

Bipolar Disorder Practice Guidelines for Adults

Introduction

PerformCare’s condensed guidelines for the treatment of Bipolar Disorder are derived from the American Psychiatric Association (APA) Guidelines for the treatment of Bipolar Disorder in Adults compiled in 2002 as well as recent updates published in the scientific literature. We adopt the position expressed by the American Psychiatric Association:

“Practice Guidelines are not intended to be construed or to serve as a standard of medical care. . . . Adherence to them will not ensure a successful outcome for every individual... The ultimate judgment regarding a particular clinical procedure or treatment plan must be made by the psychiatrist in light of the clinical data presented by the patient and the diagnostic and treatment options available.”

Our intent is to present advocate summary of expert recommendations based on research and accumulated clinical experience. We report those treatments the guidelines identify as supported by the strongest evidence, based on clinical trials and substantial clinical experience. The reader can consult the original documents cited in the references for a listing of treatment options with less clinical support, or for details about the processes that were undertaken to formulate the guidelines.

Diagnostic options:

Diagnostic options have recently changed with the publication of DSM-5 in 2013. The criteria for diagnosis in the Bipolar Disorder spectrum have been modified to avoid under diagnosis of Bipolar II Disorder and over diagnosis of Bipolar Disorder NOS. A key change is the requirement in DSM-5 requiring mood change (elation/euphoric or irritable mood) to be accompanied by persistently increased activity or energy levels.

DSM-5 still requires patients with **Bipolar I Disorder** to have experienced at least one episode of mania as well as mixed, hypomanic, and depressive. Patients with **Bipolar II Disorder** must have experienced hypomanic and depressive episodes.

Cyclothymic Disorder:

Cyclothymic disorder may be diagnosed in those patients who have never experienced a manic, mixed or major depressive episode but who have experienced numerous periods of depressive symptoms and numerous periods of hypomanic symptoms for at least two years, with no symptom-free period greater than two months.

It is now the case that patients with depressive symptoms and periods of mood elevation who do not meet criteria for Bipolar Disorder I, II or Cyclothymia are no longer to be diagnosed with **Bipolar Disorder Not Otherwise Specified (NOS)**. They may be diagnosed with either **Other Specified Bipolar and Related Disorder** or **Unspecified Bipolar and Related Disorder**.

DSM-5 diagnostic options are summarized below and permit detailed characterization of the patient’s condition. For example, someone diagnosed with bipolar I disorder would be categorized with reference to current or most recent episode, severity, the presence of psychosis, remission status, and any other applicable specifiers. For details of the diagnostic criteria the reader should consult the DSM-5 Handbook.

DSM-5 Diagnosis	Current/ Recent Episode	Severity	Psychosis	Remission	Specifiers (Associated With)
Bipolar I Disorder	Manic	Mild	With or	Partial	Anxious Distress
Bipolar II Disorder	Depressed	Moderate	Without	Full	Mixed Features
Cyclothymic Disorder	Mixed	Severe	Psychotic	Unspecified	Rapid Cycling
	Hypomanic		Features		Melancholic Features
					Atypical Features

Substance/Medication-Induced Bipolar and Related Disorder <i>(must specify substance or medication)</i>					Mood-Congruent Psychosis Mood-Incongruent Psychosis Catatonia Peripartum Onset Seasonal Pattern
Bipolar and Related Disorder Due to Another Medical Condition <i>(must specify medical condition)</i>					
Other Specified Bipolar And Related Disorder					
Unspecified Bipolar and Related Disorder					

General Diagnostic Considerations

Bipolar I disorder affects approximately 0.8 percent of the adult population, with estimates from community samples ranging between 0.4percent and 1.6percent. These rates are consistent across diverse cultures and ethnic groups. Bipolar II disorder affects approximately 0.5percent of the population. Generally speaking bipolar disorders types I and II affect about 2% of the world’s population, with subthreshold forms of the disorder affecting another 2 percent.

Patients with Bipolar Disorder most often exhibit symptoms of depression but may also exhibit substance abuse, impulsivity, irritability, agitation, insomnia and problems with relationships. Patients rarely volunteer information about manic or hypomanic episodes, so clinicians must inquire about time periods with mood dysregulation, lability or both that are accompanied by associated manic symptoms (e.g., decreased need for sleep, increased energy). Culture can influence the experience and communication of symptoms of depression and mania. African-Americans and Hispanic-Americans with Bipolar Disorder tend to be misdiagnosed with schizophrenia.

In addition to looking for evidence of the existence of a mood disorder, the initial evaluation requires:

- Assessment of the safety of the patient and those around him or her in order to make a decision about the appropriate setting for treatment (e.g., outpatient, day program or inpatient).
- Assessment of the presence of an alcohol or substance use disorder.
- Assessment of additional somatic factors that may contribute to the disease process or complicate its treatment.

Suicide rates in patients with bipolar I disorder may be as high as 10 percent to 15percent; thus, a careful assessment of the patient’s risk for suicide is critical. The ability to predict suicide or violence risk from clinical data is limited. Consequently, patients who exhibit suicidal or violent ideas or intent require close monitoring.

Characteristics to evaluate in an assessment of suicide risk in patients with Bipolar Disorder include the following:

- Presence of suicidal or homicidal ideation, intent or plans.
- Access to means for suicide and the lethality of those means.
- Presence of command hallucinations, other psychotic symptoms or severe anxiety.
- Presence of alcohol or substance use.
- History and seriousness of previous attempts.
- Family history of or recent exposure to suicide.

When patients are taking more than one medication, the possibility of adverse drug-drug interactions should always be considered. Clinicians should also inquire about patient use of herbal preparations and over-the-counter medications.

General Approach to Treatment

At this time, there is no cure for Bipolar Disorder; treatment can decrease the associated morbidity and mortality. However, it must be emphasized that variability is the hallmark of this illness. Even with treatment, about 37 percent of patients relapse into depression or mania within one year of diagnosis, and 60 percent within two years.

Psychiatric management (physician) must establish and maintain a therapeutic alliance, monitor the patient's psychiatric status, provide education regarding bipolar disorder, enhance treatment compliance, encourage regular patterns of activity and of sleep, help anticipate stressors, and detect new episodes early, and limit functional impairments. Establishing and maintaining a supportive and therapeutic relationship is critical. A crucial element of this alliance is the knowledge gained about the course of the patient's illness that allows new episodes to be identified as early as possible. As early as possible the physician should communicate to the bipolar patient and significant others regarding how information about the patient will be shared. The physician should emphasize the importance of sharing information about risks and the need for significant others to understand the patient's perspective. Additionally, the physician should foster collaboration intended to support all concerned parties.

Recognizing early signs and symptoms of manic or depressive episodes can help the patient enhance mastery over his or her illness and can help ensure that adequate treatment is instituted as early as possible in the course of an episode. Early markers of episode onset vary from patient to patient but are often usefully predictable across episodes for an individual patient.

Patients with Bipolar Disorder benefit from education and feedback regarding their illness, prognosis, and treatment. Similar educational approaches are also important for family members and significant others. Patients and families can benefit from an understanding of the role of psychosocial stressors. Psychosocial stressors are consistently found to be increased before both manic and depressive episodes in all phases of the illness. Social rhythm disruption with disrupted sleep-wake cycles may specifically trigger manic (but not depressive) episodes.

Physician should advise patients and their families about what can happen during manic episodes. Patients may engage in reckless behavior and, at times, steps should be taken to limit access to cars, credit cards, bank accounts, telephones, and computers. During manic episodes, for example, patients may spend money unwisely, damage important relationships, lose jobs, or commit sexual indiscretions.

Medication side effects, cost and other demands of long-term treatment may be burdensome and need to be discussed realistically with the patient and family members. Following extreme mood episodes, patients may require assistance in addressing the psychosocial consequences of their actions.

Hospitalization is usually indicated for patients who are considered to pose a serious threat of harm to themselves or others. If patients refuse, they can be hospitalized involuntarily if their condition meets criteria of the local jurisdiction for involuntary admission. The optimal treatment setting and the patient's ability to benefit from a different level of care should be reevaluated on an ongoing basis throughout the course of treatment.

Patients with Bipolar Disorder are frequently ambivalent about treatment. This ambivalence often takes the form of noncompliance with medication and other treatments, which is a major cause of relapse. Patients who do not

believe that they have a serious illness are not likely to be willing to adhere to long-term treatment regimens. Another important factor for some patients is their reluctance to give up the experience of hypomania or mania. The increased energy, euphoria, heightened self-esteem, and ability to focus may be very desirable. Patients with Bipolar Disorder may benefit from regular patterns of daily activities, including sleeping, eating, physical activity, and social and emotional stimulation.

Acute Pharmacological Treatment (RECOMMENDED WITH SUBSTANTIAL CLINICAL CONFIDENCE)

Manic or mixed episodes:

The first-line pharmacological treatment for more severe manic or mixed episodes is the initiation of lithium plus an antipsychotic or valproate (Depakote) plus an antipsychotic. These antipsychotics include olanzapine (Zyprexa), quetiapine (Seroquel), aripiprazole (Abilify), risperidone (Risperdal) or haloperidol (Haldol). Atypical antipsychotics are preferred over typical antipsychotics because of their more benign side effect profile.

For less ill patients, monotherapy with lithium, valproate, or an atypical antipsychotic such as olanzapine may be sufficient. Monotherapy with asenapine (Saphris), paliperidone (Invega) extended release (ER), and divalproex ER (Depakote ER), as well as adjunctive asenapine, have been added as first-line options.

With adequate dosing and serum levels, medications for the treatment of mania generally exert some appreciable beneficial effect by the 10th to the 14th day of treatment. When first-line medication treatment at optimal doses fails to control symptoms, recommended treatment options include addition of another first-line medication or adding an antipsychotic if not already prescribed. Severely ill or agitated patients may also require short-term adjunctive treatment with a benzodiazepine. Electroconvulsive therapy (ECT) may be considered for patients with severe or treatment-resistant mania or if preferred by the patient in consultation with the psychiatrist.

Antidepressants may precipitate or exacerbate manic or mixed episodes, and generally should be tapered and discontinued if possible. Medications not recommended in patients with mania or mixed episode include topiramate (Topomax), lamotrigine (Lamictal) and gabapentin (Neurontin).

Depressive episodes:

First line options for the management of bipolar depression include lithium, lamotrigine, and quetiapine monotherapy. Olanzapine plus selective serotonin reuptake inhibitor (SSRI), and lithium or divalproex plus SSRI / bupropion (Wellbutrin) also remain first-line options.

Combining lithium with lamotrigine can be considered for patients with Bipolar Disorder- Depression who do not respond to monotherapy. Depressive episodes with psychotic features usually require adjunctive treatment with an antipsychotic medication

Antidepressant monotherapy is not recommended. Aripiprazole is NOT recommended for monotherapy in the treatment of acute bipolar depression. Ziprasidone alone or as adjunctive therapy, and adjunctive levetiracetam (Keppra) are not recommended for the treatment of bipolar depression. Gabapentin and the tricyclic antidepressants (TCAs) are not recommended for monotherapy or augmentation in the treatment of acute bipolar depression.

ECT should be considered for patients with severe or treatment-resistant depression, depression with psychotic or catatonic features or life-threatening symptoms.

Maintenance Pharmacological Treatment (recommended with substantial clinical confidence)

Patients who have had an acute manic episode should be treated for at least six months after the initial episode is controlled, and encouraged to continue on life-long prophylactic treatment with medication. Patients who have had more than one manic episode, have had one manic and one depressive episode or have had three or more depressive episodes should be advised to continue on life-long prophylactic treatment, as the benefits outweigh the risks.

For patients who, despite receiving maintenance medication treatment, experience a manic or mixed episode (i.e., a “breakthrough” episode), the first-line intervention should be to optimize the medication dose. Optimization of dosage entails ensuring that the blood level is in the therapeutic range and in some cases achieving a higher serum level (although one still within the therapeutic range).

Lithium, lamotrigine, valproate, olanzapine, quetiapine, aripiprazole, risperidone long-acting injection and adjunctive ziprasidone continue to be first-line options for maintenance treatment of Bipolar Disorder. Lithium or olanzapine should be considered as first-line maintenance treatment for adults with Bipolar Disorder to delay/prevent the recurrence of mania. The medications with the best empirical evidence to support their use in maintenance treatment are lithium and valproate. Risperidone long-acting Intra Muscular) injection should be considered for patient with frequent relapses.

Lithium, or lamotrigine, should be considered as a first-line treatment to prevent or delay the recurrence of bipolar depression. Quetiapine augmentation of valproate or lithium should be considered a first-line maintenance treatment for adults with Bipolar Disorder to maintain remission and prevent new episodes of all types. If one of these medications was used to achieve remission from the most recent depressive or manic episode, it generally should be continued.

For patients treated with an antipsychotic medication during the preceding acute episode, the need for ongoing antipsychotic treatment should be reassessed upon entering maintenance treatment; antipsychotics should be discontinued unless they are required for control of persistent psychosis. If medications are to be discontinued they should be slowly and gradually tapered over at least a two to four week period, unless medically contraindicated, in order to prevent an episode of Bipolar Disorder and/or increase the risk of suicide.

Adherence to medication therapy should be routinely evaluated at each visit. Reasons for noncompliance should be explored with the patient. The physician should monitor serum concentration for lithium, carbamazepine, or valproate and other appropriate blood work every three to six months to maintain efficacy and avoid toxicity.

Patients with Bipolar Disorder are rarely likely to gain some additional benefit during the maintenance phase from a concomitant psychosocial intervention that addresses illness management (i.e., adherence, lifestyle changes and early detection of prodromal symptoms) and interpersonal difficulties. When the functional impairments of Bipolar Disorder are severe and persistent, other services may be necessary such as case management, assertive community treatment, psychosocial rehabilitation and supported employment.

Psychosocial Treatment

Treatment guidelines increasingly suggest that optimum management of Bipolar Disorder needs integration of pharmacotherapy with targeted psychotherapy. The main goals of adjunctive psychotherapy for Bipolar Disorder include the education of patients, and when possible caregivers, about strategies for the management of stress, the identification and intervention of early signs of recurrence and how to keep regular lifestyle (e.g., sleep and exercise) habits. Moreover, in view of the high rate of non-adherence to drug treatments (up to 60 percent after acute episodes), psychosocial treatments emphasize consistency with pharmacotherapy. Evidence-based models

include cognitive-behavioral therapy, family-focused therapy, interpersonal and social rhythm therapy, group psychoeducation, and systematic care management.

Additional Treatment Considerations/Co-Occurring Disorders

Substance abuse:

Bipolar Disorder with a comorbid substance use disorder is a very common presentation. Co-occurring alcohol abuse or dependence is found in 46 percent of patients with a bipolar disorder. The prevalence of drug abuse or dependence is 41 percent in the bipolar population. Co-occurring substance use is typically associated with fewer and slower remissions, greater rates of suicide and suicide attempts, and poorer outcome. Treatment for substance abuse and Bipolar Disorder should proceed concurrently when possible. Generally, practitioners treat the mood instability and address any immediate needs or detoxification for a given patient. Once stabilized, the substance abuse or dependence takes on a more primary focus of the treatment plan. Alcohol or substance abuse may interfere with pharmacotherapy for Bipolar Disorder due to dehydration which may raise lithium levels to toxicity or hepatic dysfunction which may also alter plasma levels of pharmacological agents.

Other co-occurring psychiatric disorders:

Patients with Bipolar Disorder are at greater risk for comorbid anxiety disorders, especially panic disorder and obsessive-compulsive disorder. Comorbid anxiety may lead to longer recovery times from mood episodes. Patients with comorbid personality disorders generally have greater symptom burden, lower recovery rates from episodes, greater functional impairment, a higher risk for relapse and more difficulty adhering to treatment.

Other co-occurring medical disorders:

Somatic disorders, if present, or the medications used to treat them should always be considered as possible causes of a manic episode. For example, the course of Bipolar Disorder may be exacerbated by any condition that requires intermittent or regular use of steroids (e.g., asthma, inflammatory bowel disease), or that leads to abnormal thyroid functioning. Neurological conditions commonly associated with secondary mania are multiple sclerosis, lesions involving right-side subcortical structures, and lesions of cortical areas with close links to the limbic system. The treatment of Bipolar Disorder may be complicated by conditions such as chronic kidney disease or hypertension that require the use of diuretics, angiotensin-converting enzyme inhibitors. Treatment of conditions that are associated with abnormal cardiac conduction or rhythm or that affect hepatic function may further limit the choice or dosage of effective Bipolar Disorder medications.

Gender Related Treatment Considerations

Hypothyroidism is more common in women who may be more susceptible to the anti-thyroid effects of lithium. Additionally, the psychiatrist should encourage effective contraceptive practices for all female patients of childbearing age who are receiving pharmacological treatment because many medications used to treat Bipolar Disorder are associated with a higher risk of birth defects. The postpartum period is consistently associated with a markedly greater risk for relapse into mania, depression, or psychosis. It is generally considered that prophylactic medications such as lithium or valproate may prevent postpartum mood episodes in women with Bipolar Disorder. All medications used in the treatment of Bipolar Disorder are secreted in breast milk in varying degrees, thereby exposing the neonate to maternally ingested medication and conceivably affecting central nervous system functioning in the infant.

Age Related Treatment Considerations

Children and adolescents:

Bipolar Disorder in children and adolescents and its treatment is discussed in a separate guideline based on the recommendations of the American Academy of Child and Adolescent Psychiatry (2005) and more recent updates.

Geriatric patients:

Manic syndromes in geriatric patients may also be associated with general medical conditions, neurological conditions, medications used to treat those conditions, or substance use. General principles for treating geriatric mania are similar to those for younger adults. However, older patients will usually require lower doses of medications, since aging is associated with reductions in renal clearance and volume of distribution. Concomitant medications and medical conditions may also alter the metabolism or excretion of psychotropic medications. Polypharmacy in older adults should be avoided.

The preferred treatment for older adults with acute mania is an atypical antipsychotic (e.g. risperidone, quetiapine, olanzapine, and aripiprazole) combined with a mood stabilizer. Comorbid medical conditions such as diabetes, constipation, hypotension, and weight may influence medication choice. All pharmacological interventions for older adults with Bipolar Disorder should be combined with psychosocial therapies, psychoeducation and chronic disease case management.

Lithium can be used in older adults to treat acute mania, as maintenance, and also to treat bipolar depression. Overall, valproate appears to be better tolerated than lithium in older adult patients with Bipolar Disorder. Carbamazepine (Tegretol) is an alternative treatment to lithium for older patients with severe cardiovascular or renal disease. Generally, benzodiazepines should be used with caution if needed to treat extreme agitation.

Older adults are more likely than younger adults to develop initial manic episodes during antidepressant therapy. However, older adults with Bipolar Disorder treated with a mood stabilizer and an antidepressant may be less likely to attempt suicide. Mood stabilizers may impact cognitive functioning in older adults. Adverse effects were least likely for lamotrigine and oxcarbazepine, intermediate with lithium, and greatest with valproate, carbamazepine, and topiramate.

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