

**CME Article**

# Ministry of Health Clinical Practice Guidelines: Bipolar Disorder

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**ABSTRACT**

The Ministry of Health (MOH) has published clinical practice guidelines on Bipolar Disorder to provide doctors and patients in Singapore with evidence-based guidance on the management of bipolar disorders. This article reproduces the introduction and executive summary (with recommendations from the guidelines) from the MOH clinical practice guidelines on Bipolar Disorder, for the information of readers of the Singapore Medical Journal. Chapters and page numbers mentioned in the reproduced extract refer to the full text of the guidelines, which are available from the Ministry of Health website: [http://www.moh.gov.sg/content/moh\\_web/home/Publications/guidelines/clinical\\_practiceguidelines/2011/bipolar\\_disorder.html](http://www.moh.gov.sg/content/moh_web/home/Publications/guidelines/clinical_practiceguidelines/2011/bipolar_disorder.html). The recommendations should be used with reference to the full text of the guidelines. Following this article are multiple choice questions based on the full text of the guidelines.

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**INTRODUCTION**

Bipolar disorder is a chronic relapsing illness, and if left untreated, may pose significant morbidity and suicide risks. Global estimates suggest that 1%–2% of people may suffer from bipolar disorder over their lifetimes. The age of onset for bipolar disorder ranges from childhood to 50 years of age, with a mean age of approximately 21 years. Most cases commence when individuals are aged 15–19 years. The second most frequent age range of onset is 20–24 years.

Bipolar disorder has significant morbidity and mortality rates. The cost of lost productivity resulting from this illness in the United States during the early 1990s was estimated at \$15.5 billion annually. Many studies show that sufferers of bipolar disorder who are not fully stabilised (i.e. adequately treated) have a lower quality of life compared to those who are generally considered symptom free. Studies

have also shown that even the patients who are considered symptom free and in remission continue to have a poorer quality of life compared with the general population.

**1.1 Objectives and scope of guidelines**

These guidelines are not to be viewed as a protocol, but they provide a framework to:

- Diagnose and initiate treatment for adult patients with bipolar disorder.
- Continue maintenance treatment.

Although bipolar disorder can present in children, there is still ongoing debate on the diagnostic criteria for classifying bipolar disorder in children and adolescents. The treatment of children and adolescents with bipolar disorder presents many challenges. There is understandably limited evidence regarding the use of medications in this population. The treatment and follow-up should be provided by a specialist in this field.

**1.2 Target group**

The target group of the guidelines are general practitioners and clinicians involved in the diagnosis and treatment of patients with bipolar disorder.

**1.3 Guideline development**

These guidelines were compiled by a committee comprising a family physician, pharmacists, psychologists, psychiatrists and a patient representative appointed by the Ministry of Health. They were developed based on the best available current evidence and expert opinion.

**1.4 Review of guidelines**

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence may supersede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review three years after publication, or if new evidence appears that requires substantive changes to its recommendations.

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Institute of Mental Health  
Jurong Health  
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## EXECUTIVE SUMMARY OF RECOMMENDATIONS

Details of the recommendations listed can be found in the main text as the pages indicated.

### Definitions and diagnosis

**GPP** When diagnosing bipolar disorder, a careful clinical assessment that includes a longitudinal history, as well as obtaining a history of mania and hypomania in patients with a first presentation of depression, should be performed (pg 15).

**C** The use of screening instruments in day-to-day practice in primary and tertiary settings is not recommended (pg 15).

**Grade C, Level 2+**

### Acute treatment

**A** Haloperidol may be used for the treatment of acute mania (pg 16).

**Grade A, Level 1+**

**A** Aripiprazole, olanzapine, quetiapine, risperidone or ziprasidone may be used for the treatment of acute mania (pg 17).

**Grade A, Level 1+**

**A** Combination pharmacotherapy with an antipsychotic and a mood stabiliser may be used for patients showing inadequate response to mood stabiliser monotherapy (pg 17).

**Grade A, Level 1+**

**A** Combination pharmacotherapy with an antipsychotic and a mood stabiliser may be used for patients showing inadequate response to mood stabiliser monotherapy (pg 17).

**Grade A, Level 1+**

**A** Sodium valproate monotherapy may be used for the treatment of acute mania (pg 18).

**Grade A, Level 1+**

**A** Carbamazepine monotherapy may be used for the treatment of acute mania (pg 18).

**Grade A, Level 1+**

**A** Lamotrigine should not be used for the treatment of acute mania, as it lacks efficacy in this area (pg 18).

**Grade A, Level 1+**

**A** Clonazepam or lorazepam (IM or oral) may be used in the acute treatment of agitation in mania (pg 19).

**Grade A, Level 1+**

**A** Haloperidol (IM or oral), olanzapine (IM or oral), quetiapine (oral) or aripiprazole (IM) may be used in the acute treatment of agitation in mania (pg 19).

**Grade A, Level 1+**

**A** If antidepressants are to be used in combination with mood stabilisers as first-line treatment for the acute treatment of bipolar depression, they should be used cautiously due to conflicting evidence of efficacy (pg 20).

**Grade A, Level 1+**

**GPP** The lowest therapeutic dosage of antidepressants, for the shortest required period of time, should be used for patients who continue to be depressed despite the optimal use of mood stabilisers (pg 21).

**GPP**

**A** Quetiapine monotherapy, olanzapine monotherapy or olanzapine-fluoxetine combination may be used in the treatment of bipolar depression (pg 21).

**Grade A, Level 1+**

**A** Monotherapy with sodium valproate or carbamazepine is not recommended in the treatment of bipolar depression due to conflicting evidence regarding efficacy (pg 21).

**Grade A, Level 1+**

**A** There is insufficient evidence to recommend lamotrigine monotherapy in the treatment of bipolar depression. However, it is recommended as an add-on for patients already on lithium for treatment of bipolar depression (pg 21).

**Grade A, Level 1+**

**A** Lithium may be used in the treatment of bipolar depression (pg 21).

**Grade A, Level 1+**

**A** Consider using sodium valproate or quetiapine as first-line treatment in patients with rapid cycling. This may be combined with lithium (pg 22).

**Grade A, Level 1+**

**A** A combination of lithium and lamotrigine may be considered as an alternative treatment for rapid cycling (pg 22).

**Grade A, Level 1+**

**GPP** Non-pharmacological treatments should not be used for patients with rapid cycling bipolar disorder due to insufficient evidence (pg 22).

**GPP**

**A** Mood stabilisers may be used when treating mixed states. Of these, valproate and carbamazepine should be preferred over lithium, as there is more evidence for the efficacy of valproate and carbamazepine than for lithium (pg 22).

**Grade A, Level 1+**

**B** Electroconvulsive therapy can be considered for manic and depressive episodes that are severe or that fail to respond to pharmacological interventions, or when pharmacological interventions are not possible (pg 23).

**Grade B, Level 2++**

**C** Consider the use of electroconvulsive therapy as anti-manic and anti-depressive treatment in mixed states that are severe or fail to respond to pharmacological interventions, or when pharmacological interventions are not possible (pg 23).

**Grade C, Level 2+**

#### Maintenance

**A** Lamotrigine can be used for prophylaxis in patients who have initially stabilised with lamotrigine (pg 24).

**Grade A, Level 1+**

**A** Lithium, valproate or olanzapine may be used as maintenance therapy in preventing relapse to either pole of illness in patients with bipolar disorder (pg 25).

**Grade A, Level 1+**

**A** Aripiprazole may be used as maintenance therapy in bipolar patients with recent manic or mixed episode (pg 25).

**Grade A, Level 1+**

**A** Quetiapine, in combination with lithium or valproate, may be used as maintenance therapy in patients with bipolar I disorder (pg 25).

**Grade A, Level 1+**

**A** To minimise the risk of manic switching and/or rapid cycling, patients whose depressive symptoms have remitted for at least eight weeks from an acute depressive episode may have their antidepressant medication gradually discontinued over several weeks while maintaining them on their mood stabiliser medication (pg 26).

**Grade A, Level 1+**

**A** Patients should not be routinely continued on their antidepressant treatment for long-term, as they offer minimal to no significant continuing benefits or effects on depressive episode prevention or enhanced remission rates (pg 26).

**Grade A, Level 1+**

**A** Maintenance medications for bipolar disorder should not be discontinued in view of the high risk of relapse (pg 26).

**Grade A, Level 1+**

**A** If discontinuation of maintenance medications is planned, it should be performed by gradual tapering of the dosage over several weeks (pg 26).

**Grade A, Level 1+**

**A** Lithium and valproate may be used as maintenance therapy for patients with rapid cycling bipolar disorder (pg 27).

**Grade A, Level 1+**

**B** Patients with rapid cycling bipolar disorder should not be routinely continued on antidepressant therapy after achieving remission, as it does not offer significant clinical benefit in preventing relapse (pg 27).

**Grade B, Level 2++**

#### Definitions and diagnosis

**GPP** Whenever possible, health professionals should provide psychoeducation to patients with bipolar disorder and their families/caregivers (pg 28).

**GPP**

**A** Upon identification of early warning signs/relapse signatures by individuals or family members/caregivers, individuals can use the plan of action that they developed based on these early warning signs. This plan of action should be a collaborative effort

between the patient, family members/caregivers and healthcare professionals (pg 29).

**Grade A, Level 1+**

- A** Quetiapine, in combination with lithium or valproate, may be used as maintenance therapy in patients with bipolar I disorder (pg 25).

**Grade A, Level 1+**

- A** Cognitive behavioural therapy, family therapy or interpersonal social rhythms therapy may be considered as part of the treatment plan for bipolar depression (pg 31).

**Grade A, Level 1+**

### Reproductive health issues

- A** Women on combined oral contraceptive pills who are concurrently taking carbamazepine and/or lamotrigine should be advised of the risk of decreased contraceptive effect as a result of drug interactions (pg 32).

**Grade A, Level 1+**

- B** Use of sodium valproate in women of childbearing age should be balanced against the risk of decreased fertility, foetal malformations and perinatal complications (pg 33).

**Grade B, Level 1+**

- A** Periconceptional folate supplementation should be prescribed to protect against neural tube defects (pg 34).

**Grade A, Level 1+**

- D** Abrupt discontinuation (i.e. less than two weeks) of mood stabilisers should be avoided, if possible, in order to lessen the chance of relapse (pg 34).

**Grade D, Level 3**

- GPP** Consider switching to antipsychotic treatment, or gradual decrement (over 15–30 days) of monotherapy mood stabiliser to the lowest effective amount in divided doses during pregnancy; concurrent careful foetal monitoring is recommended (pg 34).

**GPP**

- GPP** Consider resuming mood stabiliser treatment immediately postpartum, as this is a period of vulnerability to relapse (pg 34).

**GPP**

- B & GPP** Sodium valproate and carbamazepine are preferable to lithium and lamotrigine during breastfeeding;\* mothers who require the latter two medications may be advised to consider abstinence from breastfeeding for the infant's safety (pg 34).†

**\*Grade B, Level 2++**

**†GPP**

- GPP** In the event of breastfeeding while taking mood stabilisers, consider administering feeds before taking medication and discarding the first post-dose batch of expressed milk, so as to minimise the infant's consumption of medication via breast milk (pg 34).

**GPP**

- B** First-trimester paroxetine use should be avoided, as it is associated with increased risk of serious congenital (particularly cardiac) defects (pg 35).

**Grade B, Level 2++**

- B** Selective serotonin reuptake inhibitors should be used judiciously in late pregnancy because of associations with persistent pulmonary hypertension of the newborn and neonatal behavioural syndrome (pg 35).

**Grade B, Level 2++**

- GPP** While there is no evidence for routine monitoring for congenital malformations during antenatal use of antidepressants, careful foetal monitoring is recommended nonetheless (pg 35).

**GPP**

- D** Women who are planning conception should be advised that antipsychotics are associated with hyperprolactinaemia and amenorrhoea, which may affect fertility (and predispose toward premature bone loss) (pg 37).

**Grade D, Level 3**

- D** Typical antipsychotics, such as chlorpromazine and haloperidol, may be considered for treatment of pregnant women with bipolar disorder, as they appear less likely than atypical antipsychotics to cause metabolic complications and other serious adverse effects (pg 37).

**Grade D, Level 3**

**GPP** When considering antipsychotics for pregnant women, the clinical presentation and side effect profile should also be considered. For instance, previous poor response or side effects to typical antipsychotics should merit consideration of an atypical antipsychotic (pg 37).

**GPP** Weight, blood sugar and blood pressure should be monitored in pregnant women on atypical antipsychotics (pg 37).

**GPP** When antipsychotics are used in pregnant women, close and careful foetal monitoring via regular visits and scans is recommended (pg 37).

**GPP** In the event of breastfeeding while taking antipsychotics, consider administering feeds before taking medication and discarding the first post-dose batch of expressed milk to minimise the infant's consumption of medication via breast milk (pg 37).

**C** Benzodiazepines should be avoided in pregnancy (pg 38).

**Grade C, Level 2+**

**D** Electroconvulsive therapy may be considered as a treatment option in pregnancy for the same indications as in nonpregnant patients (pg 38).

**Grade D, Level 3**

#### Substance misuse

**A** Addiction disorders in patients with bipolar disorder should be treated (pg 39).

**Grade A, Level 1+**

**GPP** Patients with dual diagnosis of bipolar disorder and addiction disorders should be treated in an integrated specialist treatment centre (pg 39).

**GPP**

#### Suicide prevention

**C** Clinicians should routinely assess risk of suicide in all patients with bipolar disorder (pg 40).

**Grade C, Level 2+**

#### Monitoring

**B** During each review, clinical assessment of cardiovascular risk factors (e.g. obesity, smoking) should be performed for all patients with bipolar disorders (pg 41).

**Grade B, Level 2++**

**GPP** Prior to starting treatment, doctors should obtain a patient's personal and family history of obesity, diabetes mellitus, dyslipidaemia, hypertension and cardiovascular disease (pg 41).

**GPP**

**GPP** A patient's alcohol and smoking history, height, weight (including the calculation of body mass index) and blood pressure measurements, together with fasting blood (plasma) glucose level and lipid profile assessment, should be obtained at baseline. This clinical monitoring should also be repeated at regular planned intervals (pg 42).

**GPP**

**GPP** Consider using the Clinical Global Impression scales (both severity and improvement component scales) to measure illness severity and treatment progress during consultations (pg 43).

**GPP**

## SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME

### Multiple Choice Questions (Code SMJ 201112C)

These questions are based on the full text of the guidelines which may be found at [http://www.moh.gov.sg/content/moh\\_web/home/Publications/guidelines/clinical\\_practiceguidelines/2011/bipolar\\_disorder.html](http://www.moh.gov.sg/content/moh_web/home/Publications/guidelines/clinical_practiceguidelines/2011/bipolar_disorder.html)

	True	False
<b>Question 1.</b> Based on current knowledge, bipolar disorder:		
(a) Is a chronic, relapsing illness.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Only begins in adolescence.	<input type="checkbox"/>	<input type="checkbox"/>
(c) If severe, may present with psychotic symptoms.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Is easily diagnosed at first presentation.	<input type="checkbox"/>	<input type="checkbox"/>
<b>Question 2.</b> Appropriate acute treatment options for bipolar disorder include:		
(a) Intramuscular lorazepam for agitation.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Combination of an antipsychotic and a mood stabiliser for patients showing inadequate response to mood stabiliser monotherapy.	<input type="checkbox"/>	<input type="checkbox"/>
(c) Lamotrigine monotherapy for mania.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Lithium for bipolar depression.	<input type="checkbox"/>	<input type="checkbox"/>
<b>Question 3.</b> With regard to the prevention of relapse in patients with bipolar disorder:		
(a) Lithium, valproate and olanzapine may be used as maintenance therapy in preventing relapse.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Quetiapine may be used alone as maintenance therapy in patients with bipolar I disorder.	<input type="checkbox"/>	<input type="checkbox"/>
(c) Bipolar patients whose depressive symptoms have remitted for at least eight weeks may have their antidepressant medications stopped.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Maintenance medications should not be discontinued in view of the high risk of relapse.	<input type="checkbox"/>	<input type="checkbox"/>
<b>Question 4.</b> A 28-year-old married female patient with bipolar disorder is currently on lamotrigine only as maintenance therapy. She is now interested in family planning. Evaluate the following statements:		
(a) Combined oral contraceptive pills will be more effective in her case.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Peri-conceptual folate supplementation is contraindicated.	<input type="checkbox"/>	<input type="checkbox"/>
(c) Breastfeeding is not advised.	<input type="checkbox"/>	<input type="checkbox"/>
(d) If she is pregnant and suffers a major depressive episode, there are no antidepressants that she can use.	<input type="checkbox"/>	<input type="checkbox"/>
<b>Question 5.</b> A 21-year-old male bipolar patient is on follow-up with you. Evaluate the following statements:		
(a) If he presents with comorbid alcohol addiction, he should be treated for substance abuse.	<input type="checkbox"/>	<input type="checkbox"/>
(b) Suicide risk assessment should be done only if the patient expresses suicide ideology.	<input type="checkbox"/>	<input type="checkbox"/>
(c) Cognitive behavioural therapy can be considered as part of the treatment plan for bipolar depression.	<input type="checkbox"/>	<input type="checkbox"/>
(d) Clinical assessment of cardiovascular risk factors should be done only when he is at least 45 years old.	<input type="checkbox"/>	<input type="checkbox"/>

#### Doctor's particulars:

Name in full: \_\_\_\_\_

MCR number: \_\_\_\_\_ Specialty: \_\_\_\_\_

Email address: \_\_\_\_\_

#### SUBMISSION INSTRUCTIONS:

(1) Log on at the SMJ website: <http://www.sma.org.sg/cme/smj> and select the appropriate set of questions. (2) Select your answers and provide your name, email address and MCR number. Click on "Submit answers" to submit.

#### RESULTS:

(1) Answers will be published in the SMJ February 2012 issue. (2) The MCR numbers of successful candidates will be posted online at [www.sma.org.sg/cme/smj](http://www.sma.org.sg/cme/smj) by 13 January 2012. (3) All online submissions will receive an automatic email acknowledgment. (4) Passing mark is 60%. No mark will be deducted for incorrect answers. (5) The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council. (6) One CME point is awarded for successful candidates.

**Deadline for submission: (December 2011 SMJ 3B CME programme): 12 noon, 06 January 2012.**