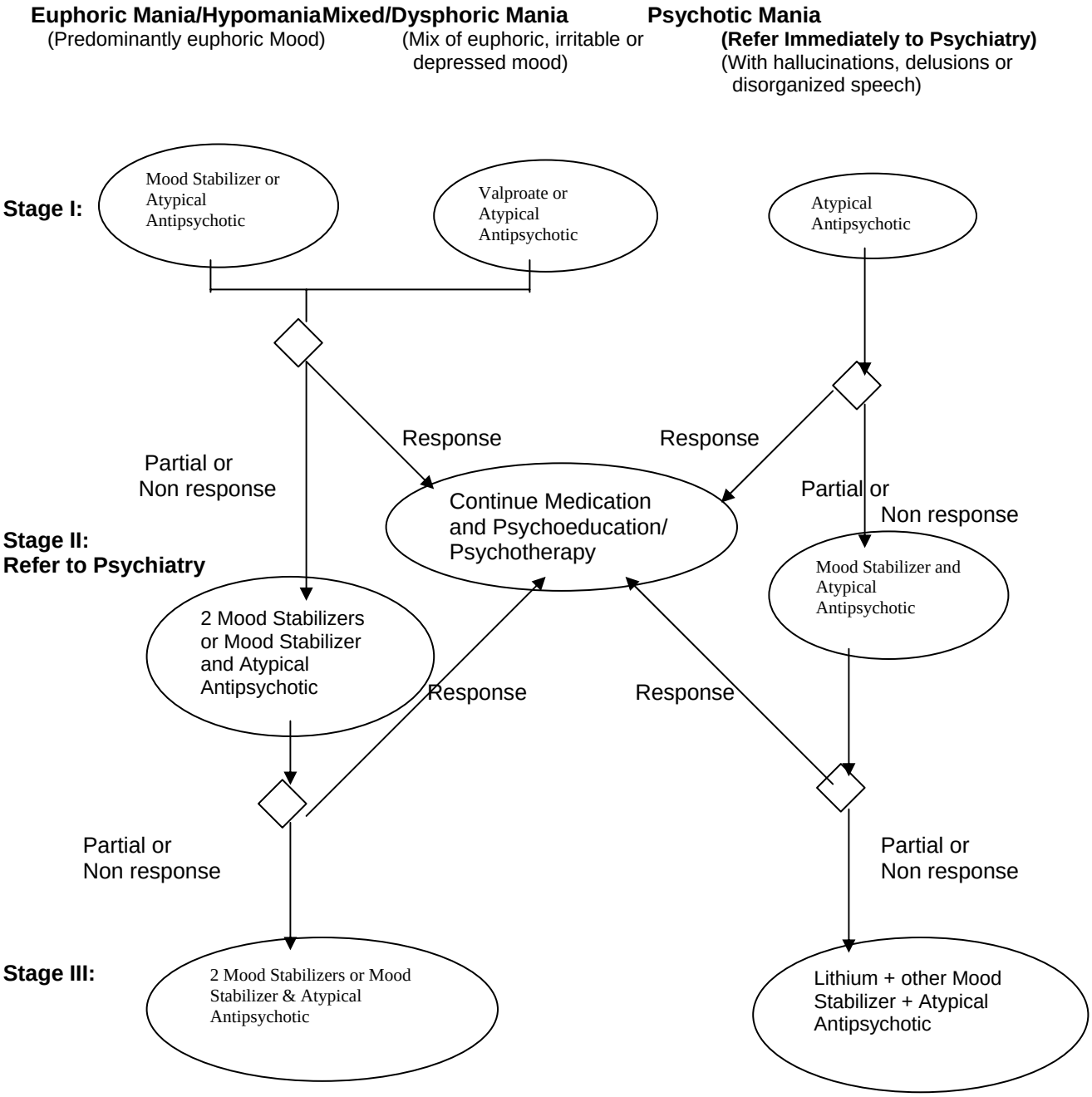
Guideline for the Treatment of Bipolar Disorder, Manic Episodes in Adults

Definition	Bipolar Disorder as defined in the DSM-IV is a severe mood disorder that involves episodes of mania or hypomania, and major depression. The condition can be disabling and may present with psychotic symptoms.
Differential Diagnosis	Secondary mania due to medications, other medical condition, or substance abuse must be ruled out. Rapid shifts of mood that continue to swing up and down every few hours or which are situational are less likely to indicate bipolar disorder than more persistent episodes that meet the duration criteria above.
Evaluation	The diagnosis of mania or hypomania is based on the presence of affective symptoms and four (if euphoric) or five (if irritable) of the following cognitive and behavioral symptoms. A week's duration is required to diagnose a manic episode (or a shorter time if the patient is arrested or hospitalized), if these symptoms cause vocational or social disability. If they do not cause disability, and last at least 4 days, hypomania may be diagnosed. The DSM-IV emphasizes the need to get third party corroboration of the intensity and duration of the symptoms. **Affective Symptoms (must be present):** 1. Euphoria or irritability; mood may be changing mix of euphoria and depression **Cognitive Symptoms:** 2. Rapid Speech 3. Distractibility 4. Ideas jump illogically **Behavioral Symptoms:** 5. Insomnia, not feeling a need for sleep 6. Intense goal directed activity (money, sex, etc) 7. Excessive involvement in pleasurable activities with a high risk of negative consequences **Precipitating Factors:** Mania or hypomania may develop after periods of extreme stress, and have developed following head trauma. Mania or hypomania may develop in response to general medical illnesses, antidepressants, steroids, dopamine agonists and other stimulants, and rarely other medications. Substance abuse can provoke mania in susceptible individuals. **Risk Factors**: • Substance Abuse, especially alcohol or stimulants • Family History of Bipolar Disorder • Recurrent episodes of depression • Treatment resistant depression
Treatment	All patients and their families or support people should have psychoeducation regarding bipolar disorder at the time the diagnosis is made and as needed in an ongoing fashion. All patients should be encouraged to keep mood charts. Psychotherapy using a cognitive behavioral approach should be considered. Alcohol and drugs should be avoided. Referral for dual diagnosis (mood disorder and substance dependence) treatment should be made if clinically indicated. Referral to psychiatry is always appropriate at Stage I and strongly recommended by Stage II. Patients with mania frequently meet criteria for hospitalization until the mania is under control, and mania is a very significant risk factor for suicidal or homicidal behavior, especially when psychosis is present. A careful evaluation of risks must precede any treatment plan.
Laboratory Testing and Monitoring	**The APA guidelines of 2002 recommend serum levels of lithium, carbamazepine and valproate at least twice a year once therapeutic serum levels are obtained during initial titration.** Other recommended labs: **Lithium:** Baseline serum creatinine, electrolytes, and TSH. EKG if over 50, then monitor creatinine and TSH q 6 months. **Valproate:** Baseline LFT's and CBC, then monitor q 6 months **Carbamazepine:** Baseline LFT's, CBC and electrolytes. May need more frequent serum levels that valproate and lithium due to its tendency to induce its own metabolism, and its levels are effected by many factors, including smoking, diet, and other medications. 12 hour trough levels are the standard, and patients may need to be reminded about this: always suspect a peak level if an unexpectedly high value is obtained. Labs may be needed more frequently if there is a question of efficacy or adherence or if there is a trend toward abnormal values in associated labs. **All Atypical Antipsychotics:** The FDA has recommended that all patients taking these agents be monitored for glucose intolerance and increased blood lipids. All patients on medications for mania and bipolar disorder should be weighed regularly to monitor medication related weight gain.

Guideline for the Treatment of Bipolar Disorder, Manic Episodes in Adults

Treatment Algorithm for Mania/Hypomania in Primary Care
Adapted from the TMAP algorithm of 2002 with changes



Beyond the above options, there are many combinations of mood stabilizers, antipsychotics, other drugs and ECT to be tried, at this point the patient should have been referred to psychiatry for consultation and/or direct treatment.

Guideline for the Treatment of Bipolar Disorder, Manic Episodes in Adults

Clinical Pearls	• Moods can change rapidly in bipolar disorder. Patients should be seen frequently if they are in an episode of mood instability, and may need to be seen on short notice if mania or suicidal ideation develop. Real time communication between prescribing clinicians and other mental health providers working with the patient is essential. • Adequate sleep is very important in treating mania. If the patient does not get significant sedation and improved sleep after starting an antimanic medication, aggressive augmentation with benzodiazepines at bedtime may help normalize sleep quickly and reduce daytime agitation. Patients with Bipolar Disorder may need to avoid shift work. • Atypical antipsychotics, especially the more sedating ones, Olanzapine, Quetiapine and Risperidone, are easier to titrate quickly on an outpatient basis in moderate to severe mania or if psychosis is present. Valproate may be increased faster than Lithium due to a wider therapeutic index. • It is more common for people with bipolar disorder to be depressed than manic, and depression is more likely to be spontaneously reported than mania or hypomania. Mania can present with predominantly irritable, rather than euphoric mood. • The natural frequency of episodes in untreated patients is about twice a year on average, though there is a wide variation. Thus it may be a year or more before there is reason to believe that maintenance treatment is effective in preventing or reducing further episodes. Mood charting is recommended for every patient taking a mood stabilizer, especially for the first few years after the diagnosis of bipolar is made. Regular patterns of relapse according to time or season may be observed, but are not to be expected. • Patients who have two or more episodes of mania should be on lifelong treatment with mood stabilizers; those with one episode should be followed closely if they elect not to take maintenance mood stabilizers. • Every patient with bipolar disorder should know the prodromal signs of illness to try to develop a network of support people who are knowledgeable about these signs and empowered to report them to the treating clinicians. A written treatment plan in the patient and families' possession spelling out who to call in an emergency can help facilitate prompt attention early in an exacerbation. • About 50% of bipolar patients respond adequately to the first medication tried; polypharmacy may be necessary. Medication non-adherence and substance use are common causes of failure to respond to treatment. Serum levels may be useful to assess adherence. • Substance abuse is a problem in more than 50% of people with bipolar disorder; continue to ask your patients about this and continue to educate about the toxicity of substance use with this disorder, including "social drinking". • Pregnancy is a relative contraindication to the use of mood stabilizers due to the risk of birth defects, although the risks are greater in the first trimester. Women of child-bearing age should take supplemental folate with Valproate. Lithium may have lower risks than Valproate; agents with the lowest risk to the fetus are the older antipsychotics like Haloperidol.
Screening Tools	Mood Charting is recommended. http://www.manicdepressive.org/moodchart.html has useful information. The format can be simplified to meet the needs and capacity of the patient; a calendar with daily global mood ratings by patient and support person may suffice. The Young Mania rating scale is commonly used to rate the intensity of mania in research. A self-scoring mania screening questionnaire is available at http://www.psycom.net/depression.central.bipolar-screening.html. Episodes of hypomania are harder to identify reliably than mania when taking a history.
Resources	Always provide direct education and written materials about bipolar disorder and its treatment. The following websites may be useful for patients who use the internet: http://www.manicdepressive.org/moodchart.html http://www.dbsalliance.org http://www.nami.org http://www.psycom.net/depression.central.bipolar.html http://www.manicdepressive.org/aboutbp.html The following books are recommended to patients and their families: Living Without Depression and Manic-Depression, by Mary Ellen Copeland Manic-Depressive Illness, second edition by Fred Goodwin and Kay Jameson

Sources:

Practice guideline for the treatment of patients with bipolar disorder (revision). American Journal Psychiatry 2002 Apr;159(4 Suppl):1-50 (472 References)

TMAP(Texas Medication Algorithm Project) Procedural Manual Bipolar Disorder Algorithms and Mania/Hypomania Algorithms, Trisha Suppes, MD, Ph.D., Ellen Dennehy, Phd, August 2002

Guideline for the Treatment of Bipolar Disorder, Manic Episodes in Adults

Supplement to Guideline

Medication for the Treatment of Mania

Proven Mood Stabilizers:
Advantages: Less expensive than atypical antipsychotics, with more extensive evidence of efficacy for both acute mania and long term maintenance (except for Lamotrigine). Lithium and Lamotrigine have antidepressant effects. Serum levels to some extent predict response.
Disadvantages: Require serum levels (except Lamotrigine, may cause a variety of side effects some of which have significant medical risk) Weight gain, tremor & GI side effects common with Lithium and Valproate; Lithium may effect thyroid or kidney and may interact with NSAIDs or diuretics causing high blood levels. Rare liver and pancreatic reactions occur with Valproate, which may also cause low blood platelets. Carbamazepine may cause toxic rash or liver reactions. Valporate and Carbamazepine may interact with other medications to change serum levels. Lamotrigine must be titrated slowly over months to avoid rash, does not seem to prevent mania.

Medication	Brand Name(s)	Starting dose (mg/d)	Usual dosage (mg/d)	Serum Levels (General Adult)	How Supplied
Lithium	Eskalith Lithobid	600 mg-900 mg/d	900 mg tid	0.6 - 1.2	150 mg,300 mg,450 mg, liquid
Valproate	Depakote	750 mg/d	2800 mg/qd	50 - 125	125 mg spinkles, 250 mg , 500 mg Extended release, liquid
Carbamazepine	Tegretol	100-200 mg (1-2 xqd)	800-1200 mg qd	4 - 12	100 mg, 200 mg long acting, Liquid

Probable Mood Stabilizer

Advantages: Does not require serum levels. Unlikely to cause weight gain. Overall level of side effects less than proven mood stabilizers.
Disadvantages: Less evidence of efficacy, not FDA approved for mania. Oxcarbazepine may cause hyponatremia, may cause rash.

Medication	Brand Name(s)	Starting dose (mg/d)	Usual dosage	How Supplied
Oxcarbazepine	Trileptal	300 mg/bid	Not more than 2400 mg	150 mg, 300 mg

Atypical Antipsychotics
Advantages: Can be titrated quickly, will treat any associated psychotic symptoms. Risperidone can be given in long acting IM form, Ziprasidone in a short acting IM form. Most of the atypical antipsychotics have been approved by the FDA for the treatment of mania or bipolar disorder.
Disadvantages: Very expensive, may cause weight gain (Olanzapine, Quetiapine and Clozapine), may cause akithesia(Resperidone, Olanzapine and Aripiprazole). FDA suggests monitoring for increased serum glucose and fats when atypical antipsychotics are used. There is a small risk of persistent movement disorders such as tardive dyskinesia or tardive dystonia.

Medication	Brand Name(s)	Starting dose (mg/d)	Usual dosage	How Supplied
Risperidone	Risperdal/Consta	1 mg bid	3 mg	0.25 mg, 0.5 mg, 1-4 mg tabs, oral solution, long-acting injection
Olanzapine	Zyprexa	10-15 mg/qd	20 mg/ max dose	2.5mg, 5 mg, 10 mg, 15 mg, 20 mg
Quetiapine	Seroquel	25 mg bid	800 mg/ max dose	25 mg, 100 mg, 200 mg, 300 mg
Ziprasidone	Geodon	20 mg bid	20 – 80 mg bid	20 mg, 40 mg, 60 mg, 80 mg, IM short acting
Abilify	Aripiprazole	10-15 mg/qd	10-30 mg/qd	5 mg, 10 mg, 15 mg, 20 mg, 30 mg

Medications not recommended for Mania: Gabapentin is not effective for mania. Lamotrigine is effective for preventing bipolar depression but not mania. Topiramate has not been demonstrated in controlled studies to be effective for mania.

Guideline for the Treatment of Bipolar Disorder, Manic Episodes in Adults

Other medication commonly used to treat bipolar disorder:
Chlorpromazine, Haloperidol and Fluphenzine are commonly used to treat acute mania, and the latter two medications come in depot long acting forms which can be given IM every 2 to 4 weeks for maintenance treatment. While often effective for mania they have more risk of long-term movement disorders and may cause more affective flattening and dysphoria than atypical antipsychotics.
Benzodiazepines such as Lorazepam and Clonazepam are frequently useful to treat insomnia and agitation of bipolar disorder, especially during exacerbations. However, it must be remembered that there is a high rate of substance abuse amongst people with bipolar disorder so chronic use is generally not advisable.