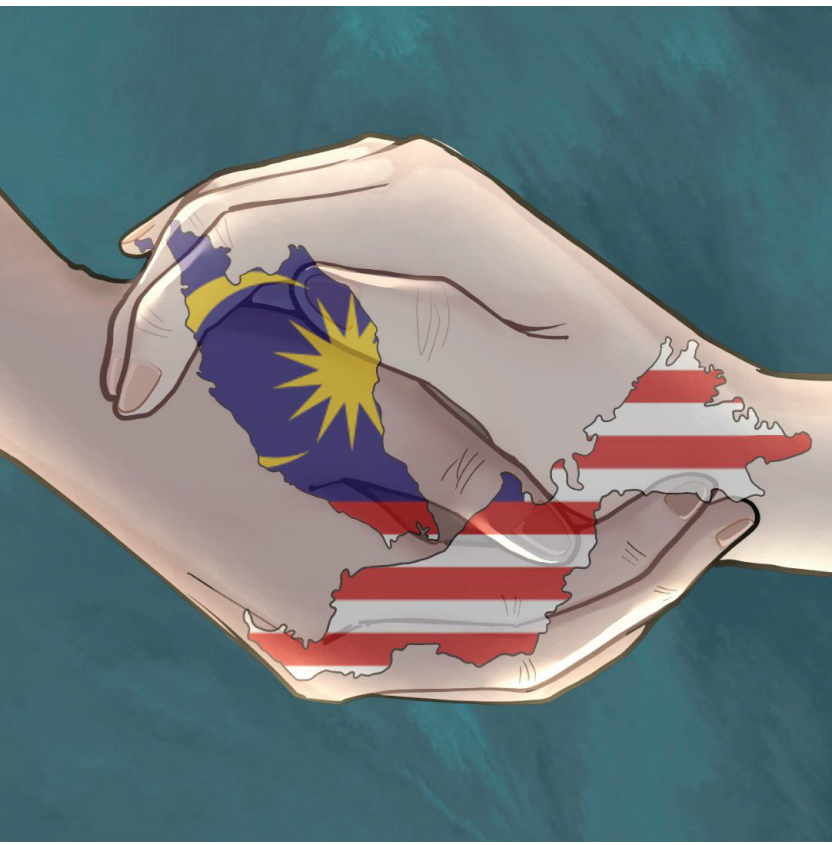
QUICK REFERENCE FOR HEALTHCARE PROVIDERS

MANAGEMENT OF SCHIZOPHRENIA

(SECOND EDITION)



Ministry of Health Malaysia

Malaysian Psychiatric Association

Academy of Medicine Malaysia

KEY MESSAGES

1. Schizophrenia is a major psychiatric disorder that alters an individual's perception, thought, affect & behaviour which are manifested by positive symptoms, negative symptoms, cognitive dysfunction, mood symptoms & motor symptoms.
2. The clinical importance of duration of untreated psychosis is that it is a prognostic factor which can be altered through changes in health service delivery. Thus, health education or promotion, early referral and reducing stigma can address this issue.
3. People with possible schizophrenia should be assessed thoroughly by history taking (self-report & collateral), physical examination, mental state examination & relevant investigations.
4. Substance-induced psychoses associated with cannabis, hallucinogens & amphetamines have an increased risk of transition to schizophrenia. Schizophrenia with co-morbid substance use disorder should be managed by psychiatrist.
5. In acute & relapse prevention phases, the modalities of treatment in schizophrenia are pharmacological, physical, psychosocial & service level interventions.
6. Antipsychotics (APs) should be offered in schizophrenia as it is the mainstay of the treatment in acute & relapse prevention. Second-generation APs are the preferred choice. Clozapine should be offered in treatment-resistant schizophrenia & persistent suicidal risk.
7. Psychosocial interventions should be offered in schizophrenia particularly psychoeducation (which includes early warning signs interventions) & supported employment.
8. Service level interventions e.g. crisis intervention, assertive community treatment, intensive case management & early intervention in psychosis services should be offered for people with schizophrenia.
9. Pre-pregnancy care which includes counselling & multi-disciplinary care during pregnancy should be offered to all women in reproductive age with schizophrenia.
10. Awareness towards patient's rights in schizophrenia should be incorporated in the training & service assessment to health care providers.

This Quick Reference provides key messages & a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Schizophrenia (Second Edition)

Details of the evidence supporting these recommendations can be found in the above CPG, available on the following websites:

Ministry of Health Malaysia: www.moh.gov.my

Academy of Medicine Malaysia: www.acadmed.org.my

CLINICAL PRACTICE GUIDELINES SECRETARIAT

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ASSESSMENT

History Taking	
History of present illness	Reason for current visit
	Current symptom
	Precipitating factor
Past psychiatric history	Hospitalisation & emergency visit for psychiatry issues including substances abuse
	Psychiatric treatment including type & duration, treatment setting, dose of medication, & response & adherence to treatment
	Prior psychiatric diagnosis & symptom including hallucination, delusion, negative symptom, aggressive idea or behaviour, suicidal idea or attempt, impulsivity
Substance use history	Tobacco, alcohol or illicit substance
	Recent or current substance use
Medical history	Allergy or drug sensitivity
	All current medication use & side effect including non-prescribed medication or supplement
	Current or past medical/surgical illness including related hospitalisation
	Traditional & complementary medicine
Family history	History of mental illness including history of suicidal or aggressive behaviour
Social history	Presence of psychosocial stressors e.g. financial, housing, legal, school/occupation, interpersonal relationship, social support, disfiguring or terminal illness
	Exposure to physical, sexual or emotional trauma or childhood abuse
Pre-morbid personality	Temperament, stress management, interest or hobby, relationship, beliefs & personality traits. These include highest & current level of functioning/education/vocation, interpersonal relationship & independent living
Physical examination	Full physical examination including height, weight & body mass index, vital signs, cardiovascular & neurological examinations
Mental State Examination	
Appearance & behaviour	• Level of consciousness • General appearance - body build, posture, cleanliness, dressing, evidence of weight loss, self-harm • Face - eye contact, emotional expression • Posture & movement - posture of depressed or anxious person, agitated, restless, biting nails, etc. • Motor - fast or slow movement, choreoathetosis, tardive dyskinesia, dystonias, abnormal movement • Attitude to examination & social behaviour - friendly, hostile, suspicious

Speech	• Production - spontaneity, speed, loudness, quantity, tone, quality (dysarthria) • Forms - neologism, punning & clang associations, expressive dysphasia • Content - obscene words, poor fluency, coherence, relevance
Mood & affect	• Mood - euthymic, depressed, elevated • Affect - type, range, stability/lability, appropriateness/congruity
Thought disturbances	• Abnormal thought content - delusional, non-delusional a. Delusion b. Non-delusional - phobia, obsession, suicidal ideation • Abnormal thought form - fluency, flow, word • Suicidal thought • Homicidal thought
Perceptual disturbance	• Hallucination - auditory, visual, olfactory, gustatory, tactile • Illusion • Pseudo-hallucination • Depersonalisation, derealisation
Cognitive function	Orientation/memory/attention & concentration/abstract thinking/general knowledge
Judgement	Patient's recognition of consequences of action
Insight	Patient's awareness & understanding of illness & need for treatment

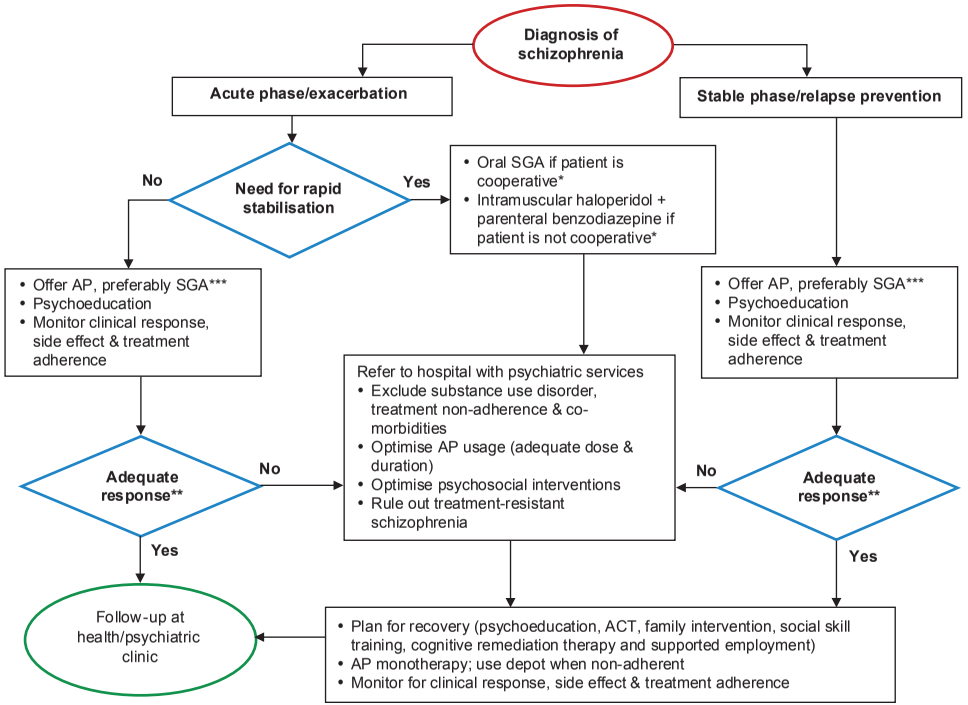
REFERRAL

- For people with schizophrenia treated in primary care, early referral to psychiatric service should be considered in the following circumstances:
  - presence of prodromal or attenuated symptoms
  - unclear diagnosis
  - plan for psychosocial rehabilitation
  - treatment adherence issues
  - poor response to treatment
  - potential violent behaviour to self or others
  - intolerable side effects from medication
  - co-morbid substance use disorder
  - special group e.g. pregnancy, paediatric & geriatric age

DIAGNOSIS

Schizophrenia should be diagnosed using either Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) or International Classification of Diseases and Related Health Problem 10th Revision (ICD-10).

ALGORITHM 1. MANAGEMENT OF SCHIZOPHRENIA

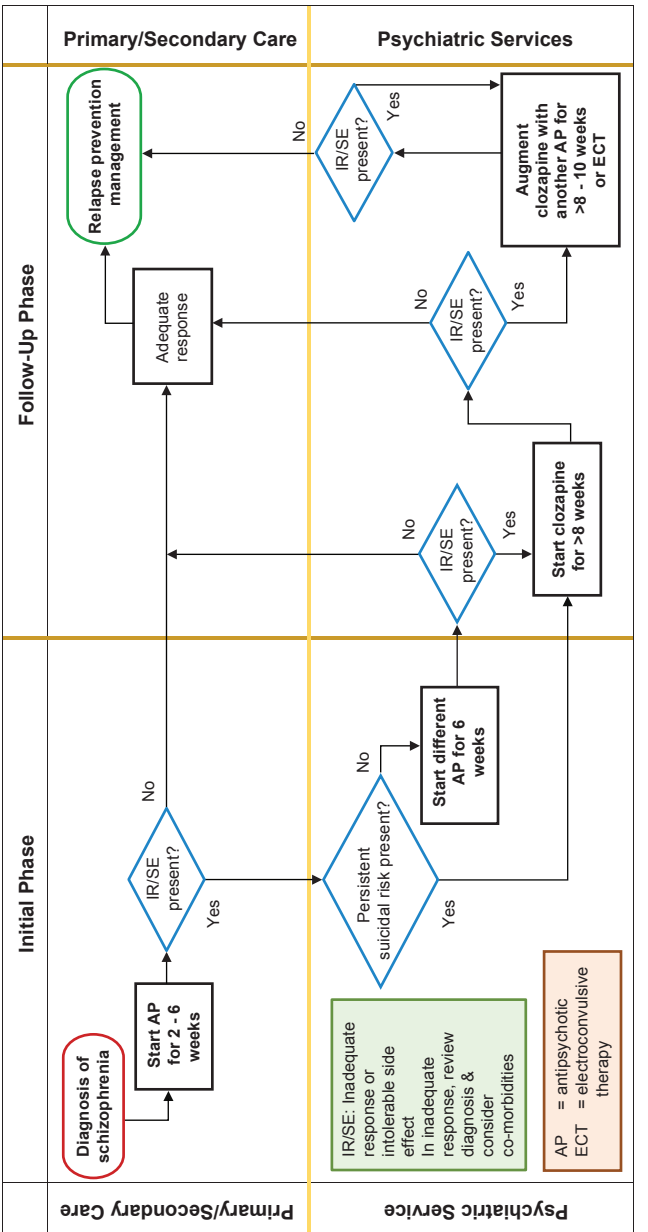


*Cases to be referred urgently to psychiatric services
**Adequate response: A reduction in symptoms as a result of treatment that is associated with clinically significant benefit in functioning and/or quality of life

***Prevention & management of side effect of AP at all phases
- Monitor EPS/akathisia/ weight gain/diabetes/ cardiovascular disease/ sexual dysfunction
- Follow schedule of physical care

AP = antipsychotic
SGA = second-generation AP
ACT = assertive community treatment
EPS = extrapyramidal side effects

ALGORITHM 2. PHARMACOTHERAPY FOR SCHIZOPHRENIA



DOSING REGIMEN FOR ANTIPSYCHOTICS

Oral APs	Daily starting dose (mg/day)	Titration (mg)	Minimum effective dose (mg/day)	Maximum daily dose (mg/day)	Regimen frequency	Pregnancy safety category[a]	Lactation risk[b]
Chlorpromazine	50 - 100	50 - 200/day	200	1000	TDS	C	L3
Haloperidol	2 - 5	2 - 5 every 1 - 7 days	2	20	OD/BD	C	L2
Perphenazine	4 - 8	4 - 8/day	16	24 (64 mg - hospitalised patients)	TDS	C	NA
Sulpiride	200 - 400	200 every 3 - 7 days	400	2400	BD	NA	NA
Amisulpride	50	50 - 100 every 2 - 3 days	300	1200	BD	NA	NA
Aripiprazole	10 - 15	10 - 15 after 2 weeks	10	30	OD	C	L3
Clozapine	12.5	Refer to CPG	300 - 900	900	OD/BD	B	L3
Olanzapine	5 - 10	5/day for every 1 week	5	20	OD	C	L2
Quetiapine	IR: 50 ER: 300	Refer to CPG	IR: 300 - 450 ER: 600 - 800	IR: 750 ER: 800	IR: BD ER: OD	C	L4
Risperidone	1 - 2	1 every 2 - 3 days	2 - 4	16	OD/BD	C	L3

Depot APs	Starting dose	Titration (mg)	Dose range (per injection)	Maximum dose	Interval between injections	Pregnancy safety category[a]	Lactation risk[b]
Flupenthixol decanoate	20 mg (elderly - quarter to half adult dose)	Test dose 20 mg, then 20 - 40 mg after at least 7 days, then 20 - 40 mg every 2 - 4 weeks	50 mg every 4 weeks to 300 mg every 2 weeks	400 mg/week	2 - 4 weeks	C	NA
Fluphenazine decanoate	12.5 mg (elderly - 6.25 mg)	Test dose 12.5 mg, then 12.5 - 100 mg after 4 - 7 days, then 12.5 - 100 mg every 14 - 35 days	12.5 - 100 mg	100 mg/2 weeks	14 - 35 days	NA	L3
Zuclopenthixol decanoate	100 mg (elderly - quarter to half adult dose)	Test dose 100 mg, then 200 - 500 mg after at least 7 days, then 200 - 500 mg every 1 - 4 weeks	200 - 500 mg every 1 to 4 weeks	600 mg/week	1 - 4 weeks	NA	NA

IR: immediate release, ER: extended release, OD: once daily, BD: twice daily, TDS: thrice daily, NA: not available

[a]United States Food & Drug Administration (US FDA) categorisation of risk of drug use in pregnancy:

A= Controlled studies fail to demonstrate a risk to the foetus in the first trimester & the possibility of foetal harm remains remote

B= Either animal-reproduction studies have not demonstrated a foetal risk but there is no controlled in human

C= Either study in animals have revealed adverse effects on the foetus (teratogenic or embryocidal or other) & there are no controlled studies in human

D= There is positive evidence of human foetal risk

X= Studies in animals or human beings have demonstrated foetal abnormalities

[b]American College of Obstetricians and Gynecologists lactation risk categories: L1= Safest; L2= Safer; L3= Moderately safe; L4= Possibly hazardous; L5= Contraindicated

COMMON SIDE EFFECTS OF ANTIPSYCHOTICS & THEIR MANAGEMENT STRATEGIES

Side effects	Management strategies			Comments
	First choice	Second choice	Third choice	
Constipation	• Ensure adequate fibre, fluid & exercise • Osmotic laxatives (e.g. lactulose)/ stimulant laxatives (e.g. senna)	Change to AP with lower risk	-	• Clozapine-induced gastrointestinal hypomotility is a common AE, 3 times that seen with other APs • Avoid bulk-forming laxatives • Stop other medicines that may contribute to constipation if possible
EPS: Dystonia	Anticholinergic medication (e.g. trihexyphenidyl, procyclidine)	Antihistaminic medication (e.g. diphenhydramine)	Benzodiazepine (e.g. clonazepam, diazepam)	Where symptoms do not respond to simpler measures, including switching to an AP with low propensity for EPS, botulinum toxin may be effective
EPS: Pseudo-parkinsonism (tremor, rigidity, bradykinesia)	Reduce dose of AP	Change to AP with lower risk	Anticholinergic medication (e.g. trihexyphenidyl, benztropine)	Majority of patients do not require long-term anticholinergic medication (its use should be reviewed at least every 3 months & not to be not to be taken at night)
Akathisia	Reduce dose of AP	Change to AP with lower risk	Beta-blockers (e.g. propranolol)	• 5-HT_2 antagonists e.g. cyproheptadine, mirtazapine, trazodone & mianserin may help • Antimuscarinic or benzodiazepine may also be useful • Anticholinergics are generally unhelpful
Tardive dyskinesia	• Reduce dose of AP • Stop anticholinergic if prescribed	Change to AP with lower risk	Valbenazine, tetrabenazine or deutetrabenazine	Change to AP with lower propensity for TD e.g. clozapine & quetiapine.
Sedation	Dose at night before sleep	Reduce dose	Change to less sedating APs	Stimulants have unclear benefit
Diabetes mellitus	Change to AP with lower risk (haloperidol, aripirazole, amisulpride, ziprasidone)	Treat accordingly & refer to CPG Management of Type 2 Diabetes Mellitus (6th Edition)		-
Weight gain	Behavioural modification (diet, exercise)	Behavioural modification + change AP	Add aripiprazole to existing treatment	Medication e.g. metformin should be considered only where behavioural methods or switching of AP have failed or where obesity presents clear and immediate physical risk to the patient
Dyslipidaemia	Behavioural modification (diet, exercise) + change AP	Treat accordingly & refer to CPG on Management of Dyslipidaemia (5th Edition)		-
Hyperprolactinaemia	Change to 'prolactin-sparing' APs (aripiprazole, quetiapine, clozapine)	Add aripiprazole	Consider dopamine agonists or referral to endocrinologist	Metformin has been shown to improve prolactin-related symptoms & levels
Orthostatic hypotension	Adjust dose or slow dose titration	Adequate hydration	Change to AP with lower risk	Avoid APs that are potent α_1-adrenergic receptor antagonist (clozapine, quetiapine) and/or concomitant intake of medications that can reduce BP
ECG changes - QT prolongation	• >440 ms (men)/>470 ms (women) but <500 ms: reduce dose or switch AP with lower risk • >500 ms: ○ repeat ECG ○ stop suspected causative drugs & switch to lower risk AP ○ immediately refer to cardiologist • Abnormal T-wave morphology: review treatment, consider reduce dose or switching to lower risk AP			Risk is high with any intravenous AP or combination of APs with doses exceeding recommended maximum