DSM-5 Criteria: Bipolar Disorders

Box 2.

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.

Box 3.

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 4 on page 30 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

Note: *Treatment recommendations are based on levels of evidence and expert opinion. For a description of the criteria for each level, see page 4.*

Conduct comprehensive assessment and use measurement-based care. Refer to Principles of Practice on pages 6–11.

The primary therapeutic objectives of bipolar disorder care are to achieve symptomatic remission, promote syndromal recovery, prevent recurrence, and facilitate 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.
- Revisit the appropriateness of current regimen (e.g. inappropriate polypharmacy)

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

Level 1 Initial treatment:

- Lurasidone or cariprazine monotherapy*

  **Note: Lurasidone and cariprazine have better metabolic profiles than quetiapine.*
- Lamotrigine monotherapy
- Quetiapine monotherapy - *If the patient has bipolar II depression*
- Lithium monotherapy
- Lurasidone or lamotrigine** adjunctive to lithium or divalproex if index agent (lithium or divalproex) has been previously prescribed and optimized. Adjunctive data for cariprazine not available, but cariprazine could be considered as alternative adjunct.

  ***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 pages 24–25.*
- Do not utilize conventional antidepressants (e.g., SSRIs, SNRIs, TCAs, MAOIs) as a first-line therapy.

Level 2 If Level 1 is ineffective and/or not well tolerated:

- Divalproex + lurasidone
- Olanzapine + fluoxetine (bipolar I disorder)

  **Note: Tolerability limitations include weight gain and metabolic concerns.*
- Two (2) drug combination of Level 1 medications but **NOT TWO** antipsychotic medications.

  **Note: Efficacy limitations, relatively few positive randomized controlled trials.*

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

- Electroconvulsive therapy (ECT)

  **Note: Consideration is merited due to clinical need, despite even greater efficacy/tolerability limitations than Level 1 and 2 treatments.*

Treatment of Acute Bipolar Disorder - Depression *(continued)*

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

- Intravenous racemic ketamine and/or esketamine
- FDA-approved agent for bipolar disorder + conventional antidepressant (e.g., SSRI)*
- Pramipexole
- Adjunctive: modafinil, thyroid hormone (T3), or stimulants
- Three (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.*
- *Antidepressant monotherapy is not recommended in bipolar I depression; recommendation is for adjunctive mood stabilizer with antidepressant.*
- *The safety and efficacy of antidepressant monotherapy in bipolar II depression is uncertain but may be appropriate in select circumstances.*

Treatment of Acute Bipolar Disorder - Mania

Note: *Treatment recommendations are based on levels of evidence and expert opinion. For a description of the criteria for each level, see page 4.*

Conduct comprehensive assessment and use measurement-based care. Refer to Principles of Practice on pages 6–11.

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 concern, 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 Initial Treatment:

Mild to moderate severity and/or not requiring hospitalization

- 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 If Level 1A is ineffective and/or not well tolerated:

Mild to moderate severity

- Monotherapy with 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*

Treatment of Acute Bipolar Disorder - Mania *(continued)*

	Level 4 **If Levels 1 – 3 are ineffective and/or not well tolerated:** ✦ A three (3)-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 risk 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 available at* ***floridamedicaidmentalhealth.org.*

***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 > 6mg has some data supporting efficacy.

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

Bipolar 1 Disorder Continuation / Maintenance Therapy

Note: *Treatment recommendations are based on levels of evidence and expert opinion. For a description of the criteria for each level, see page 4.*

Conduct comprehensive assessment and use measurement-based care. Refer to Principles of Practice on pages 6–11.

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 treat by a non-psychiatrist.

Level 1 Initial Treatment:

- Periodic evaluation: frequency based on clinical needs
- Continue with effective and well-tolerated treatment
- Lithium* monotherapy
- Quetiapine monotherapy
- Lamotrigine* (evidence strongest for prevention of depression)
- If initially stabilized on divalproex*†, maintain.
- Oral aripiprazole or aripiprazole long-acting injectable, long-acting risperidone monotherapy
- Quetiapine (for recurrence prevention) or ziprasidone (for relapse prevention) adjunctive to (lithium* or divalproex*†)
- Asenapine monotherapy
- Manual-based psychotherapy (e.g., interpersonal social rhythm therapy, CBT, mindfulness best evidence along with psychoeducation during the maintenance phase)

†*Note: Be aware that there are limited data on long-term efficacy of divalproex.*

Level 2A If Level 1 is ineffective and/or not well tolerated:

- Olanzapine monotherapy
- Olanzapine adjunctive to lithium* or divalproex*†

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

- Continue effective and well-tolerated acute treatment(s) if not listed in Level 1
- Lithium* and divalproex*† combination
- Follow acute mania/bipolar depression guidelines to achieve remission or partial remission

Bipolar 1 Disorder Continuation / Maintenance Therapy
(Continued)

→	**Level 3** **If Levels 1 and 2 are ineffective and/or not well tolerated:** ✦ Adjunctive clozapine (avoid combining with another antipsychotic) ✦ Electroconvulsive therapy (ECT)†

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 available at* ***floridamedicaidmentalhealth.org****.*

***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 2. Recommended Medications for the Treatment of Bipolar Disorder – Mood Stabilizers

Medication	Dosage	Comments
Lithium	**In acute mania:** 1,200–2,400 mg/day (serum level 0.8–1.2 mEq/L)	✦ Initial titration for tolerability: ✧ Start 600–900 mg/day, increase 300 mg/day every 5 days. ✧ Check levels 5 days after initiation/dose change (ideally, trough lithium levels 12 hours after last dose). ✧ Check blood levels more frequently if signs or suspicion of clinical toxicity. ✦ Lower doses/levels may be necessary in non-manic compared to manic patients. ✦ Monitor renal and thyroid functions. ✦ 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.
Divalproex	**In acute mania:** 5–60 mg/kg/day; 1,000–2,500 mg/day (serum level 85–125 µg/mL)	✦ Initial dosing: ✧ Initial loading may be tolerated, but some patients need initial titration for tolerability. ✧ Lower doses/levels may be necessary in non-manic compared to manic patients. ✧ Check levels 48 hours after initiation and adjust dose accordingly. ✦ Side-effects (especially gastrointestinal) are more evident above 100 µg/ml. ✦ More teratogenic than other mood stabilizers. ✦ Serious side effects include hepatotoxicity, thrombocytopenia, pancreatitis, and hyperammonemic encephalopathy.

Table 2. Recommended Medications for the Treatment of Bipolar Disorder – Mood Stabilizers *(continued)*

Carbamazepine	**In acute mania:** 200–1,600 mg/day (serum level 6–12 µg/mL)	✦ 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*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*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, 2C9, and 2C19.
Lamotrigine	**In bipolar maintenance:** 100–400 mg/day	✦ Initial titration to reduce risk of Stevens-Johnson syndrome and Toxic Epidermal Necrolysis (TEN) [serious rash]: ✧ Start 25 mg/day (12.5 mg/day if taken with divalproex). ✧ Increase by 25 mg/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.

**mg/day= milligrams per day; mEq/L = milliequivalents per Liter; mg/kg/day = milligram per kilogram per day; µg/ml = microgram per millimeter*

Table 3. Recommended Medications for the Treatment of Bipolar Disorder – Second Generation Antipsychotics (SGAs) and Antidepressants

Medication	Dosage	Comments
Second Generation Antipsychotics (SGA)	**In acute mania:** • Aripiprazole: 15–30 mg/day • Asenapine: 10–20 mg/day • Olanzapine: 6–20 mg/day • Paliperidone 3–12 mg/day • Quetiapine: 400–800 mg/day • Risperidone: 2–6 mg/day • Ziprasidone: 80–160 mg/day **In acute bipolar depression:** • Quetiapine: 200–600 mg/day • Olanzapine/Fluoxetine: 3 mg/12.5 mg–12 mg/50 mg per day • Lurasidone: 40–120 mg/day • Clozapine: 50–400 mg/day (if treatment resistant)	✦ 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.
Antidepressants	**In acute bipolar depression:** As dosed for major depression. (No specific dosing recommendations can be given for bipolar depression.)	✦ Larger trials have not found a benefit of antidepressant 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. ✦ Antidepressant 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 antidepressants and have stable mood.

**mg/day = milligrams per day*

Summary for Treatment of Bipolar Disorder *(continued)*

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Introduction

Bipolar disorder (BD) is a severe, lifelong group of disorders with an estimated prevalence of approximately 2%. Approximately three-quarters of individuals with BD exhibit features of the disorder prior to the age of 25 highlighting the neurodevelopmental aspects of the disorder as well as the importance for screening and timely diagnosis, especially in younger populations presenting in clinical settings with clinically significant depressive and anxiety symptoms. Misdiagnosis representing a conflation of both false positives and false negatives continue to be one of the greatest unmet needs in BD. The consequences of missed and delayed diagnosis are protean and include the accumulation of comorbidities (e.g., obesity, substance abuse), unmitigated suicide risk, erroneous treatment selections, human suffering, and increased morbidity.

The panel agreed that screening for BD is essential for any person presenting with mood related symptoms and/or in clinical scenarios wherein conventional treatments for a mood disorder are inadequate. Results from longitudinal studies consistently report that most individuals with BD exhibit depression, depressive symptoms, and/or episodes as the predominant presentation of the illness as well as polarity at first presentation. Consequently, many adults with BD transition from the diagnosis of Major Depressive Disorder (MDD) to BD over multiple years of prospective follow-up. For example, it is reported that approximately 1% of adults with "MDD" transition to BD annually underscoring the importance of vigilance for hypo/manic presentations in adults originally diagnosed with having MDD.

In addition to misdiagnosis as well as delayed diagnosis, insufficient attention to comorbidity in BD is identified as an unmet need. Adults with BD are affected by a large number of medical and mental comorbidities with at least half of patients meeting criteria for three or more concurrent conditions. It is not uncommon for the comorbid conditions to be a phenomenological antecedent to BD and, not infrequently, obscuring the underlying diagnosis of BD.

Similar to adults with MDD, it is recognized that the vast majority of adults with BD are not achieving full syndromal and functional recovery. This deficiency is in part explained by inadequate/inappropriate treatments, treatment non-concordance, as well as insufficient attention to comorbidities and relevant psychosocial factors. It is additionally recognized that for a substantial population of adults with BD, enduring deficits across multiple domains of cognitive function remain a source of distress and mediator of functional impairment. In some cases, the severity, persistence, and complexity of cognitive impairment in BD phenotypically mimics attention deficit hyperactivity disorder (ADHD). Hitherto, there are no United States Food and Drug Administration (FDA)-approved treatments for cognitive dysfunctions in BD nor are there any evidence-based and proven treatments for cognitive impairment in BD.

Results from the extant literature indicate that outcomes in BD are optimal when individuals are diagnosed timely and accurately and receive guideline-informed measurement based, integrated, and multidisciplinary care. For individuals with treatment-resistant BD, evidence also supports cognitive and functional remediation as a manual-based intervention. Response rates to conventional treatments for BD, both pharmacologic and psychosocial, are diminished

in subpopulations with higher episode frequency. Moreover, populations with greater episode frequency exhibit greater susceptibility to additional disorders including, but not limited to, cardiovascular disease, obesity, and dementia.

Principles of Treatment

The unmet need regarding timely and accurate diagnosis instantiates the importance of using screening tools (e.g., Mood Disorder Questionnaire; MDQ) in adults with BD. Screening should take place at initial assessments and any scenarios wherein inadequate outcomes are being observed. Screening does not supplant a careful and comprehensive clinical evaluation which is sine qua non to establishing the diagnosis of BD. The use of measurement to track symptoms (e.g., mood diaries) is encouraged and attempts to prevent comorbidities should be a clinical focus at initial presentations. Recognition that BD is an independent risk factor for cardiovascular disease further underscores the importance of holistic approaches to the assessment, prevention, and management of BD. Individuals with BD report much higher rates of physical and sexual trauma in the recent or distant past as well as describe psychosocial stressors as associated with episode recurrence. In addition to targeting key features of BD, the management of BD also needs to include psychoeducation, improvement of diagnosis and treatment literacy, conflict and stress management skills, as well as lifestyle improvement with focus on diet as well as sleep hygiene.

Pharmacologic Treatment of Acute Bipolar Depression

The panel recommends cariprazine and lurasidone monotherapy as initial treatment for bipolar depression. Lurasidone is also recommended in combination with lithium or divalproex. The panel recognizes that lurasidone is not FDA-approved for mania; cariprazine and quetiapine are approved for acute bipolar mania/mixed states. Cariprazine was FDA approved in 2019 for the acute treatment of bipolar depression. The panel recognizes that cariprazine and lurasidone have lower propensity to weight gain and are metabolically similar to placebo in the treatment of adults with BD. These observations differentiate these second-generation antipsychotics (SGAs) from quetiapine and olanzapine-fluoxetine combination which are susceptible to clinically significant weight gain and/or metabolic shift. It was the view of the panel that consideration of weight gain and metabolics is paramount in selecting treatments for bipolar depression. The panel also recommends lithium or lamotrigine as possible first-line treatments for bipolar depression. The anti-suicide effects of lithium, not seen with other FDA-approved treatments for BD, are an important attribute of lithium.

The panel recognizes that antidepressant monotherapy in Bipolar I Disorder is to be discouraged. Conventional antidepressants are not recommended in Bipolar I Disorder for adults manifesting mixed features, rapid cycling, and/or histories of previous antidepressant-associated emergence of hypo/mania. For adults with Bipolar II Disorder, preliminary evidence suggests that some adults may be safely and effectively treated with antidepressant monotherapy. The lack of empirically supported response predictors to antidepressant monotherapy in BD implies that it is unknown a priori which individuals with Bipolar II Disorder may be safely treated with antidepressant monotherapy. The panel also recognizes that there is a paucity of long-term treatments with antidepressants in BD. The recommendation to continue antidepressants will be determined on an individual basis.

Pharmacologic Treatment of Acute Bipolar Mania

The ***2019-2020 Florida Best Practice Psychotherapeutic Medication Guidelines for Adults*** has retained similar guidance with respect to pharmacologic treatments of bipolar mania. Bipolar mania is recognized as a medical emergency requiring, in many cases, a higher intensity of treatment. Safety is of paramount importance of mania and, where applicable, inpatient stay and specialist consultation is encouraged. The panel also recognizes that for many adults with bipolar mania, the predominant presentation is dysphoric and mixed with many adults manifesting non-specific symptoms (e.g., anxiety, agitation, irritability, anger) that often obscure the underlying diagnosis of mania. SGA monotherapy as well as lithium or divalproex are recommended in cases of mania of milder severity (e.g., non-psychotic mania). In situations where patients have severe mania (e.g., psychosis, need for hospitalization), combination SGA and additional mood stabilizing agent (e.g., lithium) is recommended.

Maintenance Pharmacological Treatment of Bipolar Disorder

More than 90% of individuals with BD will experience recurrence of illness. Episode recurrence in BD is highly associated with progressive changes to brain structure and function, as well as the accumulation of multiple comorbidities. Further evidence also suggests that greater episode frequency is associated with more pronounced cognitive deficits in BD. Moreover, it is not frequent in BD to witness a phenomenological shift across time where patients manifest increasing depressive symptom burden. A clinical impression awaiting cogent empirical confirmation is that, increasingly, clinicians are encountering a higher percentage of individuals with BD presenting with mixed features during the acute or maintenance phase. It is uncertain what is causing this, but, certainly, antidepressant utilization, drug and alcohol misuse and obesity are contributing causes. For most adults with BD, multi-year/lifetime pharmacotherapy is recommended, integrated with lifestyle interventions targeting healthful living, diet, exercise, and sleep hygiene. For many adults, manual-based psychosocial treatments (e.g., cognitive therapy), interpersonal social rhythm therapy and psychoeducation, are critical adjuncts to pharmacotherapy to improve overall psychosocial function and wellbeing. During the acute and maintenance phase of BD, careful attention to suicidality is paramount.

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