QUICK REFERENCE FOR HEALTHCARE PROVIDERS

MANAGEMENT OF MAJOR DEPRESSIVE DISORDER

(Second Edition)

Ministry of Health Malaysia

Malaysian Psychiatric Association

Academy of Medicine Malaysia

KEY MESSAGES

1. Major Depressive Disorder (MDD) is characterised by persistent low mood, loss of interest, difficulty in concentrating, sleep disturbances, fatigue & in more severe form, functional impairment & suicidal ideations.
2. Screening for depression using Whooley Questions in primary care may be considered in people at risk (refer to Screening & Assessment).
3. Screening for perinatal depression may be done in two-stage approach. Use brief screening tools e.g. Patient Health Questionnaire-2 or Whooley Questions in the first stage & followed by Edinburgh Postnatal Depression Scale.
4. Psychoeducation should be offered early & continuously throughout the management of MDD.
5. Psychosocial interventions & psychotherapy should be offered throughout all severity, while combination of pharmacological intervention & psychotherapy should be offered in moderate to severe MDD.
6. Second-generation antidepressants may be considered as the initial treatment medication, while the older antidepressants e.g. tricyclic antidepressants (TCAs) & monoamine oxidase inhibitors (MAOIs) are considered for subsequent choice (refer to **Table 1**).
7. Short-term benzodiazepines (not more than 2 - 4 weeks) may be used in MDD with anxiety, agitation or insomnia.
8. Antidepressants should be continued for at least 6 - 9 months after remission & at least 2 years if there is high risk of relapse or recurrence.
9. Women in their reproductive age with MDD should receive pre-pregnancy care. Benefits & risks of treatment to mother & baby in both short- & long-term; & possible consequences of no treatment or if treatment is changed or stopped abruptly should be considered throughout perinatal period (refer to **Algorithm 2**).
10. Monitoring requirements for some drugs are needed (refer to **Table 2**).

This Quick Reference provides key messages & a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Major Depressive Disorder (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
Malaysian Psychiatric Association: www.psychiatry-malaysia.org/

CLINICAL PRACTICE GUIDELINES SECRETARIAT
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SCREENING & ASSESSMENT

Screening for MDD should be done in high risk individuals* using the following tool:

- Whooley Questions on depression:
  1. "During the past month, have you often been bothered by feeling down, depressed or hopeless?"
  2. "During the past month, have you often been bothered by having little interest or pleasure in doing things?"

*High risk individuals are:

- first-degree relative with history of depression
- chronic pain (e.g. backache, headache)
- experiencing major life changes
- multiple vague symptoms
- loss of interest in sexual activity
- chronic diseases
- impoverished home environment
- pregnant or postpartum period
- sleep disturbance
- old age
- obesity
- financial constrain
- socially-isolated
- substance abuse e.g. alcohol, illicit drugs

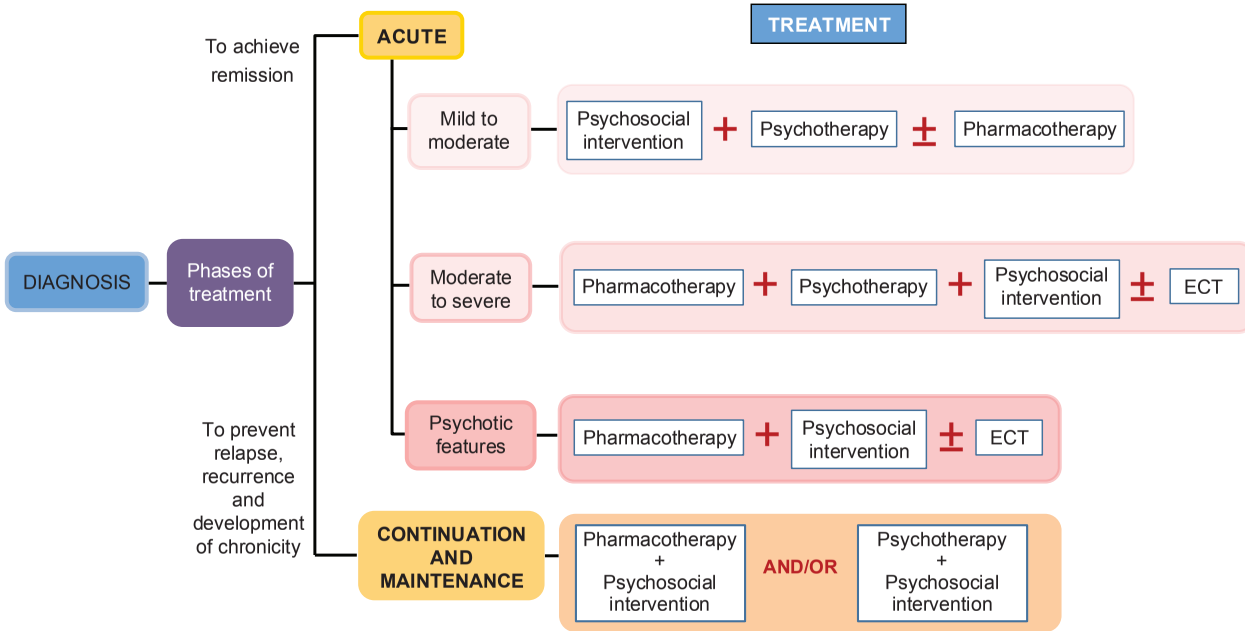
The diagnosis of MDD is made using internationally accepted diagnostic criteria i.e. either the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) or the ICD-10 Classification of Mental and Behavioural Disorder: Clinical Description & Diagnostic Guidelines.

- The severity of MDD should be assessed to determine the mode of treatment.

REFERRAL CRITERIA

- In local setting, referral to the psychiatric services may be done through the emergency & trauma department or directly to the psychiatric clinic. Indications for referral to psychiatric services include:
  - unsure of diagnosis
  - attempted suicide
  - active suicidal ideas
  - failure of treatment
  - advice on further treatment
  - clinical deterioration
  - recurrent episode within 1 year
  - psychotic symptoms
  - severe agitation
  - self-neglect

ALGORITHM 1. TREATMENT OF MAJOR DEPRESSIVE DISORDER



ECT = electroconvulsive therapy

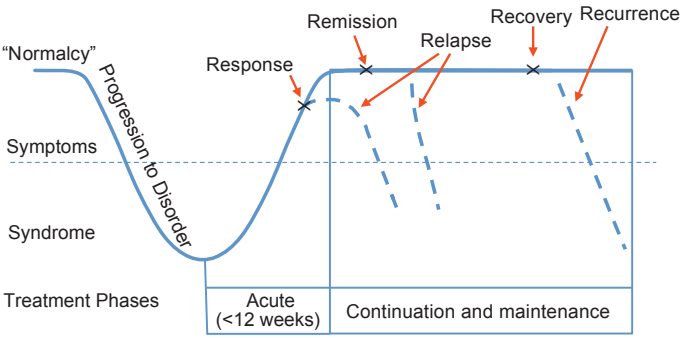


FIGURE 1. PHASES OF TREATMENT OF MAJOR DEPRESSION

TREATMENT

ACUTE PHASE

- **Mild To Moderate**

- In mild to moderate MDD, psychosocial intervention & psychotherapy should be offered, based on resource availability, but not restricted to the following:
  - cognitive behavioural therapy
  - interpersonal therapy
  - problem-solving therapy
  - behavioural therapy
  - internet-based cognitive behavioural therapy

- **Moderate To Severe**

- In moderate to severe MDD, a combination of pharmacotherapy & psychotherapy should be offered.
- In moderate to severe MDD, exercise may be offered as an adjunct treatment.
- In moderate to severe MDD, one of the second-generation antidepressants should be prescribed:
  - selective serotonin reuptake inhibitors
  - serotonin noradrenaline reuptake inhibitors
  - noradrenergic and specific serotonergic antidepressants
  - melatonergic agonist and serotonergic antagonist
  - multimodal serotonin modulator
  - noradrenaline/dopamine-reuptake inhibitor

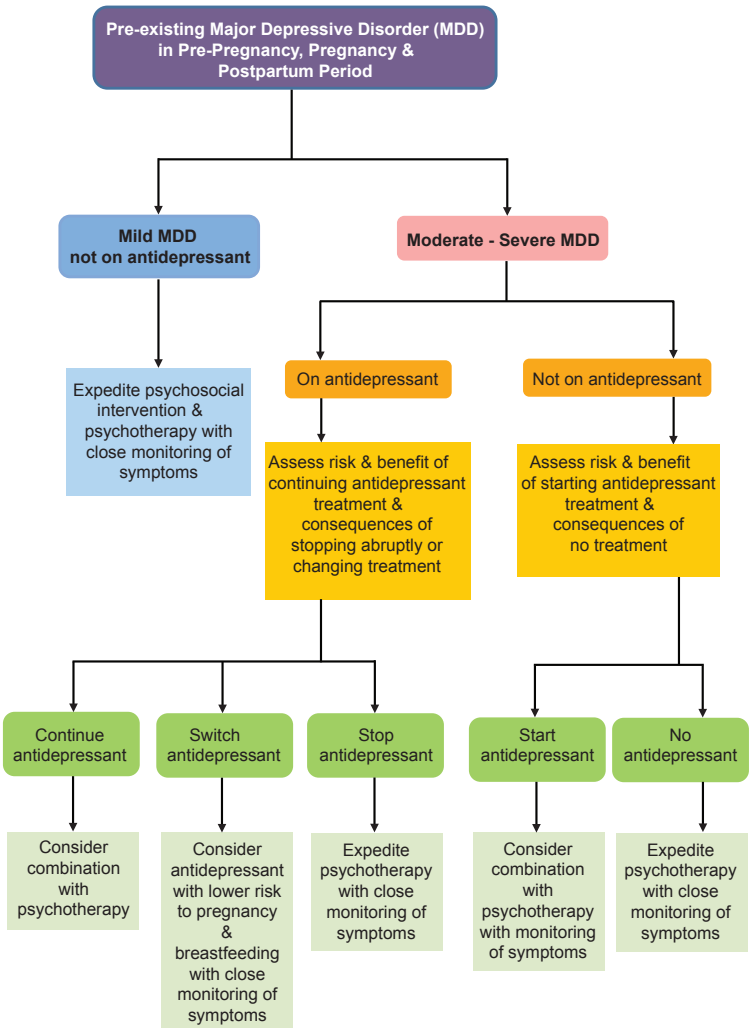
MAINTENANCE & CONTINUATION PHASE

- Antidepressants should be continued for at least 6 - 9 months after remission, & at least 2 years if there is high risk of relapse or recurrence.

TABLE 1. COMMONLY USED ANTIDEPRESSANTS, DOSAGES & ADVERSE EFFECTS

Name	Starting Usual dose (mg/day)	Usual dose range (mg/day)	Common adverse effects	Pregnancy Category
Selective serotonin reuptake inhibitors (SSRIs)				
Escitalopram	10	10 - 20	Nausea, diarrhoea, headache, constipation, dry mouth, insomnia, somnolence	C
Fluoxetine	20	20 - 60		C
Fluvoxamine	50 - 100	50 - 300		C
Sertraline	50	50 - 200		C
Serotonin & noradrenaline reuptake inhibitors (SNRIs)				
Duloxetine	20 - 60	60 - 120	Hypertension, dizziness, constipation, dry mouth, insomnia, somnolence, nausea, anorexia, sexual dysfunction	C
Venlafaxine	37.5 - 75	75 - 225 (up to 375 mg for in-patients)		C
Noradrenergic & specific serotonergic antidepressant (NaSSA)				
Mirtazapine	15	15 - 45	Constipation, weight gain, dry mouth, oedema, dizziness, increased liver enzyme levels, jaundice, somnolence, hyponatraemia	C
Melatonergic agonist & serotonergic antagonist				
Agomelatine	25	25 - 50	Increased liver enzymes, constipation, nausea, diarrhoea, vomiting, abdominal pain, dry mouth, headache, dizziness, insomnia, somnolence, fatigue, jaundice, tremor, agitation, blurred vision	B
Multimodal serotonin modulator				
Vortioxetine	10	10 - 20	Constipation, nausea, diarrhoea, vomiting, dry mouth, night sweating, dizziness, sexual dysfunction	B
Tricyclics & tetracylic antidepressants (TCAs)				
Amitriptyline	50 - 75	75 - 150 (up to 300 mg for in-patients)	Constipation, hypotension, tachycardia, arrhythmias, dizziness, drowsiness, tremor, dry mouth, blurred vision, urinary retention	C
Dothiepin	50 - 75	75 - 225		C
Imipramine	25 - 50	50 - 200 (up to 300 mg for in-patients)		C
Monoamine oxidase inhibitors (MAOIs)				
Moclobemide	150	150 - 600	Hypertensive crisis, tachycardia, dizziness, headache, abdominal pain, nausea, diarrhoea, vomiting, sleep disturbances, constipation, somnolence, agitation, anxiety, increased appetite, blurred vision	B

ALGORITHM 2. TREATMENT OF PRE-EXISTING MAJOR DEPRESSIVE DISORDER IN PRE-PREGNANCY, PREGNANCY & POSTPARTUM PERIOD



FOLLOW-UP & MONITORING

TABLE 2. ONGOING MONITORING DURING TREATMENT OF MDD

Parameter	Agent	Frequency of the monitoring parameter	Comments
Body Mass Index & waist circumference	NASSAs MAOIs TCAs	At baseline & at 6-monthly	
Blood pressure	Venlafaxine TCAs MAOIs	At baseline, with significant dose increase & 3 to 6-monthly after stabilisation	Closer monitoring of MAOIs in first weeks until tolerance occurs
Electro-cardiogramme for QT prolongation	TCAs	At baseline, after initial dose titration & at change of dose	In individuals over 45 years of age or with cardiovascular (CV) disorders
	SNRIs SSRIs	At baseline	In individuals with CV risk
Liver function test	Agomelatine	At baseline, 3, 6, 12 & 24 weeks after initiation dosage, after dosage increment or when clinically indicated	Treatment should be discontinued if transaminases exceed three times upper limit of normal
Electrolytes	SSRIs Mirtazapine SNRIs TCAs	At baseline & at 1 month after treatment initiation or clinically indicated in high risk groups*	• More frequent monitoring in elderly or those with existing hyponatraemia • Need to monitor together with urine & serum osmolality since SSRIs can induce hypovolemic hyponatremia via Syndrome of Inappropriate Antidiuretic Hormone Secretion
Full blood count	Mirtazapine Mianserin	If clinically indicated	To detect blood dyscrasia (e.g. neutropenia & thrombocytopaenia)
Bone mineral density	SSRIs	As clinically indicated in high risk groups for osteoporosis**	Refer to Fracture Risk Assessment Tool Score in Ministry of Health CPG Management of Osteoporosis, 2012

*previous history of antidepressant-induced hyponatremia, advanced age, low body weight, thiazide & carbamazepine use

**based on Fracture Risk Assessment Tool Score