DSM-5 Criteria: Bipolar Disorders

Box 1.

**DSM-5 Diagnosis: Bipolar I Disorder**

**Bipolar I Disorder:**

For a diagnosis of bipolar I disorder, it is necessary to meet the following criteria for a manic episode. The manic episode may have been preceded by and may be followed by hypomanic or major depressive episodes.

**Manic Episode:**

- A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased goal-directed activity or energy, lasting at least 1 week and present most of the day, nearly every day (or any duration if hospitalization is necessary).
- During the period of mood disturbance and increased energy or activity, 3 (or more) of the following symptoms (4 if the mood is only irritable) are present to a significant degree and represent a noticeable change from usual behavior:
  - Inflated self-esteem or grandiosity
  - Decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
  - More talkative than usual or pressure to keep talking
  - Flight of ideas or subjective experience that thoughts are racing
  - Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed
  - Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation (i.e., purposeless, non-goal-directed activity)
  - Excessive involvement in activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)
- The mood disturbance is sufficiently severe to cause marked impairment in social or occupational functioning, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.
- The episode is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment) or to another medical condition.

*Note: A full manic episode that emerges during antidepressant treatment [e.g., medication, electroconvulsive therapy (ECT)], but persists at a fully syndromal level beyond the physiological effect of treatment is sufficient evidence for a manic episode, and therefore, a bipolar I diagnosis.*
DSM-5 Criteria: Bipolar Disorders (continued)

Box 2.

DSM-5 Diagnosis: Bipolar II Disorder

**Bipolar II Disorder:**

- Criteria have been met for at least one hypomanic episode and at least one major depressive episode
- There has never been a manic episode
- The occurrence of the hypomanic episode(s) and major depressive episode(s) is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorder.
- The symptoms of depression or the unpredictability caused by frequent alternation between periods of depression and hypomania causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

For a diagnosis of bipolar II disorder, it is necessary to meet the following criteria for a current or past hypomanic episode and the criteria for a current or past major depressive episode (See Box 3 on page 24 for Major Depressive Episode criteria).

**Hypomanic Episode:**

- A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least 4 consecutive days and present most of the day, nearly every day.
- During the period of mood disturbance and increased energy and activity, 3 (or more) of the above symptoms (4 if the mood is only irritable) have persisted, represent a noticeable change from usual behavior, and have been present to a significant degree.
- The episode is associated with an unequivocal change in functioning that is uncharacteristic of the individual when not symptomatic.
- The disturbance in mood and the change in functioning are observable by others.
- The episode is not severe enough to cause marked impairment in social or occupational functioning or to necessitate hospitalization. If there are psychotic features, the episode is, by definition, manic.
- The episode is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment).

*Note:* A full hypomanic episode that emerges during antidepressant treatment (e.g., medication, ECT) but persists at a fully syndromal level beyond the physiological effect of that treatment is sufficient evidence for a hypomanic episode diagnosis. However, caution is indicated so that one or two symptoms (particularly increased irritability, edginess or agitation following antidepressant use) are not taken as sufficient for a diagnosis of a hypomanic episode nor necessarily indicative of a bipolar diathesis.
Treatment of Acute Bipolar Disorder - Depression

Conduct comprehensive assessment and use measurement-based care. Refer to Principles of Practice on pages 6-10.

The primary therapeutic objectives of bipolar disorder care are remission, maintenance of remission, prevention of recurrence, and full functional recovery.

- Selection of acute treatment should take maintenance treatment goals into account.
- Be aware of safety and tolerability concerns, evidence for maintenance use, and acute efficacy.

**Strongly recommend psychiatric consultation prior to initiation of therapy + psychotherapeutic medication using a multi-disciplinary approach if treated by a non-psychiatrist.**

<table>
<thead>
<tr>
<th>Level 1</th>
<th>Established efficacy:</th>
</tr>
</thead>
<tbody>
<tr>
<td>♦ Optimize index mood stabilizer if already prescribed a mood stabilizer. Check blood levels if appropriate.</td>
<td></td>
</tr>
<tr>
<td>♦ Quetiapine or lurasidone monotherapy*</td>
<td></td>
</tr>
<tr>
<td>*Notes: Only quetiapine has established efficacy for bipolar II disorder. Lurasidone has a better metabolic profile than quetiapine.</td>
<td></td>
</tr>
<tr>
<td>♦ Lamotrigine monotherapy</td>
<td></td>
</tr>
<tr>
<td>♦ Lurasidone or lamotrigine** adjunctive to lithium or divalproex if index mood stabilizer has been optimized.</td>
<td></td>
</tr>
<tr>
<td>**Caution: There is a drug-drug interaction with use of lamotrigine and divalproex together that requires reducing the lamotrigine dose by 50% of the typical lamotrigine dose. For dosing recommendations, refer to Table 2 on page 19.</td>
<td></td>
</tr>
<tr>
<td>♦ Do not utilize conventional antidepressants (e.g., SSRIs, SNRIs, TCAs, MAOIs) as a first-line therapy.</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Level 2A</th>
<th>Established efficacy, but with safety concerns*:</th>
</tr>
</thead>
<tbody>
<tr>
<td>♦ Olanzapine + fluoxetine (bipolar I disorder)</td>
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<tr>
<td>*Note: Tolerability limitations include weight gain and metabolic concerns.</td>
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<tr>
<th>Level 2B</th>
<th>Better tolerability, but limited efficacy*:</th>
</tr>
</thead>
<tbody>
<tr>
<td>♦ Lithium (bipolar 1 disorder)</td>
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<tr>
<td>♦ 2 drug combination of above medications. Drugs may include either a first generation antipsychotic (FGA) or second generation antipsychotic (SGA) but NOT TWO antipsychotic medications</td>
<td></td>
</tr>
<tr>
<td>*Note: Efficacy limitations, relatively few positive randomized controlled trials.</td>
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<tr>
<th>Level 3</th>
<th>If Levels 1 and 2 are ineffective and/or not well tolerated*:</th>
</tr>
</thead>
<tbody>
<tr>
<td>♦ Electroconvulsive therapy (ECT)</td>
<td></td>
</tr>
<tr>
<td>*Note: Consideration is merited due to clinical need, despite even greater efficacy/tolerability limitations than Level 1 and 2 treatments.</td>
<td></td>
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</tbody>
</table>
Treatment of Acute Bipolar Disorder - Depression (continued)

Level 4  If Levels 1 – 3 are ineffective and/or not well tolerated:

- Cariprazine
- FDA-approved agent for bipolar disorder + conventional antidepressant (e.g., SSRI)*
- Pramipexole
- Adjunctive: modafinil, thyroid hormone (T3), or stimulants
- 3 drug combination
- Transcranial magnetic stimulation (TMS)

*Notes:

- There is inadequate information (including negative trials) to recommend adjunctive antidepressants, aripiprazole, ziprasidone, levetiracetam, armodafinil, or omega-3 fatty acids for bipolar depression.
- Preliminary evidence is available for cariprazine in the treatment for bipolar I depression.
- Antidepressant monotherapy is not recommended in bipolar I depression; recommendation is for adjunctive mood stabilizer with antidepressant.
- Superiority (in other words, efficacy and safety) of antidepressant monotherapy versus adjunctive mood stabilizer with antidepressant for treatment of bipolar II depression is uncertain.
Treatment of Acute Bipolar Disorder - Mania

Conduct comprehensive assessment and use measurement-based care. Refer to Principles of Practice on pages 6-10.

The primary therapeutic objectives of bipolar disorder care are safety, symptomatic improvement, and patient psychoeducation.

- Selection of acute treatment should take maintenance treatment goals into account.
- Be aware of safety and tolerability concerns, evidence for maintenance use, and acute efficacy.

Strongly recommend psychiatric consultation prior to initiation of therapy + psychotherapeutic medication using a multi-disciplinary approach if treated by a non-psychiatrist.

Level 1A Established efficacy:

Mild to moderate severity and/or not requiring hospitalization
- Optimize mood stabilizer (lithium*, divalproex*, or carbamazepine*) if already prescribed. Check blood levels if appropriate.
- Lithium* monotherapy
- Monotherapy with aripiprazole, asenapine, divalproex*, quetiapine, risperidone, ziprasidone, or cariprazine.

Severe and/or requiring hospitalization
- Lithium* or divalproex* + aripiprazole, asenapine, quetiapine, or risperidone
- Electroconvulsive therapy (ECT) is recommended if medical emergency/patient welfare at risk and pharmacotherapy is insufficient.

Level 1B Established efficacy, but with safety concerns**: 

Mild to moderate severity and/or not requiring hospitalization
- Monotherapy with either haloperidol or olanzapine

Severe and/or requiring hospitalization
- Lithium* or divalproex* + either haloperidol or olanzapine

Level 2 If Levels 1A and 1B are ineffective and/or not well tolerated:

- Combination treatment with lithium* + divalproex*
- Combination with lithium* and/or divalproex* + second generation antipsychotic (SGA) other than clozapine
- Carbamazepine* monotherapy

Level 3 If Levels 1 and 2 are ineffective and/or not well tolerated:

- Electroconvulsive therapy (ECT)
- Clozapine + lithium* or divalproex*
- Lithium* + carbamazepine*
- Divalproex* + carbamazepine*
Level 4  If Levels 1 – 3 are ineffective and/or not well tolerated:

- A three-drug combination of Level 1, 2, and 3. Drugs may include first generation antipsychotic (FGA) or second generation antipsychotic (SGA) but **NOT TWO** antipsychotic medications.

Example: lithium* + (divalproex* or carbamazepine*) + antipsychotic

Notes:

*Caution should be used when prescribing lithium, lamotrigine, divalproex or carbamazepine to women of reproductive age due to increased risks to the fetus with use during pregnancy, including neural tube and other major birth defects. Please see Florida Best Practice Recommendations for Women of Reproductive Age with Serious Mental Illness and Comorbid Substance Use Disorders and online guideline on the Pharmacological Treatment of Mood Disorders During Pregnancy.

**Side-effect concerns with these agents include weight gain, metabolic syndrome, and extrapyramidal symptoms (EPS). Side-effects warrant vigilance and close monitoring on the part of the clinicians.

Data for use of paliperidone to treat bipolar mania are mixed. Paliperidone >6 mg has some data supporting efficacy.

Benzodiazepines may be used as an adjunct treatment for acute treatment of bipolar mania.

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**Florida Clozapine Hotline**

727-562-6762
Rhemsath@aol.com

The Clozapine Hotline is operated by Randolph Hemsath, M.D., Medical Director of Boley Centers, a CARF-accredited community mental health center in St. Petersburg, FL. Dr. Hemsath has over 30 years’ experience as a psychiatrist and extensive experience utilizing clozapine as an option for individuals with treatment-refractory schizophrenia.

The hotline is funded by the Florida Medicaid Drug Therapy Management Program for Behavioral Health through a contract with the Florida Agency for Healthcare Administration.

Calls and emails will be answered on non-holiday weekdays between 8:00am and 5:00pm. **No registration is required and the service is free.**
Bipolar 1 Disorder Continuation / Maintenance Therapy

Conduct comprehensive assessment and use measurement-based care. Refer to Principles of Practice on pages 6-10.

The list of possible treatments in the prevention of bipolar disorder is comprised of many treatment options; therefore, the regimen that stabilizes a patient should be strongly considered for continuation and maintenance (monitoring for efficacy and adverse events).

Strongly recommend psychiatric consultation prior to initiation of therapy + psychotherapeutic medication using a multi-disciplinary approach if treated by a non-psychiatrist.

<table>
<thead>
<tr>
<th>Level 1</th>
<th>Established efficacy:</th>
</tr>
</thead>
<tbody>
<tr>
<td>✦ Periodic evaluation: frequency based on clinical needs</td>
<td></td>
</tr>
<tr>
<td>✦ Continue with effective and well-tolerated treatment</td>
<td></td>
</tr>
<tr>
<td>✦ Lithium* monotherapy</td>
<td></td>
</tr>
<tr>
<td>✦ Quetiapine monotherapy</td>
<td></td>
</tr>
<tr>
<td>✦ Lamotrigine* (evidence strongest for prevention of depression)</td>
<td></td>
</tr>
<tr>
<td>✦ If initially stabilized on divalproex*†, maintain.</td>
<td></td>
</tr>
<tr>
<td>✦ Aripiprazole or aripiprazole long-acting injectable, long-acting risperidone monotherapy</td>
<td></td>
</tr>
<tr>
<td>✦ Quetiapine (for recurrence prevention) or ziprasidone (for relapse prevention) adjunctive to (lithium* or divalproex*‡)</td>
<td></td>
</tr>
<tr>
<td>✦ Asenapine monotherapy</td>
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</tbody>
</table>

\[\text{\textsuperscript{1}}\text{Note: Be aware that there are limited data on long-term efficacy of divalproex.}\]

<table>
<thead>
<tr>
<th>Level 2A</th>
<th>Established efficacy, but with safety concerns**:</th>
</tr>
</thead>
<tbody>
<tr>
<td>✦ Olanzapine monotherapy</td>
<td></td>
</tr>
<tr>
<td>✦ Olanzapine adjunctive to lithium* or divalproex*‡</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Level 2B</th>
<th>If Level 1 is ineffective and/or not well tolerated:</th>
</tr>
</thead>
<tbody>
<tr>
<td>✦ Continue effective and well-tolerated acute treatment(s) if not listed in Level 1</td>
<td></td>
</tr>
<tr>
<td>✦ Lithium* and divalproex*‡ combination</td>
<td></td>
</tr>
<tr>
<td>✦ Follow acute mania/bipolar depression guidelines to achieve remission or partial remission</td>
<td></td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Level 3</th>
<th>If Levels 1 and 2 are ineffective and/or not well tolerated:</th>
</tr>
</thead>
<tbody>
<tr>
<td>✦ Adjunctive clozapine (avoid combining with another antipsychotic)</td>
<td></td>
</tr>
<tr>
<td>✦ Electroconvulsive therapy (ECT)*†</td>
<td></td>
</tr>
</tbody>
</table>

Notes:

* Caution should be used when prescribing lithium, lamotrigine, divalproex or carbamazepine to women of reproductive age due to increased risks to the fetus with use during pregnancy, including neural tube and other major birth defects. Please see Florida Best Practice Recommendations for Women of Reproductive Age with Serious Mental Illness and Comorbid Substance Use Disorders and online guideline on the Pharmacological Treatment of Mood Disorders During Pregnancy.

**Side-effect concerns with these agents include weight gain, metabolic syndrome, and extrapyramidal symptoms (EPS). Side-effects warrant vigilance and close monitoring on the part of the clinician.

†Long-term efficacy data are limited for the following: divalproex monotherapy, carbamazepine (drug interaction risk), antidepressants, and electroconvulsive therapy (inconvenience/expense).
<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>In acute mania: 1,200 - 2,400 mg/day (serum level 0.8 - 1.2 mEq/L)</td>
<td>Initial titration for tolerability - start 600-900 mg/day, increase 300 mg/day every 5 days. Check levels 5 days after initiation/dose change. Check levels frequently if clinical toxicity. Monitor renal and thyroid functions. Lower doses/levels may be necessary in non-manic compared to manic patients. For maintenance, some patients require serum levels of 0.8 to 1.2 mEq/L, others can be maintained with lower levels, but not below 0.6 mEq/L. In older individuals, start with lower lithium dose, titrate more slowly, and target lower serum lithium levels.</td>
</tr>
<tr>
<td>Divalproex</td>
<td>In acute mania: 5 - 60 mg/kg/day; 1,000 - 2,500 mg/day (serum level 85 - 125 µg/mL)</td>
<td>Initial loading may be tolerated, but some patients need initial titration for tolerability. Check levels 48 hours after initiation and adjust dose accordingly. Side-effects (especially gastrointestinal) are more evident above 100µg/ml. More teratogenic than other mood stabilizers. Lower doses/levels may be necessary in non-manic compared to manic patients.</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>In acute mania: 200 - 1,600 mg/day (serum level 6 - 12 µg/mL)</td>
<td>Initial titration for tolerability due to hepatic auto-induction: Start 200 - 400 mg/day and increase 200 mg/day every 3 days. Lower doses/levels may be necessary in non-manic compared to manic patients. Monitor for blood dyscrasias and serious rash. Screen individuals of Asian descent for HLA-B<em>1502 (serious rash risk indicator) due to high risk for Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). Patients testing positive for the HLA-B</em>1502 allele should not be treated with carbamazepine unless benefits clearly outweigh risks. Carbamazepine decreases serum levels of multiple other CYP450-metabolized drugs due to induction of CYP450 enzymes 3A4, 1A2, 2C19, and 2C19.</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>In bipolar maintenance: 100 - 400 mg/day</td>
<td>Initial titration to reduce risk of Stevens-Johnson syndrome (serious rash): Start 25 mg/day (12.5 mg/day if taken with divalproex). Increase by 25mg/day (12.5 mg/day if taken with divalproex) after 2 and 4 weeks and weekly thereafter. Initial target dose 200 mg/day, but final doses may be 100 - 400 mg/day. May be used in some patients with acute bipolar depression (despite acute efficacy limitation) due to good tolerability and depression prevention efficacy.</td>
</tr>
</tbody>
</table>

*mg/day = milligrams per day; mEq/L = milliequivalents per Liter; mg/kg/day = milligram per kilogram per day; µg/ml = microgram per milliliter
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<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
<th>Comments</th>
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<tbody>
<tr>
<td><strong>Second Generation Antipsychotics (SGA)</strong></td>
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<td></td>
</tr>
<tr>
<td>Second Generation Antipsychotics (SGA)</td>
<td>In acute mania:&lt;br&gt;• Aripiprazole: 15 - 30 mg/day&lt;br&gt;• Asenapine: 10 - 20 mg/day&lt;br&gt;• Olanzapine: 6 - 20 mg/day&lt;br&gt;• Paliperidone 3 - 12 mg/day&lt;br&gt;• Quetiapine: 400 - 800 mg/day&lt;br&gt;• Risperidone: 2 - 6 mg/day&lt;br&gt;• Ziprasidone: 80 - 160 mg/day</td>
<td>Initial titration may be necessary for tolerability. Lower doses may be necessary in depressed patients (e.g., quetiapine 300 mg/day). Ziprasidone should be taken with food. Asenapine is sublingual. Monitor for side effects, including sedation (especially with quetiapine and clozapine), weight gain (especially with olanzapine and clozapine), akathisia (especially with aripiprazole and ziprasidone) and extrapyramidal symptoms (EPS), especially with risperidone. Monitor weight and body mass index (BMI) at each visit and laboratory metabolic indices at baseline, 3 months, and yearly thereafter.</td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
<td>In acute bipolar depression:&lt;br&gt;As dosed for major depression. (No specific dosing recommendations can be given for bipolar depression.)</td>
<td>Larger trials have not found a benefit of antidepressants when added to mood stabilizers/antimanics for bipolar depression (other than olanzapine/fluoxetine combination). May be used in combination with antimanic drugs in some patients with acute bipolar depression, but should not be prescribed as monotherapy in patients with bipolar I disorder due to manic switch risk. Serotonin-norepinephrine reuptake inhibitors (SNRIs) and tricyclic antidepressants (TCAs) may have greater manic switch risk. Antidepressants carry an FDA boxed warning for increased suicidality risk in pediatric and young adult patients (under age 25). May be continued in patients who are on them and have stable mood.</td>
</tr>
</tbody>
</table>
Pharmacological Treatment of Bipolar Disorder: 2017-2018 Update Summary

Roger S. McIntyre, M.D., FRCPC
Professor of Psychiatry and Pharmacology, University of Toronto
Head, Mood Disorders Psychopharmacology Unit (MDPU), University Health Network
Chairman and Executive Director, Brain and Cognition Discovery Foundation (BCDF)
Director, Depression and Bipolar Support Alliance (DBSA), Chicago

INTRODUCTION

Bipolar disorders (BD) are associated with high rate of non-recovery, inter-episodic dysfunction, and chronicity. Mortality studies indicate that the rate of premature mortality is significantly elevated in bipolar disorder with a widening chasm in the mortality rate between affected individuals and persons in the general population. Convergent and replicated evidence indicates that utilization of a chronic disease model is an integral component to improving health outcomes in bipolar disorder, with salutary effects on both morbidity and mortality outcomes. Moreover, by improving precision, consistency, and appropriateness of treatment selection, decision support with evidence informed guidelines have demonstrated to reduce both individual and societal costs attributable to bipolar disorder.

The update of the 2017-2018 Florida Best Practice Psychotherapeutic Medication Guidelines for Adults represents the most up-to-date treatment recommendations and decision support for multiple stakeholders involved with, and who provide care for, individuals diagnosed with bipolar disorder. This current iteration provides a further refinement, in some cases differential emphasis, from the previous published version (Ostacher, Tandon, and Suppes 2016). In contradistinction from most treatment guidelines in bipolar disorder, the 2017-2018 Florida Best Practice Psychotherapeutic Medication Guidelines for Adults represents a synthesis of evidence and multi-disciplinary opinion from multiple stakeholders, including, but not limited to academicians, clinicians, and experts in private and public healthcare policy. The current portrait sketched of bipolar disorder as a common, complex, and lifelong disorder that significantly curtails human capital invites the need for multi-disciplinary consensus on pragmatic and scalable interventions. The updated version of the 2017-2018 Florida Best Practice Psychotherapeutic Medication Guidelines for Adults provides an update of pharmacologic, psychosocial, and neurostimulatory treatment approaches for symptom management.

PRINCIPLES OF TREATMENT

There are several guiding principles of treatment that are emphasized in the 2017-2018 guidelines. A particular emphasis is made on the importance of timely and accurate diagnosis. It remains a modifiable deficiency in bipolar disorder that the majority of affected individuals continue to be misdiagnosed and/or diagnosed long after observable characteristics and service utilization related to bipolar disorder have appeared. Safety assessment continues to be a priority and guiding principle in bipolar disorder, with emphasis not only on suicide and risk reduction, but also an urgency given to risk factor modification for common and chronic non-communicable comorbid physical health conditions (e.g., cardiovascular disease, metabolic syndrome). A third guiding principle is the importance of careful calculus of benefit of treatment expected compared to the holistic appraisal of treatment-related side effects and safety concerns. It is the view of the
Pharmacological Treatment of Bipolar Disorder:  
2017-2018 Update Summary (continued)

authorship of the guideline, that collective treatments for acute-based management (i.e., acute mania, acute bipolar depression) need to anticipate both short- and long-term side effects and safety concerns (e.g., weight gain). Priority is always given to safe, well-tolerated treatments that are supported by rigorous, randomized, double-blind, placebo-controlled trials.

Moreover, the guiding principle of integrating multimodality treatments in bipolar disorder is emphasized in light of the evidence supporting and the rationale for considering manualized-based psychosocial treatments (e.g., cognitive behavioral therapy, interpersonal social rhythm therapy). The 2017-2018 guideline further presses the principle on the importance of giving equal priority to somatic health (e.g., cardiovascular disease) as is given to conventional treatment targets in bipolar disorder (e.g., mania, sleep, cognitive impairment). Finally, patient health management, locus of care (e.g., medical home), and the importance of functional recovery and positive mental health and resiliency, are emphasized.

Pharmacological Treatment of Acute Bipolar Depression

Bipolar depression is the predominant therapeutic target in bipolar disorder in most early and later phases of the illness. Furthermore, depressive symptoms as part of bipolar disorder are often chronic, and highly associated with risk, comorbidity (e.g., cardiovascular disease), functional impairment, and suicidality. The United States Food and Drug Administration (FDA) has approved three psychotherapeutic agents of bipolar depression (i.e., lurasidone, quetiapine, and olanzapine-fluoxetine combination). The expert panel for the Florida Guidelines consensually agree to also list lamotrigine as a possible first-line treatment strategy in bipolar depression. The expert panel recognizes that lamotrigine has not received regulatory approval for marketing in bipolar depression. Notwithstanding, results conducted in large academic centers, as well as meta-analyses, indicate that lamotrigine is an effective agent for both acute and recurrence prevention of bipolar depression (lamotrigine is currently FDA-approved for recurrence prevention in bipolar disorder). Cariprazine, a D3 preferring D2/D3 partial agonist is currently approved for mania and mixed states in bipolar disorder, but not for bipolar depression. At the time of completing the 2017-2018 Florida Guidelines, results from two pivotal registration trials in adults with bipolar I depression indicate that cariprazine is efficacious in the acute treatment of bipolar I depression. The 2017-2018 guidelines re-emphasize the ubiquity and hazards posed by mixed features in bipolar disorder. Hitherto, no safe and reliable treatment is unequivocally established and efficacious in mixed bipolar depression (McIntyre, 2017). Notwithstanding, select atypical antipsychotics are likely the initial treatments of choice for many individuals with bipolar depression and mixed features. Select second generation antipsychotics are also recommended as first-line treatment for mania with mixed features.

Antidepressant utilization remains an understudied and controversial issue in bipolar disorder. No single antidepressant or class of antidepressants are approved for bipolar disorder. It is recognized by the Florida Expert Panel that antidepressants continue to be utilized at a high rate in adults with bipolar disorder. The guiding principle of utilizing antidepressants in bipolar disorder is that they should not be prioritized over better established and FDA-approved treatment, and should be utilized as adjunctive treatment strategies. The use of antidepressant monotherapy is highly discouraged in bipolar I disorder, while the safe and effective use of antidepressants in bipolar II disorder remains a possibility, but still requires replicated empirical evidence. Psychosocial treatments, like pharmacotherapeutic treatments for bipolar disorder, are recognized to be more effective earlier in the illness course. For treatment-resistant bipolar depression, electroconvulsive
therapy (ECT) remains the recommended treatment option, with evidence also supporting alternate neurostimulatory approaches (e.g., rTMS).

PHARMACOLOGICAL TREATMENT OF ACUTE BIPOLAR MANIA

The expert panel recognizes that mania is not only a defining feature of bipolar I disorder, but is a medical emergency requiring urgent detection, establishment of safety, appropriate setting assignment for care, and evidence-based treatments. No substantive changes were made to the acute mania guidelines when compared to the 2015 iteration, with an ongoing emphasis on FDA-approved second-generation antipsychotics, lithium, and divalproex, as the most commonly recommended first-line strategies.

CONTINUATION AND MAINTENANCE PHARMACOLOGICAL TREATMENT OF BIPOLAR DISORDER

Bipolar disorder is a highly progressive condition, as evidenced by greater episode frequency, duration, and complexity, as well as diminished treatment response across the illness trajectory. It is also recognized in bipolar disorder that best practices utilizing integrated multimodality therapies reduce and forestall risk of recurrence, and speculatively, neurobiological progression and cumulative illness load. Since the publication of the 2015 guidelines, the FDA has approved aripiprazole long-acting injectable (LAI) as a recurrence prevention treatment in bipolar disorder. The FDA has also approved aripiprazole proteus (Abilify MyCite®), which may be extrapolated to the bipolar population. Aripiprazole proteus (Abilify MyCite®) is a combination product comprised of oral aripiprazole embedded with an ingestible digital sensor to record and communicate medication ingestion events. Whether digital sensory detection improves compliance and health outcomes in bipolar disorder, however, is not well known. As per the previous guidelines, key therapeutic targets during long-term treatment of bipolar include subsyndromal depression, affective instability, cognitive impairment, sleep disturbance, comorbidity (e.g., substance use disorder, anxiety disorder, cardiovascular disease, obesity), as well as interpersonal, social and workplace dysfunction (Miskowiak et al., 2017). Multimodality interventions incorporating pharmacotherapy, psychosocial treatment, cognitive remediation, lifestyle modification (e.g., exercise), are critical components of long term care. As with major depressive disorder (MDD), it is also recommended by the expert panel that advocacy, for example, the Depression and Bipolar Support Alliance (DBSA), can play a critical role in education support service access and illness/treatment literacy and should be considered an integral component of care for any person affected by bipolar disorder.

REFERENCES:

