Bipolar disorder is a common illness that affects 1%–2% of the general population, it is therefore often first assessed, and frequently managed, by general practitioners. It usually presents with symptoms of depression, but a diagnosis of bipolar disorder is contingent on the occurrence of an episode of mania or hypomania. Consequently, many cases of bipolar disorder remain undetected or are misdiagnosed as major (unipolar) depression. Further, individuals with hypomania rarely seek help, and those with comorbid anxiety or symptoms of depression that do not respond to treatment often resort to self-medication with alcohol or illicit substances. Equally, bipolar disorder is thought to be overdiagnosed in some populations such as adolescents and young adults.

Sufficient to say the clinical picture of bipolar disorder is complex and its treatment is necessarily sophisticated. In recent years, the importance of psychological and social interventions in the successful management of bipolar disorder has been increasingly recognised; however, pharmacotherapy remains the mainstay of treatment for most patients.

Traditionally, bipolar disorder is partitioned according to its phases of illness — depression, mania and euthymia (normal mood stated) — and its treatment is considered in corresponding stages. Here, we summarise the pharmacological management of adults with bipolar disorder in primary care in relation to its phases of illness. We do not discuss complex presentations, treatment non-response and comorbidities, as these are normally managed by psychiatrists, but we do briefly mention mixed states and rapid cycling.

METHODS

We synthesised recommendations from recently published guidelines for the treatment of bipolar disorder. Treatment recommendations are therefore divided into sections on acute bipolar mania, acute bipolar depression and maintenance.

We also conducted a literature search of articles on pharmacological treatment of bipolar disorder that were published up to May 2009 — using electronic databases (MEDLINE, PubMed, PsycINFO), book chapters and articles known to the authors — to identify Cochrane reviews, meta-analyses, review articles and reports from randomised controlled trials. The search terms bipolar disorder, mania, pharmacotherapy, general practice, manic–depressive illness and depression were used. Key recommendations relevant to GPs were synthesised and rated according to National Health and Medical Research Council (NHMRC) levels of evidence.

Over 500 articles were reviewed, with an emphasis on meta-analyses and systematic reviews of randomised controlled trials. Where evidence was more limited, open trials and non-controlled data were also reviewed. We distilled the key recommendations and clinical messages relevant to the pharmacological management of bipolar disorder in primary care. However, the majority of the available evidence did not satisfy NHMRC levels I or II; consequently, much of the advice is based on lower levels of evidence than would normally be ideal.

ABSTRACT

Objective: To provide a practical overview of the pharmacological management of adults with bipolar disorder in primary care and the role of general practitioners in the pharmacotherapy of this complex disorder.

Data sources: Published guidelines for the treatment of bipolar disorder, plus Cochrane reviews, meta-analyses, review articles and reports from randomised controlled trials that were published up to May 2009.

Study selection: Over 500 articles on the treatment of bipolar disorder were reviewed, with an emphasis on meta-analyses and systematic reviews of randomised controlled trials. Where evidence was more limited, open trials and non-Controlled data were also reviewed.

Data extraction: Key recommendations relevant to GPs were synthesised and rated according to National Health and Medical Research Council levels of evidence.

Data synthesis: Lithium, valproate and atypical antipsychotics are first-line treatment options for acute mania, and monotherapy is ideal if it produces an adequate response. For depressive episodes, recommendations are less definitive and the use of antidepressants is controversial. Most patients require maintenance treatment, during which pharmacotherapy should be used to prevent relapse, and psychological and social interventions should be considered.

Conclusions: Bipolar disorder is a lifelong episodic illness that affects 1%–2% of the population, many of whom are principally managed by their GPs. Pharmacological treatment with mood-stabilising agents is the primary form of management, although this is ideally provided in conjunction with psychosocial interventions.

RESULTS

The role of the GP

GPs are integral to the management of bipolar disorder, often with involvement from the initial detection and assessment of the illness through to longer-term management. The GP is usually the first healthcare professional from whom the patient will seek assistance. Alternatively, in instances where the illness emerges insidiously, it may be the GP’s long-term knowledge of the patient that assists in detecting subtle changes in mood and behaviour.

The GP’s role in managing bipolar disorder will vary according to the patient, the severity of the illness and the level of available support. The GP may take on the primary role of treating the patient, with the option of referral to specialist services if and when required. Alternatively, the patient may be primarily managed by an external team, such as a community mental health service, but with links to the GP maintained. Further, multiple professionals are typically
involved in working with patients who have a mental illness, including professionals who primarily target clinical interventions and those who target more broad aspects of life affected by the illness, such as social and occupational functioning. While many of the professionals who work with these patients should also communicate with one another, the GP often serves as the focal point around which the other services are provided, including contact with family and carers (Box 1). With respect to pharmacological management, the main priorities for the GP are to assess efficacy, encourage adherence to treatment and monitor for potential side effects. Ideally, treatment plans are developed and initiated following consultation with a psychiatrist, particularly when more specialist input is necessary or greater severity of illness, or the risk of suicide is an ongoing consideration throughout all stages of treatment. Pharmacotherapy remains the primary treatment modality, but ideally it is supplemented with psychological interventions; in some instances, specialist physical measures such as electroconvulsive therapy may also be useful. Box 4 provides a detailed overview of side effects and recommended therapeutic dosing for agents commonly used in bipolar disorder.

Models of treatment
If a diagnosis of bipolar disorder is suspected, the first imperative is to act. Action involves careful assessment so as to provide individualised care and effective treatment. Box 2 provides an overview of the management of bipolar disorder, adapted from previously published recommendations. In all cases, management should begin with a detailed clinical assessment that includes diagnostic formulation, assessment of safety and risk, a brief medical examination (including baseline investigations and screening for medical illnesses), and implementation of any necessary action such as facilitating an emergency assessment for hospitalisation. Guidelines for baseline and ongoing monitoring in bipolar disorder have been reviewed in detail recently and are summarised in Box 3. The care principles outlined in Box 2 are applicable throughout all stages of treatment and are essential for effective long-term management. An effective collaborative alliance is important for increasing the likelihood that the patient remains engaged in treatment; this can be fostered by providing emotional support and education to the patient and his or her family. Much of this can be initiated by a GP, but prompt transition to joint involvement of a psychiatrist is recommended, especially when affirming diagnosis and planning future management.

Treatment involves implementing strategies to achieve remission of symptoms of acute manic episodes and/or depressive episodes, as well as longer-term maintenance treatment to optimise social and occupational functioning and prevent relapse. In addition, ensuring safety and specifically reducing the risk of suicide is an ongoing consideration throughout all stages of treatment. Pharmacotherapy remains the primary treatment modality, but ideally it is supplemented with psychological interventions; in some instances, specialist physical measures such as electroconvulsive therapy may also be useful. Box 4 provides a detailed overview of side effects and recommended therapeutic dosing for agents commonly used in bipolar disorder.

Acute bipolar mania
During acute mania, an assessment of risk including personal safety, reputation and the safety of others should be undertaken. Steps may need to be taken to manage acute mania — for example, hospitalisation or referral for specialist mental health services is often necessary during this phase of illness. Treatments for acute bipolar mania should aim to treat the acute symptoms of mania and to manage any accompanying behavioural disturbance (Box 5).

What are the first-line treatment options for acute mania?
Where possible, any mania-inducing agents that the patient is already taking (eg, antidepressants and stimulants) should be tapered and ceased. The patient should also be advised to institute general measures to reduce stimulation and maintain a routine, and to delay making important decisions. Restoration of sleep is also important.

With regard to pharmacological treatments, lithium, valproate, atypical antipsychotics, haloperidol and, to a lesser extent, carbamazepine all have indications for acute mania. The choice of agent depends on episode severity, patient preference and likely side effects. While haloperidol is effective in acute mania, it is not a first-line option because of a high risk of extrapyramidal side effects and its inability to prevent depression. If a rapid response is required, valproate or the atypical antipsychotics are preferable to lithium.

If possible, monotherapy should be trialled to reduce the likelihood of adverse effects. However, when there is marked risk or greater severity of illness, or the response to an initial monotherapy trial has not been adequate, combinations such as lithium or valproate combined with an atypical antipsychotic add efficacy. In
general, about 50% of individuals with mania respond to monotherapy with an antimanic agent, and 75% respond to a combination of an atypical antipsychotic and either lithium or valproate.

Psychotic symptoms frequently occur in acute mania and symptoms are often mood congruent (eg, grandiose delusions). If antipsychotics are not already being used, short-term administration of atypical antipsychotics may be necessary.

**How should behavioural disturbance in acute mania be managed?**

The adjunctive short-term use of benzodiazepines (eg, lorazepam) may help manage additional behavioural disturbance. However, these are usually tapered within days and gradually withdrawn as symptoms start to abate. If the patient is being treated with an antipsychotic for mania, this may also provide an additional settling effect.

**Acute bipolar depression**

Depression is the predominant phase of bipolar disorder and, as such, it confers substantive risks in terms of morbidity and suicide. In comparison to acute mania, the pharmacotherapy for bipolar depression is more complicated and based on data that are less clear. This is reflected in recommendations that are generally less definitive and vary across guidelines (Box 6).

**What are the first-line treatment options for bipolar depression?**

First-line monotherapy options include lithium, valproate, quetiapine and lamotrigine. Lithium is particularly noted for its antisuicidal properties, but is disadvantaged by a delay in effect of 2–3 weeks. First-line medication combinations include olanzapine plus fluoxetine, and lithium combined with valproate or lamotrigine. Each agent, or combination of agents, has unique advantages and disadvantages in relation to clinical effectiveness, speed of antidepressant action, tolerability and prophylactic properties.

**Are the conventional antidepressants effective in bipolar depression?**

Unlike the use of antidepressants in unipolar depression, antidepressant use in bipolar disorder is a controversial issue. The effectiveness of conventional antidepressants in bipolar depression is unclear, and three recent large studies have reported no additional benefit from the adjunctive use of antidepressants in bipolar depression.

Further, in some patients, the use of conventional antidepressants is associated with an increased risk of a switch to mania. Nonetheless, antidepressants may benefit a small cohort of patients with bipolar depression but, if used, should be prescribed in combination with a mood-stabilising agent to minimise the risk of affective instability. In this regard, selective serotonin reuptake inhibitors are preferable because they are less likely to induce a switch to mania than other antidepressant classes and are less dangerous in cases of overdose.

**Maintenance treatment**

Maintenance treatment (Box 7) is likely to be necessary in most patients with an established diagnosis of bipolar disorder. Following an acute episode, conservative indications for maintenance treatment include instances where there has been at least one other prior mood episode in the past 5 years or two prior episodes across the lifetime, the acute episode was severe and included suicide risk or psychotic features, or there is ongoing functional disability.

**What are the key considerations in the long-term management of bipolar disorder?**

Bipolar disorder is a lifelong illness with episodes that can cause marked disruption and stress not only to patients but also their families. When patients present with severe illness or experience frequent relapse, the demands on the treating physician can also be significant. It may be necessary for the GP to broaden the management and include referrals to external health care providers.

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**3 International Society for Bipolar Disorders guidelines for baseline and ongoing monitoring in bipolar disorder**

**All agents**

- Obtain patient history: medical comorbidities (including cardiovascular disease risk factors), smoking status, alcohol use, pregnancy status, and family history of cardiovascular disease risk factors
- Undertake baseline investigations: waist circumference and/or body mass index, blood pressure, full blood count, electrolytes, urea and creatinine, liver function tests, fasting glucose, and fasting lipid profile

<table>
<thead>
<tr>
<th>Agent</th>
<th>Specific baseline investigations</th>
<th>Specific ongoing monitoring</th>
</tr>
</thead>
</table>
| Lithium                | Thyroid-stimulating hormone and serum calcium | • Urea and creatinine: every 3–6 months  
• Thyroid-stimulating hormone, serum calcium, and weight: at 6 months, then annually       |
| Valproate              | Identify any history of haematological or hepatic disease | • Weight, full blood count, liver function tests, and menstrual changes (for women of reproductive age): every 3 months for 1 year, then annually  
• Provide advice on bone health                                                                 |
| Carbamazepine          | Identify any history of haematological or hepatic disease | • Full blood count: monthly  
• Liver function tests, and electrolytes, urea and creatinine: monthly for 3 months, then annually  
• Review oral contraceptive efficacy  
• Inform patients of potential dermatological reactions: if rash occurs, cease medication immediately and seek emergency medical attention  
• Provide advice on bone health                                                                 |
| Lamotrigine            | None                             | • Inform patients of potential dermatological reactions: if rash occurs, cease medication immediately and seek emergency medical attention |
| Atypical antipsychotics| Identify any family history of cardiac problems, including congenital long QT syndrome | • Weight: monthly for 3 months, then every 3 months  
• Blood pressure and fasting glucose: every 3 months for 1 year, then annually  
• Fasting lipid profile: at 3 months, then annually  
• Electrocardiogram and prolactin levels where clinically indicated |

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4 Side effects and therapeutic dosing for agents commonly used in bipolar disorder*8-10

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Common (incidence ≥ 1%)</th>
<th>Uncommon or rare (incidence &lt; 1%)†</th>
<th>Dose range and serum levels</th>
<th>Therapeutic dosing</th>
<th>Dosing considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>＊Nephrogenic diabetes insipidus, hyperparathyroidism, memory impairment, hair loss, arthrythmias, hyperthyroidism</td>
<td>Acute mania: 400–1200 mg/day</td>
<td>Lithium concentration can be affected by other medications (eg, angiotensin-converting enzyme inhibitors, non-steroidal anti-inflammatory drugs) and sodium depletion (eg, gastrointestinal disturbance) There can be a delay of 6–8 weeks for an antidepressant effect</td>
<td></td>
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</tr>
<tr>
<td>GIT: nausea, vomiting, epigastric discomfort, dry mouth, metallic taste, diarrhoea, weight gain</td>
<td>Acute mania: can consider rapid titration</td>
<td>Maintenance: reduce dose to maintain serum level within therapeutic range</td>
<td>Lithium toxicity: signs include loss of balance, increasing diarrhoea, vomiting, anorexia, weakness, ataxia, blurred vision, tinnitus, polyuria, coarse tremor, muscle twitching, irritability and agitation. Drowsiness, psychosis, disorientation, seizures, coma and renal failure may also occur.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNS: fatigue, headache, difficulty concentrating, vertigo, fine tremor</td>
<td>Therapeutic levels: 0.6–0.8 mmol/L</td>
<td>(lower end of range recommended for maintenance)</td>
<td>Valproate</td>
<td></td>
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</tr>
<tr>
<td>Skin: dry skin, exacerbation of psoriasis or acne, rash</td>
<td>Risk of toxicity increases markedly at &gt; 1.5 mmol/L (&gt; 3.5 mmol/L is potentially lethal), toxicity can also occur within the therapeutic range (particularly in older patients) Abrupt reduction of &gt; 0.2 mmol/L increases risk of relapse</td>
<td>Severe hepatic dysfunction, pancreatitis, extrapyramidal syndrome, hyperammonaemic encephalopathy</td>
<td>Maintenance: usually 1000–2000 mg/day, divided doses, titrated gradually</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolic: hypermagnesaemia, hypercalcaemia, hypothyroidism</td>
<td>Therapeutic levels: 350–700 mmol/L (guide only)‡</td>
<td>Maintenance: 200–400 mg/day</td>
<td>Therapeutic levels: 350–700 mmol/L (guide only)‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other: benign electromyogram changes, leukocytosis</td>
<td>Acute mania: 400–1200 mg/day, titrated gradually</td>
<td>Maintenance: 200–400 mg/day</td>
<td>Carbamazepine impacts on the cytochrome p450 system and can affect other drugs that are metabolised by this system (eg, antidepressants, anticonvulsants, risperidone, haloperidol)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GIT: dry mouth, vomiting, diarrhoea, anorexia, constipation, abdominal pain</td>
<td>Acute mania: 400–1200 mg/day, titrated gradually</td>
<td>Maintenance: 200–400 mg/day</td>
<td>Carbamazepine impacts on the cytochrome p450 system and can affect other drugs that are metabolised by this system (eg, antidepressants, anticonvulsants, risperidone, haloperidol)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNS: dizziness, headache, ataxia, drowsiness, blurred vision, diplopia</td>
<td>Therapeutic levels: 20–50 mmol/L (guide only)</td>
<td>Maintenance: 200–400 mg/day</td>
<td>Carbamazepine impacts on the cytochrome p450 system and can affect other drugs that are metabolised by this system (eg, antidepressants, anticonvulsants, risperidone, haloperidol)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin: rash</td>
<td>Maintenance: reduce dose to maintain serum level within therapeutic range</td>
<td>Maintenance: 200–400 mg/day</td>
<td>Carbamazepine impacts on the cytochrome p450 system and can affect other drugs that are metabolised by this system (eg, antidepressants, anticonvulsants, risperidone, haloperidol)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other: thrombocytopenia, elevated liver transaminase levels, asymptomatic elevations of ammonia</td>
<td>Risk of toxicity increases markedly at &gt; 1.5 mmol/L (&gt; 3.5 mmol/L is potentially lethal), toxicity can also occur within the therapeutic range (particularly in older patients) Abrupt reduction of &gt; 0.2 mmol/L increases risk of relapse</td>
<td>Agranulocytosis, aplastic anaemia, severe skin reactions (including Stevens–Johnson syndrome), SIADH, arrhythmias, orofacial dyskinesias, hepatitis</td>
<td>Carbamazepine impacts on the cytochrome p450 system and can affect other drugs that are metabolised by this system (eg, antidepressants, anticonvulsants, risperidone, haloperidol)</td>
<td></td>
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</tr>
</tbody>
</table>

GIT = gastrointestinal tract. CNS = central nervous system. SIADH = syndrome of inappropriate antidiuretic hormone secretion. ◆ This table is not exhaustive and specific product information and recognised sources of information should be consulted before prescribing. † In addition, every medication has the potential to cause a hypersensitivity syndrome (fever, severe skin reactions, lymphadenopathy, hepatitis, haematological abnormalities, facial oedema). ‡ Routine monitoring is not necessary and only recommended when initiating therapy or altering doses.

such as psychiatrists, psychologists, social workers and case managers working within community mental health teams.

Treatment non-adherence is a major risk factor for relapse. The maintenance phase is therefore an important time to re-evaluate the treatment plan, work with the patient to maintain engagement in treatment and develop a collaborative approach to care. Engagement of family members may also be particularly beneficial. The long-term nature of primary care lends itself to monitoring and supporting adherence. In particular, it is important to assess for comorbidities (such as anxiety, and drug and alcohol misuse); monitor for subsyndromal depressive symptoms; monitor side effects of medications (including cardiometabolic health risk); identify and check for early warning signs; provide education about the illness; promote a healthy lifestyle which includes good sleep, hygiene, regular exercise and routines; and foster the development of problem-solving skills. The maintenance phase is therefore the optimum time to consider incorporating adjunctive psychological and social interventions into the treatment plan.

Which treatments are recommended in the long-term management of bipolar disorder?

Following an acute episode, it is important to taper and withdraw any agents (such as benzodiazepines or antipsychotics) that were used to manage temporary behavioural or cognitive disturbance. The goal of pharmacotherapy in maintenance is to prevent...
relapse. In this regard, lithium is still considered the gold-standard treatment, although it appears to be more effective at preventing manic relapse than depression. Lamotrigine and valproate also have prophylactic properties, with lamotrigine being more efficacious at preventing depressive relapse compared with manic relapse.\textsuperscript{24,23} Other anticonvulsants (eg, carbamazepine) have been less impressive and are not consistently recommended as first-line treatment options.\textsuperscript{4,9}

There is growing interest in the use of atypical antipsychotics for maintenance treatment, and quetiapine, olanzapine and aripiprazole have been shown to have benefits. Quetiapine appears to be equally effective at preventing both manic and depressive episodes, whereas all other atypical antipsychotics are more effective at preventing manic episodes. While some longer-term evidence is beginning to emerge\textsuperscript{26–28} the long-term prophylactic properties of atypical antipsychotics are yet to be reliably established and further research is needed before such agents can be confidently recommended for long-term use in bipolar disorder, there is no clear class effect in this regard.

Again, monotherapy is considered ideal and trials of medications may take several months before effectiveness becomes clear. Nonetheless, a significant proportion of patients will not respond adequately and

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**4 Side effects and therapeutic dosing for agents commonly used in bipolar disorder (continued)**\textsuperscript{8–10}

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Uncommon or rare (incidence &lt; 1%)\textsuperscript{2}</th>
<th>Dose range and serum levels</th>
<th>Therapeutic dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamotrigine</td>
<td>Hepatic failure, blood dyscrasias, lupus-like reaction, severe skin reactions including Stevens–Johnson syndrome and Lyell syndrome</td>
<td>Acute bipolar depression: 100–200mg/day titrated upwards slowly</td>
<td>To prevent serious skin reaction, initiate at a low dose and increase slowly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No demonstratd benefits in measuring serum lamotrigine</td>
<td>Dosage may need to be adjusted if combining with other medications, particularly valproate and carbamazepine</td>
</tr>
<tr>
<td>Atypical antipsychotics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolic: weight gain, dyslipidaemia, hyperglycaemia, hyperprolactinaemia</td>
<td>Jaundice, neuroleptic malignant syndrome, seizures, tardive dyskinesia, electrocardiogram changes (increased QT interval), SIADH, temperature irregularity, blood dyscrasias, arrhythmias, cardiac arrest, seizures, hepatic fibrosis, lupus</td>
<td>Olanzapine: acute mania, 5–20mg/day; maintenance, continue at dose used for acute episode</td>
<td></td>
</tr>
<tr>
<td>Extrapyramidal symptoms: tremor, akathisia, rigidity, slowing, dystonia</td>
<td>Clozapine: agranulocytosis (1%), myocardiitis, cardiomyopathy, seizures</td>
<td>Risperidone: acute mania, usual dose 2–6 mg/day</td>
<td></td>
</tr>
<tr>
<td>Anticholinergic reactions: constipation, dry mouth, blurred vision, urinary retention</td>
<td></td>
<td>Quetiapine: acute mania, usual dose 200–800 mg/day titrated to average of 600mg/day; depression, usual dose 300–600 mg/day</td>
<td></td>
</tr>
<tr>
<td>Other: sedation, increased appetite, sexual dysfunction, gastrointestinal upset, peripheral oedema, nausea, cerebrovascular events such as stroke and TIA (especially in older patients), orthostatic hypotension, tachycardia</td>
<td></td>
<td>Ziprasidone: acute mania, 80–160 mg/day</td>
<td></td>
</tr>
<tr>
<td>SSRI antidepressants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GIT: nausea, diarrhoea</td>
<td>Extrapyramidal reactions: including tardive dyskinesia and dystonia</td>
<td>Equivalent doses used in treating major depression</td>
<td>Serotonin toxicity is a potentially life-threatening adverse drug reaction with cognitive, autonomic and somatic effects</td>
</tr>
<tr>
<td>CNS: dizziness, headache, tremor, agitation, insomnia, drowsiness</td>
<td>Other: sedation, confusion, palpitations, tachycardia, hypotension, hyponatraemia (as part of SIADH), abnormal platelet aggregation or haemorrhagic complications (eg, bruising, epistaxis, gastrointestinal and vaginal bleeding), elevated liver enzymes, hepatitis, hepatic failure, galactorrhoea, blood dyscrasias, seizures, akathisia, paraesthesia, taste disturbance</td>
<td></td>
<td>Some combinations with other drugs are contraindicated (especially MAOIs or within 14 days of stopping a MAOI, and moclobemide or within 2 days of stopping moclobemide) should be avoided</td>
</tr>
<tr>
<td>Anticholinergic reactions: dry mouth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other: myalgia, sweating, weakness, anxiety, weight gain or loss, sexual dysfunction, rhinitis</td>
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</tbody>
</table>

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\textsuperscript{2} Risk is greatest with high initial doses or when combined with valproate.\textsuperscript{2}
5 Summary of treatments for acute mania
• Focus of treatment: treat acute symptoms of mania and manage any behavioural disturbance.
• First-line treatments: lithium, valproate and atypical antipsychotics.
• Behavioural disturbance: short-term benzodiazepine or antipsychotic therapy (if not already prescribed for mania).

6 Summary of treatment for bipolar depression
• First-line monotherapy options: lithium, valproate, quetiapine and lamotrigine.
• First-line combination options: olanzapine plus fluoxetine, and lithium combined with valproate or lamotrigine.
• Antidepressants: the efficacy of antidepressants is not established in bipolar depression. If prescribing antidepressants, always do so in combination with an agent that has antimanic properties to limit the risk of affective instability or a switch to mania.

7 Summary of maintenance treatments
• Considerations: facilitate engagement in treatment, assess for comorbidities, monitor side effects, provide education about illness, identify and check for early warning signs.
• First-line treatments: lithium, lamotrigine, valproate and quetiapine.
• Second-line treatments: olanzapine, anipiprazole and carbamazepine.
• Inadequate response to treatment: seek consultation with a psychiatrist.

8 Rapid cycling and mixed episodes
During rapid cycling, individuals with bipolar disorder experience four or more mood episodes over a 12-month period, and some of these may be mixed episodes. A mixed episode is a period that lasts a week or more and satisfies criteria for both a manic and major depressive episode (except duration).

Rapid cycling
Rapid cycling is associated with poorer long-term response to treatment, higher rates of morbidity and increased suicide risk. Factors that may precipitate or exacerbate rapid cycling, such as antidepressants, substance misuse, medications and medical illness should be excluded. The evidence base for management of rapid cycling is limited and treatments appear to be less effective in treating depressive symptoms than manic symptoms.

Treatment options include:
• Pharmacological monotherapy: valproate, lithium, olanzapine, lamotrigine and quetiapine
• Pharmacological combinations: lithium plus valproate, and lithium plus carbamazepine or lamotrigine
• Adjunctive psychological interventions.

Mixed episodes
Mixed episodes can be difficult to diagnose. Initially, taper and cease all substances with a potential to elevate mood (e.g., antidepressants, stimulants).

Treatment options include:
• Pharmacological monotherapy: olanzapine, quetiapine and valproate
• Pharmacological combinations: olanzapine plus fluoxetine, and valproate plus olanzapine.

CONCLUSION
Bipolar disorder is a complex illness but, in most cases, it can be managed effectively once it is detected and the necessary supports and treatments are instituted. The role of the primary care physician is pivotal in the identification of bipolar disorder and its subsequent lifelong management. Suitable treatments are increasingly available but require sophisticated administration. Hence, it is important that health professionals in all areas of medicine are familiar with the management of this common psychiatric illness.

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COMPETING INTERESTS
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