Guideposts for the Treatment of Bipolar Disorder

Optum is committed to assuring our members are receiving the highest quality evidence based and person-centered care available. Optum recognizes the time demand on staff and providers and offers this resource to give rapid access to evidence based strategies and guidance from professional organizations. These key components from several best practice guidelines will serve as a common language among Optum, providers and members that allows us to all work together in a member-centric manner. We want to partner to provide the highest quality care to our members.

Assessment:

1. **Examination of a patient with bipolar illness should include an immediate assessment of risk of harm to self and others, degree of insight and ability to adhere to treatment, presence of comorbidities** (including substance use that may be aggravating or contributing to clinical presentation)**, and availability of psychosocial support network.** (Guidelines for the management of patients with bipolar disorder, Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD); Bipolar Disorders, 10:97-170. (CAN))

2. **Before initiating pharmacological treatment for a manic episode, it is imperative to rule out symptoms secondary to drugs of abuse, medications, other treatments, or a general medical or neurological condition (CAN)**

3. **When making a bipolar disorder diagnosis, alternative causes of mood symptoms, such as personality disorders, medical or neurological conditions, substance use, and adverse reactions to prescribed medications must be considered in addition to differentiating bipolar disorder from other psychiatric diagnoses. (CAN) Diagnosis of bipolar disorder in children should be made only after a long period of intensive, prospective longitudinal monitoring by a professional or multidisciplinary team with adequate training, and in collaboration with family.** (Bipolar Disorder: Assessment and Management, National Institute for Health and Care Excellence, 2017 (NICE))

Treatment:

1. **Medication remains a key to long term success for most patients. The objective is to achieve a personalized choice of medicine** (effective and well tolerated)**, informed adherence and an understanding of illness course shared with the patient and all most involved in their care.** (Evidence-based guidelines for treating bipolar disorder: Revised third edition recommendations from the British Association for

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2. Psychopharmacology. Journal of Psychopharmacology; 2016, Vol. 30(6) 495–553© The Author(s) 2016Reprints and permissions: sagepub.co.uk/journalsPermissions.navDOI: 10.1177/0269881116636545jop.sagepub.com (BAP))

3. **The first-line pharmacological treatment for more severe manic or mixed episodes is the initiation of either lithium or valproate, plus an antipsychotic. Electroconvulsive therapy (ECT) may also be considered for patients with severe or treatment-resistant mania or if preferred by the patient in consultation with the psychiatrist.** (Practice Guideline for the Treatment of Patients with Bipolar Disorder, 2nd Edition, American Psychiatric Association, 2010 (APA))

4. **Antidepressant monotherapy should be avoided in bipolar disorder.** (The 2020 Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders; Australian & New Zealand Journal of Psychiatry 2021, Vol. 55(1) 7 – 117(RANZ))

5. **Long acting ('depot') formulations should be considered if prophylaxis against recurrence of mania is required and adherence to oral medication is erratic or injection is preferred (BAP)**

Support:

1. **Patients with special needs may require additional considerations. These might include comorbid Personality Disorders, Intellectual Disabilities, medical comorbidities such as pregnancy, as well as children and adolescents (RANZ).**

Recovery:

1. **Successful management of bipolar disorder includes psychoeducation, social support assistance** (housing, supports, and employment issues)**, and the use of one or more evidence-based psychological interventions** (such as group psychoeducation or CBT). (RANZ))

Guideposts Details

Assessment:

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Background Information:

Overall:
It is important for clinicians to frequently monitor suicidal ideation and risk. Suicide is one of the leading causes of death in BD, with approximately 6%-7% of identified patients with BD dying by suicide; thus, suicide risk is substantially higher in BD than in the general population (10.7 per 100 000 per year). The fatality of suicide attempts is also higher in BD than in the general population. A comprehensive assessment for suicide risk should occur during all clinical interactions. Clinical assessment should focus on modifiable risk factors that could be targeted to reduce the risk.

Steps should be taken to rule out any other factors that may be perpetuating symptoms such as prescribed medication, illicit drug use/abuse or an endocrine disorder. Patients should also be encouraged to discontinue stimulant use, including caffeine and alcohol. Laboratory investigations should also be completed. Results of the overall assessment should be used to establish the most appropriate treatment setting (e. g., ambulatory or inpatient), with consideration given to management of safety risks. Course of illness and treatments used in current and prior episodes should be assessed, including past response to and tolerability of specific medications and doses, and used to direct subsequent therapeutic choices.

Manic Episode:
Examination of a patient presenting in a manic state should include an immediate assessment for risk of aggressive behavior, violence and safety threat to others, suicide risk especially in those with mixed features, degree of insight and the ability to adhere to treatment.

Any patients presenting with mania who have been taking antidepressants should have these medications discontinued. If there is a previous diagnosis of BD, it is appropriate to immediately commence antimanic agents. If this is the first emergence of manic symptoms, clinicians are advised to confirm the diagnosis of BD by monitoring patients for a period of time after antidepressant discontinuation and obtaining collateral information to confirm whether symptoms remain and antimanic treatment is necessary. Attention should be paid to managing withdrawal symptoms that may occur in manic patients with a history of substance abuse. When the symptoms of mania have remitted, behavioral and educational strategies should be applied to promote ongoing medication adherence, reduce residual symptoms, help identify early signs of relapse, and support functional recovery.

Depressed Episode:
Examination of a patient presenting in a depressed state should include an assessment of the nature and severity of depression and associated symptoms, risk of suicide/self-harm behavior, ability to adhere to a treatment plan, availability of psychosocial support network, and functional impairment. Consideration should be given to restarting medications if their recent discontinuation appeared to coincide with a depressive relapse. Psychoeducation and other psychosocial strategies should also be offered alongside pharmacological treatment to promote ongoing medication adherence, reduce residual symptoms and suicidal behavior, help identify early signs of relapse, and support functional recovery.

Treatment:

1. **Medication remains a key to long term success for most patients. The objective is to achieve a personalized choice of medicine** (effective and well tolerated)**, informed adherence and an understanding of illness course shared with the patient and all most involved in their care. (BAP)**

2. **The first-line pharmacological treatment for more severe manic or mixed episodes is the initiation of either lithium or valproate, plus an antipsychotic. Electroconvulsive therapy (ECT) may also be considered for patients with severe or treatment-resistant mania or if preferred by the patient in consultation with the psychiatrist (APA).**

3. **Antidepressant monotherapy should be avoided in bipolar disorder. (RANZ)**

Background Information:

Currently, medication remains the key to successful practice for most patients in the long term. The objective is to achieve a personalized choice of medicine (effective and well tolerated), informed adherence and an understanding of illness course shared with the patient and all most involved in their care. This needs to be established as early as possible in patients who present with severe illness. (BAP)

A strong therapeutic alliance is central to improve treatment adherence and outcomes. Providers should encourage individuals to actively participate in treatment planning, using a shared decision-making approach. Whenever possible, family members or key friends should be included as part of the care team. There is evidence that specialized, team-approach-based interventions combining pharmacotherapy and psychoeducation are more effective than standard community care. (CAN)

Several controlled studies of ECT in patients with bipolar depression were conducted several decades ago. All found ECT to be as or more effective than MAOIs, tricyclic

antidepressants, or placebo. ECT is a viable option for patients with severe bipolar depression, especially if psychotic features are present (APA).

The management of bipolar depression is inherently difficult because of the ever-present risk of inducing manic symptoms and creating either a mixed state or triggering an episode of mania. This is most likely to occur with conventional antidepressants when prescribed as monotherapy. And this type of iatrogenic switch into mania/mixed symptoms is also referred to as a treatment-emergent affective switch (TEAS). If a TEAS occurs, then antidepressant medication should be stopped immediately (RANZ).

Monoamine reuptake inhibitors, tricyclic antidepressants, and dual-action SNRI antidepressants (such as venlafaxine and duloxetine) carry a greater risk of precipitating a switch to mania than single action SSRI's.

Antidepressant drugs appear unlikely to induce mania when used in combination with a drug for mania. (BAP)

In bipolar II disorder, if an antidepressant is prescribed as monotherapy, any increase in dose should be gradual and there should be vigilance for and early management of any adverse reactions such as hypomania, mixed states, or agitation (IV). (BAP)

7. **Consider long acting ('depot') formulations if prophylaxis against recurrence of mania is required and adherence to oral medication is erratic or injection preferred (BAP)**

Background Information:

Without active acceptance of the need for long-term treatment, adherence may be poor. Consider a wider package of treatment interventions including enhanced psychoeducation, motivational and family support, especially in the early stages of illness to promote behavior change and adherence to medication.

8. **Special populations require additional considerations. These include Personality Disorders, Intellectual Disability, children and adolescents, medical comorbidity, and pregnancy. (RANZ).**

Background Information:

- **Co-morbid personality disorders:**
  It is important that clinicians regularly review both mood and personality symptoms and carefully consider the possibility of both.

- **Intellectual Disabilities:**
  Where possible the same interventions as for other people with mood disorders should be provided but the method of delivery and duration of treatment may need to be adjusted to account for the disability. Issues relating to capacity and consent may also need to be formally considered and it may be useful to consult with an intellectual disability specialist.

- **Geriatric Patients:**
  Manic syndromes in geriatric patients may also be associated with general medical conditions, medications used to treat those conditions, or substance use. The new onset of mania in later life is particularly associated with high rates of medical and neurological diseases, as well as higher risk of death. Geriatric patients should be evaluated carefully for general medical and neurological causes. Older patients will usually require lower doses of medications, since aging is associated with reductions in renal clearance and

volume of distribution. They may also be more sensitive to side effects. Many elderly patients tolerate only low serum levels of lithium (e.g., 0.4–0.6 mq/liter), and increases in dose should be made slowly. Older patients may be more likely to develop cognitive impairment with medications such as lithium or benzodiazepines. They may also have difficulty tolerating antipsychotic medications and are more likely to develop extrapyramidal side effects and tardive dyskinesia. With some antipsychotics and antidepressants, orthostatic hypotension may be particularly problematic and increases the risk of falls. Use of benzodiazepines and of neuroleptics also has been associated with greater risks of falls and hip fractures in geriatric patients.

- **Pregnancy:**
  Around the time of pregnancy, the risks and benefits of continuing versus discontinuing treatment require the most thoughtful judgment and discussion among the patient, the psychiatrist, the obstetrician, and the other parent. In clinical decision making, the potential teratogenic risks of psychotropic medications must be balanced against the risk of no prophylactic treatment, and the attendant risks of relapse and emergent acute illness.

  In patients who have been stable on a regimen of lithium, the rate of recurrent mood episodes is clearly increased by lithium discontinuation, particularly when discontinuation is abrupt. Should the decision be made to discontinue medication, the woman should be advised about the greater risk of recurrence with rapid discontinuation of lithium (and possibly other maintenance agents) compared and encouraged to consider a slower tapering strategy.

  Additionally, during a manic episode, women are at risk of increasing their consumption of alcohol and other drugs, thus conferring additional dangers to the fetus.

  First-trimester exposure to lithium, valproate, or carbamazepine is associated with a greater risk of birth defects. Exposure to carbamazepine and valproate during the first trimester is associated with neural tube defects at rates of up to 1% and 3%–5%, respectively. Caution must be exercised if they are prescribed to treat bipolar depression in pregnant women.

  Antipsychotic agents may be needed to treat psychotic features of bipolar disorder during pregnancy, but they may also be prescribed as an alternative to lithium to treat symptoms of mania.

  High-potency antipsychotic medications are preferred during pregnancy, since they are less likely to have associated anticholinergic, antihistaminergic, or hypotensive effects. In addition, there is no evidence of teratogenicity with exposure to haloperidol, perphenazine, thiothixene, or trifluoperazine. When high-potency antipsychotic medications are used near term, neonates may show extrapyramidal side effects, but these are generally short-lived. To limit the duration of such effects, however, long-acting depot preparations of antipsychotic medications are not recommended during pregnancy. For newer antipsychotic agents such as risperidone, olanzapine, clozapine, quetiapine, and ziprasidone, little is known about the potential risks of teratogenicity or the potential effects in the neonate.

  ECT is another potential treatment for severe mania or depression during pregnancy. In terms of teratogenicity, the short-term administration of anesthetic agents with ECT may present less risk to the fetus than pharmacological treatment options. The APA Task Force Report on ECT contains additional details on the use of ECT during pregnancy.

- **Children and adolescents:**
  The clinical features of childhood bipolar disorder differ from bipolar disorder in adults. Children with bipolar disorder often have mixed mania, rapid cycling, and psychosis. Although there is more information available about the use of lithium and divalproex in children and adolescents with bipolar disorder, other medication treatment options include atypical antipsychotics, carbamazepine, and combinations of these medications.

  Child and adolescent bipolar disorder is often comorbid with attention deficit and conduct disorders Psychiatric comorbidity may complicate the diagnosis and treatment of bipolar disorder in children and adolescents. The presence of ADHD, especially in children and adolescents, confounds the assessment of mood changes in patients with bipolar disorder. Early manifestations of mania and hypomania can be particularly difficult to distinguish from the ongoing symptoms of ADHD. Careful tracking of symptoms and behaviors is helpful.

  Youths with bipolar disorder are at greater risk for substance use disorders. Comorbid substance use has been shown to complicate the course of bipolar disorder and its treatment. Short-term treatment with lithium and divalproex may be useful in these conditions.

Recovery:

1. **In general, provision of psychoeducation to all patients and family members is recommended for prevention of relapse, particularly at illness onset, with selection of any additional psychosocial therapies based on individual concerns/presentations or deficits.(CAN) Actions that ideally must be implemented include providing psychoeducation, organizing social supports (housing, relationship and employment issues), and commencement of one or more evidence-based psychological interventions (such as group psychoeducation or CBT). These three interdependent sets of Actions are considered essential for the successful long-term management of bipolar disorder. (RANZ)**

Background Information:

Psychoeducation and psychological interventions such as CBT, family focused therapy, and support from family and friends are recommended modes of treatment. The goals of psychoeducation are to ensure the patient (and their natural supports) understand the nature of, and treatments for mood disorders, and to decrease stigma. Self-management skills can be addressed in individual and group therapies. CBT is the most commonly employed intervention and the most widely studied.

Social support is the provision of emotional assistance (empathy, concern, acceptance, encouragement, caring), instrumental support (financial assistance, goods, and services), informational assistance (advice, suggestions, factual information) and companionship (acceptance into a social/cultural group and environment, with identity and recognition).