QUICK REFERENCE FOR HEALTHCARE PROVIDERS

MANAGEMENT OF
SYSTEMIC LUPUS ERYTHEMATOSUS

Ministry of Health
Malaysia

Malaysian Society of
Rheumatology

Academy of Medicine
Malaysia

KEY MESSAGES

1. Systemic lupus erythematosus (SLE) is a chronic autoimmune multisystem disorder with diverse & complex clinical manifestations characterised by inflammation in a variety of organs. It has a relapsing-remitting course with a very unpredictable prognosis & considerable morbidity.
2. Diagnosis of SLE should be based on clinical manifestations supported by laboratory findings following exclusion of alternative diagnoses.
3. All patients with SLE should have clinical assessments of disease activity using validated assessment tools.
4. Patients with SLE should practise sun avoidance &, use protective clothing & broad-spectrum sunscreen with at least sun protection factor (SPF) 50.
5. Corticosteroids should be used for acute flare in SLE; the dose should be minimised accordingly & discontinued whenever possible.
6. All patients with SLE should be on hydroxychloroquine (HCQ) unless intolerant or contraindicated.
7. Immunosuppressants should be considered as add-on therapy to patients with SLE not responding to HCQ alone or in combination with corticosteroids, or when corticosteroids doses cannot be tapered.
8. Infection in patients with SLE should be identified early & treated accordingly.
9. All women with SLE in the reproductive age group should receive pre-pregnancy counselling.
10. In SLE with pregnancy, HCQ, azathioprine, calcineurin inhibitors & low dose corticosteroids should be continued.

This Quick Reference provides key messages & summarises the main recommendations in the Clinical Practice Guidelines (CPG) Management of Systemic Lupus Erythematosus.

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
Malaysian Society of Rheumatology: msr.my

CLINICAL PRACTICE GUIDELINES SECRETARIAT
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Medical Development Division, Ministry of Health Malaysia
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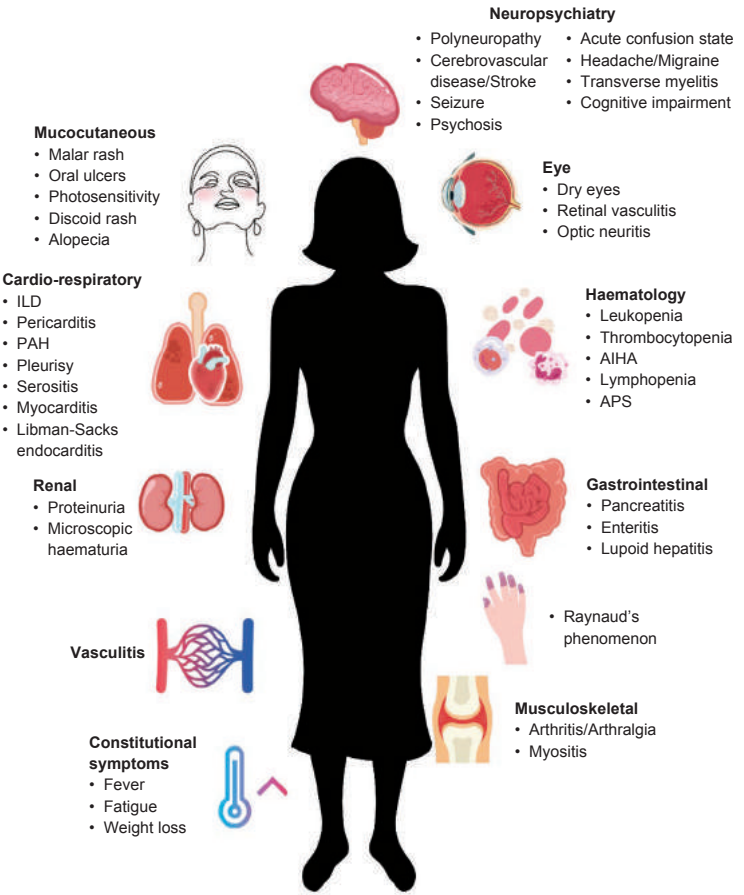
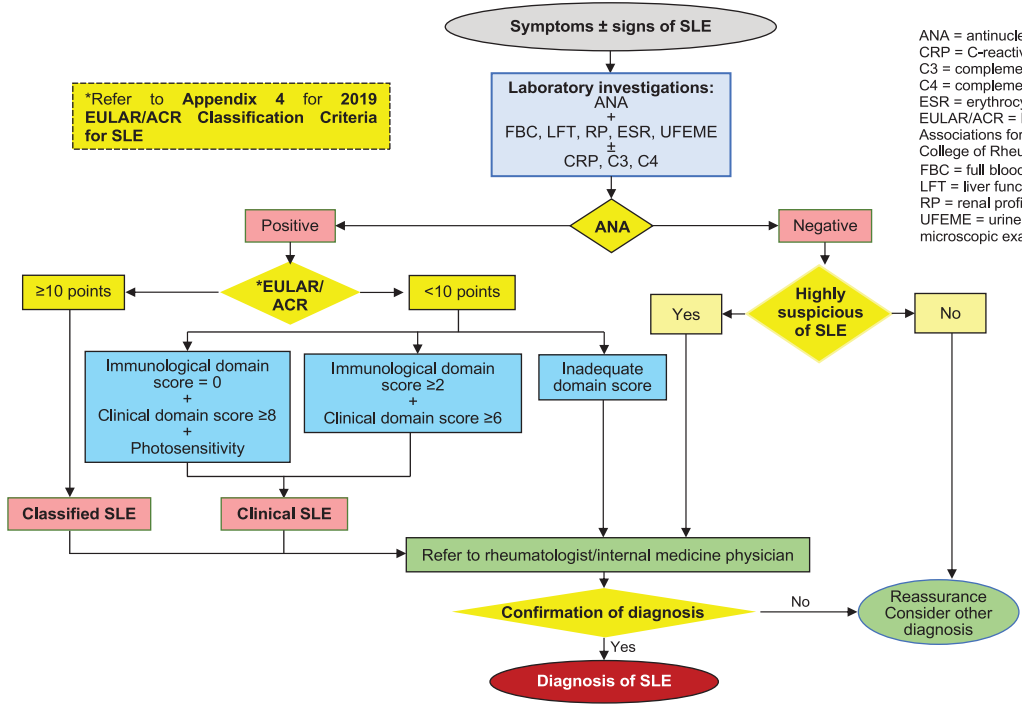
CLINICAL MANIFESTATIONS



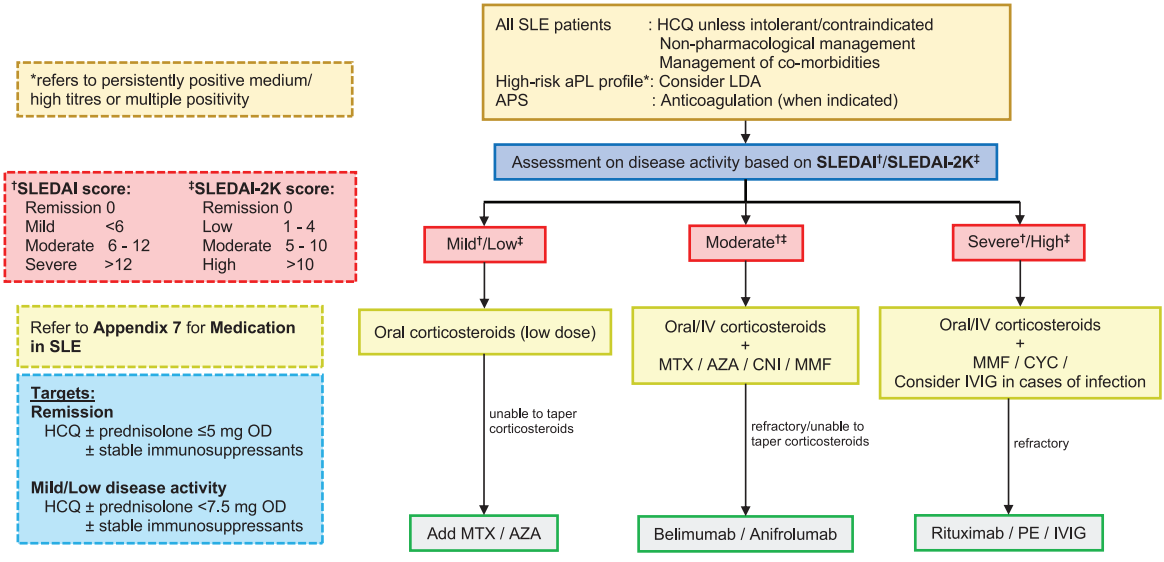
AIHA = autoimmune haemolytic anaemia; APS = antiphospholipid syndrome; ILD = interstitial lung disease; PAH = pulmonary arterial hypertension

ALGORITHM 1: DIAGNOSIS OF SLE



ANA = antinuclear antibodies
CRP = C-reactive protein
C3 = complement 3
C4 = complement 4
ESR = erythrocyte sedimentation rate
EULAR/ACR = European Alliance of Associations for Rheumatology/American College of Rheumatology
FBC = full blood count
LFT = liver function test
RP = renal profile
UFEME = urine full examination & microscopic examination

ALGORITHM 2: TREATMENT OF NON-RENAL SLE



*refers to persistently positive medium/ high titres or multiple positivity

†**SLEDAI score:**

Remission	0
Mild	<6
Moderate	6 - 12
Severe	>12

‡**SLEDAI-2K score:**

Remission	0
Low	1 - 4
Moderate	5 - 10
High	>10

Refer to **Appendix 7** for **Medication in SLE**

Targets:
Remission
HCQ ± prednisolone ≤5 mg OD
± stable immunosuppressants

Mild/Low disease activity
HCQ ± prednisolone <7.5 mg OD
± stable immunosuppressants

aPL = antiphospholipid antibody
APS = antiphospholipid syndrome
AZA = azathioprine
CNI = calcineurin inhibitors
CYC = cyclophosphamide
HCQ = hydroxychloroquine
IV = intravenous
IVIG = intravenous immunoglobulin
LDA = low dose aspirin
MMF = mycophenolate mofetil
MTX = methotrexate
OD = once a day
PE = plasma exchange
SLEDAI = Systemic Lupus Erythematosus Disease Activity Index
SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index - 2000

TREATMENT

- Principles of SLE treatment are to achieve:
  - disease remission
  - disease flare prevention
  - organ damage prevention
  - quality of life improvement
  - minimisation of drug side-effects
- If complete remission cannot be achieved, the lowest possible disease activity in all organs involved should be targeted.

FREQUENCY & PARAMETERS FOR MONITORING

Assessments	At first visit	Patients with active disease should be reviewed at least every 1 - 3 months	Patients with stable/ low disease activity should be reviewed every 6 - 12 months
Clinical			
History	✓	✓	✓
Vital signs	✓	✓	✓
Clinical examination	✓	✓	✓
Drug review	✓	✓	✓
Blood tests			
FBC	✓	✓	✓
RP	✓	✓	✓
LFT	✓	✓	✓
CRP	✓	✓[a]	✓[a]
ESR	✓	✓	✓
Bone profile	✓[a]	✓[a]	✓[a]
Vitamin D3	✓[a]	-	✓[a]
Immunology/serology			
ANA	✓	-	-
Anti-dsDNA	✓	✓[a]	✓[a]
C3/C4 levels	✓	✓[a]	✓[a]
aPL	✓	✓[a]	✓[a,p]
ENA	✓	✓[a]	✓[a,p]
Immunoglobulin A, G, M	✓[a]	✓[a]	✓[a]
Direct Coombs' test	✓	✓[a]	✓[a]
Urine			
UFEME	✓	✓	✓
Urine random protein: creatinine ratio OR 24-hour urine protein	✓[a]	✓[a]	✓[a]

✓ = indicated; ✓[a] = when indicated; ✓[a,p] = when indicated during pregnancy; - = not indicated; anti-dsDNA = anti-double stranded deoxyribonucleic acid; ENA = extractable nuclear antigen

PRE-PREGNANCY & PREGNANCY

- It is important to ensure that patients with SLE who plan to get pregnant achieve the following:
  - remission or low disease activity for ≥6 months
  - well-controlled blood pressure
  - estimated glomerular filtration rate (eGFR) >60 mL/min/1.73 m^2
  - proteinuria <1 g/day (proteinuria 2+)
- All pregnant SLE patients:
  - especially those with positive aPL should be referred to the rheumatologist at antenatal booking
  - should be under combined care of rheumatologist/physician, feto-maternal specialist/obstetrician & family medicine specialist

REFERRAL

- All cases with clinical suspicion of SLE should be promptly referred to rheumatologists for confirmation of the diagnosis & further management.

Indications for referral to rheumatologist includes to confirm diagnosis, assess disease activity & severity, provide general disease management, manage organ involvement or life-threatening disease & manage/prevent treatment toxicities. Other specific circumstances that require referral include APS, pregnancy & perioperative management.

For moderate to severe organ involvement, patients with SLE will require multidisciplinary care involving various subspecialties.

Indications for urgent referral are as listed below:
- for patients not diagnosed with SLE yet -
  - clinical suspicion of SLE with major or multisystem organ involvement
- for patients diagnosed with SLE -
  - disease flare of major organ or multisystem organ involvement
  - pregnancy (at booking)
  - severe infection

MEDICATION

Drugs	Recommended Dosages	Common Adverse Events	Pregnancy & Lactation
Corticosteroids			
Prednisolone	Low dose: <7.5 mg OD PO Intermediate dose: 7.5 - 30 mg OD PO High dose: >30 mg OD PO	• Elevated blood pressure • Infection • Acne • Hyperglycaemia • Dyslipidaemia • Osteoporosis • Muscle weakness • Fluid retention • Weight gain	Pregnancy Can be continued at lowest effective dose Lactation Compatible
Methylprednisolone	IV infusion ≥250 mg/day for 1 - 3 days (pulse)		
Hydrocortisone	IV 50 - 100 mg TDS/QID		
Antimalarial			
Hydroxychloroquine	200 - 400 mg OD PO (5 mg/kg/day actual body weight) Requires renal adjustment based on CrCl	• Skin hyperpigmentation • Prolonged QT interval • Abnormal FBC • Abnormal liver enzymes • Retinal toxicity	Pregnancy Compatible Lactation Compatible
Immunosuppressants			
Azathioprine	50 - 250 mg as a single dose or divided into 2 doses PO (1 - 2.5 mg/kg/day)	• GI intolerance • Abnormal FBC • Abnormal liver enzyme	Pregnancy Compatible Lactation Compatible
Methotrexate	7.5 - 25 mg weekly PO Requires renal adjustment based on CrCl	• Abnormal liver enzyme • Abnormal FBC • GI intolerance • Alopecia • Mucositis • Photosensitivity, rash • Interstitial pneumonia	Pregnancy • Contraindicated • Stop at least 3 months prior to conception Lactation Contraindicated
Ciclosporin	2.5 - 4 mg/kg/day in 2 divided doses PO	• Elevated blood pressure • Tremor • Hirsutism/hypertrichosis • Renal impairment • Gum hypertrophy • Abnormal liver enzymes • GI symptoms	Pregnancy Compatible Lactation Compatible
Tacrolimus	1 - 3 mg/day in 2 divided doses PO (0.1 - 0.15 mg/kg/day) *need to assess drug levels (TDM)	• GI intolerance • Peripheral oedema • Alopecia • Abnormal FBC • Renal impairment	Pregnancy Compatible Lactation Compatible
Cyclophosphamide	50 - 100 mg OD PO IV infusion follows NIH or Euro-Lupus regimen	• GI intolerance • Alopecia • Abnormal FBC	Pregnancy Contraindicated Lactation Contraindicated
Mycophenolate mofetil	1 - 1.5 g BD PO	• GI intolerance • Abnormal FBC	Pregnancy • Contraindicated • Stop at least 6 weeks prior to conception Lactation Contraindicated

BD = bis in die (twice a day); CrCl = creatinine clearance; g = gram; GI = gastrointestinal; kg = kilogram; mg = milligram; NIH = National Institutes of Health; PO = per os (by oral); QID = quarter in die (four times a day); TDM = therapeutic drug monitoring; TDS = ter die sumendum (three times a day)