid may be used or the tablets will disperse readily in water. No specific information on jejunal administration. If this route is used monitor for any loss of efficacy or increased side-effects.
- Available as: tablets 2 mg and 5 mg; oral liquid (pink syrup) 5 mg in 5 ml.

Reference: [1, 2, 10, 216, 553-561]

**Vitamin K (Phytomenadione)**
Use:
- Treatment of haemorrhage associated with vitamin-K deficiency (seek specialist advice).

Dose and routes
By mouth or intravenous:
- **Neonate:** 100 micrograms/kg.
- **Child 1 month–17years:** 250-300 micrograms/kg (maximum 10 mg) as a single dose.

Notes:
- Caution with intravenous use in premature infants <2.5 kg.
- IV injections should be given very slowly – risk of vascular collapse. Dilute with Glucose 5%.
- Available as 1 mg capsules, 200 micrograms/ml oral drops and 10 mg/ml injections. Many other forms and strengths available from special order manufacturers.

Evidence:[1, 3, 6]

# Appendix 1: Subcutaneous infusion drug compatibility

Evidence suggests that during end of life care in children, where the enteral route is no longer available, the majority of symptoms can be controlled by a combination of six “essential drugs” [562].

Ketamine can be used as an opioid adjuvant, on the advice of a specialist, and is useful for pain with a neuropathic component or to prevent opioid tolerance or opioid dose escalation [261].

Compatibility for these six drugs is given in the table 1 below[5].

Water for injection is usually the standard choice of diluent to minimise the likelihood of incompatibility. However, NaCl 0.9% should be considered if inflammation at the injection site occurs as long as the drug combinations are compatible[5]. For more detailed information professionals are advised to consult an appropriate reference source[11]

**Table 1: Syringe driver compatibility for two drugs in water for injection [5, 11, 563, 564]**

| Compatible with water for injection over 24 hours | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Diamorphine | Morphine sulphate | Oxycodone* | Midazolam | Cyclizine | Haloperidol | Levomepromazine | Hyoscine hydrobromide | |
| - | - | - | + | A | + | + | + | + |
| - | A | + | A | + | + | + | + | + |
| + | + | A | + | + | A | - | + | + |
| A | + | + | A | + | + | + | + | + |
| A | A | + | + | + | + | + | + | + |
| + | + | + | + | A | - | + | + | + |
| + | + | + | + | + | + | + | + | + |
| Compatible with NaCl 0.9% over 24 hours | | | | | | | | |
| + | + | + | + | - | + | + | No data | Ketamine |

*Data for oxycodone 10mg/mL injection. Oxycodone 50mg/mL has a differentcompatibility profile compared to the lower strength oxycodone and compatability should be considered separately and not extrapolated from one formulation to another[5].

| | |
|---|---|
| A | Laboratory data; physically and chemically compatible in water for injection but crystallization may occur as concentrations of either drug increase |
| + | Compatible in water for injection at all usual concentrations(physically and/or chemically stable) |
| - | Combination not recommended; drugs of similar class or action |

# Appendix 2: Gabapentin to Pregabalin Switch for Neuropathic Pain

Gabapentin and pregabalin have similer mechanisms of action (see APPM monographs). However, gabapentin absorption is saturable, leading to non-linear pharmacokinetics, whereas pregabalin possesses linear pharmacokinetics. As a consequence, switching between gabapentin and pregabalin is not straight-forward and there is very limited evidence in the literature with regard to managing a switch, with no evidence in children[565].

Nonetheless, many pain centres in the UK have developed local protocols for a switch in adults,with no reports of adverse effects [566, 567]. The following conversion factors have been used:

- 1/6 is generally accepted as a standard conversion however a rangeof factors from 1/4 to 1/9 have been used to accomodate practical dosingschedules
- Lower conversion factors of 1/6 to 1/9 used for higher gabapentin dosing are to accommodate the non-linear kinetics of gabapentin

Table 2 details a switch from gabapentin to pregabalin for neuropathic pain in children extrapolated from available adult data. However, caution is requied as efficacy and safety has not been established and clinical judgment with close monitoring is required. Conversion factors used in Table 2 allows for practical dosing.

**Table 2: Gabapentin to Pregabalin switch**

<table>
<tr><th>Age</th><th>Gabapentin</th><th>Conversion factor</th><th>Pregabalin</th></tr>
<tr><td rowspan="3">2-11 years</td><td>5-10mg/kg BD</td><td>1/5</td><td>1-2mg/kg BD<br>(Max single dose 100mg BD)</td></tr>
<tr><td>5-20mg/kg TID</td><td>1/5</td><td>1.5-6mg/kg BD<br>(Max single dose 100mg BD)</td></tr>
<tr><td colspan="3">For conversion:<br>• Calculate the total daily dose of gabapentin by multiplying by 2 or 3 depending on whether it is BD or TID dosing<br>• Divide by 5 to convert to total daily dose of pregabalin<br>• Divide by 2 to get BD dosing for pregabalin<br>• Remember to multiply by weight</td></tr>
<tr><td colspan="4"></td></tr>
<tr><td rowspan="3">>12 years</td><td>300mg TID</td><td>1/4.5</td><td>100mg BD</td></tr>
<tr><td>400–1200 TID</td><td>1/6 – 1/9</td><td>200mg BD</td></tr>
<tr><td colspan="3">Doses of Gabapentin above 400mg TID are capped at an equivalent of Pregabalin 200mg BD to account for the non-linear to linear pharmacokinetic switch. However, Pregabalin can be further increased on response and tolerability to a max of 300mg BD</td></tr>
</table>

Conversion for < 2 years is not provided as the APPM does not currently have evidence for the use of pregabalin in this age group (see pregabalin monograph).

Switching from Gabapentin to Pregabalin for seizure control is outside the scope of the APPM, however manufacturers do advise that doses should be tapered rather than switching directly. Seek advice from neurologists.

# Appendix 3: Benzodiazepines

**(1) Approximate equivalent oral anxiolytic-sedative doses[1,2]**

| Benzodiazepine | Dose |
|---|---|
| Clobazam | 10mg[1,2] |
| Clonazepam | 250micrograms[1,2] |
| Diazepam | 5mg[1,2] |
| Lorazepam | 500micrograms[1,2] |
| Midazolam | 5mg[2] |
| Nitrazepam | 5mg[1,2] |

**(2) Comparative pharmacokinetic data.**

**Diazepam**

| 2 | Bioavailability | Onset of action (mins) | Time to peak plasma concentration (mins) | Duration of action (hrs) | Half-life (hrs) (including active metabolites) |
|---|---|---|---|---|---|
| **Diazepam oral** | >90%[2] | 15-30[3]<br>30-90[2] | 30-90[2] | 3-30[2] | 25-50[2]<br>20-100[3] |
| **Diazepam IV** | | 1-5[2] | ≤15 (oil)[2]<br>≥15 (emulsion)[2] | 15-60[2] | |
| **Diazepam PR** | 65-85%[2]<br>90% | <30[2] | 10-30mins<br><30[2] | | |

*Metabolism and elimination in the neonate are markedly slower than in children. The half-life of diazepam is reduced in younger adults and children (approximately 18 hours)

**Lorazepam**

| 2 | Bioavailability | Onset of action (mins) | Time to peak plasma concentration (mins) | Duration of action (hrs) | Half-life (hrs) (including active metabolites) |
|---|---|---|---|---|---|
| **Lorazepam SL** | | 5[2] | 150[2] | | |
| **Lorazepam oral** | 90%[2,3] | 10-15[2] | 150[2]<br>120[3] | 6-7[2]<br>8[3] | 10-20[2,3] |
| **Lorazepam IV** | | 2-5[3]<br>10 | | 4-6[3] | 12-16 |

**Midazolam**

| 2.3 | Bioavailability | Onset of action (mins) | Time to peak plasma concentration (mins) | Duration of action (hrs) | Half-life (hrs) (including active metabolites) |
|---|---|---|---|---|---|
| **Midazolam buccal** | 85%[2] | 15[2]<br>5[3] | ≤30[2] | | |
| **Midazolam oral** | 40%[2] | 20-30<br>10-30[3] | 30-60[2] | <42<br>20-90mins[3] | 1-4[2]<br>2-5[2,3] |
| **Midazolam SC** | 95%[2] | 5-10[2] | 30[2] | | |
| **Midazolam IV** | | 2-3[2,3] | | 30-60mins[3] | |

**References:**

1. = [1]
2. = [5]
3. = [6]

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