MANAGEMENT OF MAJOR DEPRESSIVE DISORDER (MDD)

QUICK REFERENCE FOR HEALTH CARE PROVIDERS
KEY MESSAGES

• Major depressive disorder (MDD) is a significant mental health problem that disrupts a person’s mood and affects his psychosocial and occupational functioning.

• It is often under-recognised and 30-50% of MDD cases in primary care and medical settings are not detected.

• Suicide occurs in up to 15% of hospitalised patients with severe MDD.

• Management of MDD is either non-pharmacological and/or pharmacological according to severity of the disorder.

• Non-pharmacological treatment of MDD includes supportive therapy, problem-solving therapy, counselling, cognitive behavioural therapy (CBT), interpersonal therapy (IPT) and computerised CBT (CCBT).

• Selective Serotonin Reuptake Inhibitors (SSRIs) should be considered as the first line if medication is indicated.

• Clinicians may consider prescribing benzodiazepines as an adjunct to antidepressants. Avoid giving them alone, and they should not be given for more than 2 to 4 weeks as far as possible.

This Quick Reference provides key messages and a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Major Depressive Disorder (2007).

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

Ministry of Health Malaysia : http://www.moh.gov.my
Academy of Medicine : http://www.acadmed.org.my or
Malaysian Psychiatric Association : http://www.psychiatry-malaysia.org
SCREENING FOR DEPRESSION

The following two **initial** questions may be used to screen for 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?”

If the answer is “Yes” to one or both questions, assess the patient for depression.

ICD-10 DIAGNOSTIC GUIDELINES FOR DEPRESSIVE EPISODE/DEPRESSIVE DISORDER

**Typical symptoms of depressive episodes**
- Depressed mood
- Loss of interest and enjoyment
- Reduced energy

**Common symptoms of depressive episodes**
- Reduced concentration and attention
- Reduced self-esteem and self-confidence
- Ideas of guilt and unworthiness
- Bleak and pessimistic views of the future
- Ideas or acts of self-harm or suicide
- Disturbed sleep
- Diminished appetite

**Mild depressive episode**
- At least 2 typical symptoms plus 2 common symptoms; minimum duration of whole episode is at least 2 weeks

**Moderate depressive episode**
- At least 2 typical symptoms plus 3 common symptoms; minimum duration of whole episode is at least 2 weeks

**Severe depressive episode without psychotic symptoms**
- All 3 typical symptoms plus at least 4 common symptoms; minimum duration of whole episode is at least 2 weeks
MANAGEMENT OF MAJOR DEPRESSIVE DISORDER

CRITERIA FOR REFERRAL

<table>
<thead>
<tr>
<th>Criteria for referral to psychiatric services</th>
<th>Criteria for admission</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Unsure of diagnosis</td>
<td>• Risk of harm to self</td>
</tr>
<tr>
<td>• Attempted suicide</td>
<td>• Psychotic symptoms</td>
</tr>
<tr>
<td>• Active suicidal ideas/plans</td>
<td>• Inability to care for self</td>
</tr>
<tr>
<td>• Failure to respond to treatment</td>
<td>• Lack of impulse control</td>
</tr>
<tr>
<td>• Advice on further treatment</td>
<td>• Danger to others</td>
</tr>
<tr>
<td>• Clinical deterioration</td>
<td>• Any other reason that the healthcare provider deems significant</td>
</tr>
<tr>
<td>• Recurrent episode within one year</td>
<td></td>
</tr>
<tr>
<td>• Psychotic symptoms</td>
<td></td>
</tr>
<tr>
<td>• Severe agitation</td>
<td></td>
</tr>
<tr>
<td>• Self-neglect</td>
<td></td>
</tr>
</tbody>
</table>

MANAGEMENT OF MAJOR DEPRESSIVE DISORDER

<table>
<thead>
<tr>
<th>SEVERITY</th>
<th>MANAGEMENT OF MDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild MDD</td>
<td>Where patient is not started on pharmacotherapy, non-pharmacological interventions should be given. The patient should be followed up closely with a follow-up appointment within 2 weeks.</td>
</tr>
<tr>
<td></td>
<td>i. Psychological intervention:</td>
</tr>
<tr>
<td></td>
<td>- Supportive therapy</td>
</tr>
<tr>
<td></td>
<td>- Problem-solving therapy</td>
</tr>
<tr>
<td></td>
<td>- Counselling</td>
</tr>
<tr>
<td></td>
<td>- Cognitive behavioural therapy (CBT)</td>
</tr>
<tr>
<td></td>
<td>- Interpersonal therapy (IPT)</td>
</tr>
<tr>
<td></td>
<td>- Computerised CBT (CCBT)</td>
</tr>
<tr>
<td></td>
<td>ii. Other therapy:</td>
</tr>
<tr>
<td></td>
<td>- Exercise therapy</td>
</tr>
<tr>
<td></td>
<td>Pharmacotherapy – SSRIs should be considered as the first line if medication is indicated</td>
</tr>
<tr>
<td>Moderate to Severe MDD</td>
<td>Pharmacotherapy – SSRIs should be considered as the first line</td>
</tr>
<tr>
<td></td>
<td>Non-pharmacological therapy</td>
</tr>
<tr>
<td></td>
<td>i. Psychological intervention:</td>
</tr>
<tr>
<td></td>
<td>Cognitive behavioural therapy (CBT)</td>
</tr>
<tr>
<td></td>
<td>ii. Other therapy:</td>
</tr>
<tr>
<td></td>
<td>Exercise therapy</td>
</tr>
<tr>
<td></td>
<td>Electro-convulsive therapy (ECT)</td>
</tr>
</tbody>
</table>
### SUGGESTED ANTIDEPRESSANT DOSAGES AND ADVERSE EFFECTS

<table>
<thead>
<tr>
<th>NAME</th>
<th>STARTING DOSE* (mg/day)</th>
<th>USUAL DOSE (mg/day)</th>
<th>MAIN ADVERSE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escitalopram</td>
<td>10</td>
<td>10 - 20</td>
<td>Nausea, vomiting, dyspepsia, abdominal pain, diarrhoea, rash, sweating, agitation, anxiety, headache, insomnia, tremor, sexual dysfunction (male &amp; female), hyponatraemia, cutaneous bleeding disorder. Discontinuation symptoms may occur.</td>
</tr>
<tr>
<td>Sertraline</td>
<td>50</td>
<td>50 - 200</td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>20</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>50 - 100 (max 300)</td>
<td>100 - 200</td>
<td></td>
</tr>
<tr>
<td><strong>TRICYCLICS AND TETRACYCLICS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>25 - 75</td>
<td>75 - 200</td>
<td>Sedation, often with hangover, postural hypotension, tachycardia/arrhythmia, dry mouth, blurred vision, constipation, urinary retention.</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>10 - 75</td>
<td>75 - 150</td>
<td></td>
</tr>
<tr>
<td>Dothiepin</td>
<td>50 - 75</td>
<td>75 - 225</td>
<td></td>
</tr>
<tr>
<td>Imipramine</td>
<td>25 - 75 (up to 300mg for in - patients)</td>
<td>75 - 200</td>
<td></td>
</tr>
<tr>
<td>Maprotiline</td>
<td>25 - 75 (up to 225mg for in - patients)</td>
<td>75 - 150</td>
<td></td>
</tr>
<tr>
<td><strong>REVERSIBLE INHIBITOR OF MAO-A (RIMA)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moclobemide</td>
<td>150</td>
<td>150 - 600</td>
<td>Sleep disturbances, nausea, agitation, confusion. Hypertension reported may be related to tyramine ingestion.</td>
</tr>
<tr>
<td><strong>SEROTONIN AND NORADRENALINE REUPTAKE INHIBITOR (SNRIs)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venlafaxine, extended</td>
<td>37.5 - 75</td>
<td>75 - 225 (up to 375mg/day in severe depression)</td>
<td>Nausea, insomnia, dry mouth, somnolence, dizziness, sweating, nervousness, headache, sexual dysfunction.</td>
</tr>
<tr>
<td>release</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duloxetine</td>
<td>40 - 60</td>
<td>60 (max 120)</td>
<td></td>
</tr>
<tr>
<td><strong>NORADRENERGIC AND SPECIFIC SEROTONERGIC ANTIDEPRESSANT (NaSSA)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Lower starting doses are recommended for elderly patients and for patients with significant anxiety, hepatic disease, or medical co-morbidity.
ALGORITHM (1) FOR THE MANAGEMENT OF MDD

DIAGNOSIS OF MDD

Severity Assessment of MDD
(including presence of psychotic features and suicidal risk)

MILD MDD

Pharmacological Interventions
- antidepressant ± short-term benzodiazepine as adjunct

Non-pharmacological Interventions
- counselling - problem solving - psychotherapy - CCBT - exercise therapy

Moderate MDD

Pharmacological Interventions
- antidepressant ± short-term benzodiazepine as adjunct

Non-pharmacological Interventions
- counselling psychotherapy CCBT exercise therapy

Severe MDD

Pharmacological Interventions
- antidepressant ± short-term benzodiazepine as adjunct ± antipsychotics

Non-pharmacological Interventions
- counselling psychotherapy CCBT exercise therapy

Non-Psychotic

Pharmacological Interventions
- antidepressant ± short-term benzodiazepine as adjunct

Non-pharmacological Interventions
- psychotherapy

Psychotic

Pharmacological Interventions
- antidepressant ± short-term benzodiazepine as adjunct ± antipsychotics

Non-pharmacological Interventions
- psychotherapy

ECT

WITH / WITHOUT

WITH / WITHOUT

WITH / WITHOUT
**ALGORITHM (2) FOR THE PHARMACOTHERAPY OF MDD**

**Diagnosis of MDD**

- **Monotherapy with SSRIs for 1 month**
  - **Insufficient response**
    - **Optimise by titrating dose of medication as tolerated**
      - **Partial response**
        - **Continue same treatment for 2 more weeks**
          - **Partial response**
            - **Switching to another antidepressant**
              - **Non-response**
                - **Partial response**
                  - **Remission**
                    - **Continuation phase treatment: 6 - 9 months after onset of remission**
                      - **2 or more recent episodes? OR having factors associated with risk of recurrence?**
                        - **NO**
                          - **Treatment ends**
                          - **Non-response**
                            - Less than 25% decrease in baseline symptom severity
                          - **Partial response**
                            - 26-49% decrease in baseline symptom severity
                          - **Response**
                            - A 50% or more reduction in depressive symptoms and at least a moderate degree of global improvement
                          - **Remission**
                            - Absence of signs and symptoms in current episode of depression and restoration of function
                      - **YES**
                        - **Maintenance phase treatment:**
                          - at least 2 years maintenance
                          - up to 5 years or longer if increased risk of recurrence
                          - **Strategies for treatment resistance**
                            - Switching antidepressant
                            - Augment with lithium/antipsychotic
                            - Combine with second antidepressant
                    - **Partial response**
                      - **Remission**
                        - **Continuation phase treatment: 6 - 9 months after onset of remission**
                          - **2 or more recent episodes? OR having factors associated with risk of recurrence?**
                            - **NO**
                              - **Treatment ends**
                              - **Non-response**
                                - Less than 25% decrease in baseline symptom severity
                              - **Partial response**
                                - 26-49% decrease in baseline symptom severity
                              - **Response**
                                - A 50% or more reduction in depressive symptoms and at least a moderate degree of global improvement
                              - **Remission**
                                - Absence of signs and symptoms in current episode of depression and restoration of function
                          - **YES**
                            - **Maintenance phase treatment:**
                              - at least 2 years maintenance
                              - up to 5 years or longer if increased risk of recurrence
                              - **Strategies for treatment resistance**
                                - Switching antidepressant
                                - Augment with lithium/antipsychotic
                                - Combine with second antidepressant
                    - **Partial response**
                      - **Remission**
                        - **Continuation phase treatment: 6 - 9 months after onset of remission**
                          - **2 or more recent episodes? OR having factors associated with risk of recurrence?**
                            - **NO**
                              - **Treatment ends**
                              - **Non-response**
                                - Less than 25% decrease in baseline symptom severity
                              - **Partial response**
                                - 26-49% decrease in baseline symptom severity
                              - **Response**
                                - A 50% or more reduction in depressive symptoms and at least a moderate degree of global improvement
                              - **Remission**
                                - Absence of signs and symptoms in current episode of depression and restoration of function
                          - **YES**
                            - **Maintenance phase treatment:**
                              - at least 2 years maintenance
                              - up to 5 years or longer if increased risk of recurrence
                              - **Strategies for treatment resistance**
                                - Switching antidepressant
                                - Augment with lithium/antipsychotic
                                - Combine with second antidepressant
                    - **Partial response**
                      - **Remission**
                        - **Continuation phase treatment: 6 - 9 months after onset of remission**
                          - **2 or more recent episodes? OR having factors associated with risk of recurrence?**
                            - **NO**
                              - **Treatment ends**
                              - **Non-response**
                                - Less than 25% decrease in baseline symptom severity
                              - **Partial response**
                                - 26-49% decrease in baseline symptom severity
                              - **Response**
                                - A 50% or more reduction in depressive symptoms and at least a moderate degree of global improvement
                              - **Remission**
                                - Absence of signs and symptoms in current episode of depression and restoration of function
                          - **YES**
                            - **Maintenance phase treatment:**
                              - at least 2 years maintenance
                              - up to 5 years or longer if increased risk of recurrence
                              - **Strategies for treatment resistance**
                                - Switching antidepressant
                                - Augment with lithium/antipsychotic
                                - Combine with second antidepressant
                    - **Partial response**
                      - **Remission**
                        - **Continuation phase treatment: 6 - 9 months after onset of remission**
                          - **2 or more recent episodes? OR having factors associated with risk of recurrence?**
                            - **NO**
                              - **Treatment ends**
                              - **Non-response**
                                - Less than 25% decrease in baseline symptom severity
                              - **Partial response**
                                - 26-49% decrease in baseline symptom severity
                              - **Response**
                                - A 50% or more reduction in depressive symptoms and at least a moderate degree of global improvement
                              - **Remission**
                                - Absence of signs and symptoms in current episode of depression and restoration of function
                          - **YES**
                            - **Maintenance phase treatment:**
                              - at least 2 years maintenance
                              - up to 5 years or longer if increased risk of recurrence
                              - **Strategies for treatment resistance**
                                - Switching antidepressant
                                - Augment with lithium/antipsychotic
                                - Combine with second antidepressant
                    - **Partial response**
                      - **Remission**
                        - **Continuation phase treatment: 6 - 9 months after onset of remission**
                          - **2 or more recent episodes? OR having factors associated with risk of recurrence?**
                            - **NO**
                              - **Treatment ends**
                              - **Non-response**
                                - Less than 25% decrease in baseline symptom severity
                              - **Partial response**
                                - 26-49% decrease in baseline symptom severity
                              - **Response**
                                - A 50% or more reduction in depressive symptoms and at least a moderate degree of global improvement
                              - **Remission**
                                - Absence of signs and symptoms in current episode of depression and restoration of function
                          - **YES**
                            - **Maintenance phase treatment:**
                              - at least 2 years maintenance
                              - up to 5 years or longer if increased risk of recurrence
                              - **Strategies for treatment resistance**
                                - Switching antidepressant
                                - Augment with lithium/antipsychotic
                                - Combine with second antidepressant
                    - **Partial response**
                      - **Remission**
                        - **Continuation phase treatment: 6 - 9 months after onset of remission**
                          - **2 or more recent episodes? OR having factors associated with risk of recurrence?**
                            - **NO**
                              - **Treatment ends**
                              - **Non-response**
                                - Less than 25% decrease in baseline symptom severity
                              - **Partial response**
                                - 26-49% decrease in baseline symptom severity
                              - **Response**
                                - A 50% or more reduction in depressive symptoms and at least a moderate degree of global improvement
                              - **Remission**
                                - Absence of signs and symptoms in current episode of depression and restoration of function
                          - **YES**
                            - **Maintenance phase treatment:**
                              - at least 2 years maintenance
                              - up to 5 years or longer if increased risk of recurrence
                              - **Strategies for treatment resistance**
                                - Switching antidepressant
                                - Augment with lithium/antipsychotic
                                - Combine with second antidepressant
