



# RISK vs REWARD

## Treating bipolar mania in the outpatient setting

Enlist the help of family, employ evidence-based pharmacologic and psychotherapeutic strategies

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**M**anic episodes, by definition, are associated with significant social or occupational impairment.<sup>1</sup> Some manic patients are violent or engage in reckless behaviors that can harm themselves or others, such as speeding, disrupting traffic, or playing with fire. When these patients present to a psychiatrist's outpatient practice, involuntary hospitalization might be justified.

However, some manic patients, in spite of their elevated, expansive, or irritable mood state, never behave dangerously and might not meet legal criteria for involuntary hospitalization, although these criteria differ from state to state. These patients might see a psychiatrist because manic symptoms such as irritability, talkativeness, and impulsivity are bothersome to their family members but pose no serious danger (*Box, page 40*).

In this situation, the psychiatrist can strongly encourage the patient to seek voluntary hospitalization or attend a partial hospitalization program. If the patient declines, the psychiatrist is left with 2 choices: initiate treatment in the outpatient setting or refuse to treat the patient and refer to another provider.

Treating "non-dangerous" mania in the outpatient setting is fraught with challenges:

- the possibility that the patient's condition will progress to dangerousness
- poor adherence to treatment because of the patient's limited insight
- the large amount of time required from the psychiatrist and care team to adequately manage the manic episode (eg, time spent with family members, frequent patient visits, and managing communications from the patient).

continued



## Outpatient mania

### Clinical Point

At each outpatient visit, explore with the patient and family emerging symptoms that could justify involuntary hospitalization



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Box

## Manic, but refusing inpatient treatment

Accompanied by her husband and mother, Mrs. W, age 31, is seeking help for insomnia and anxiety. She reports that she has been unable to sleep more than a few hours a night for the last 2 weeks and is having spontaneous panic attacks. Her affect is elevated, she is hyperverbal and loud, and she repeatedly stands up and paces during the interview.

Mrs. W's husband tells you that she doesn't sleep, has spent \$1,000 in the last week on random items, is calling her friends and her doctors all day and night, and is so easily distracted that she cannot safely take care of their infant. These behaviors are abnormal for Mrs. W when she is well, he reports, but also occurred during a previous manic episode. He says she is doing nothing dangerous and she hasn't voiced any threats of self-harm or violence toward others. Mrs. W's family is concerned about her behavior.

Because you are unable to involuntarily commit Mrs. W to a psychiatric hospital, you recommend that she voluntarily check herself into a hospital. Her family strongly supports this idea, but Mrs. W refuses.

There are no guidelines to assist the office-based practitioner in treating mania in the outpatient setting. When considering dosing and optimal medication combinations for treating mania, clinical trials may be of limited value because most of these studies only included hospitalized manic patients.

Because of this dearth of knowledge, we provide recommendations based on our review of the literature and from our experience working with manic patients who refuse voluntary hospitalization and could not be hospitalized against their will. These recommendations are organized into 3 sections: diagnostic approach, treatment strategy, and family involvement.

### Diagnostic approach

Making a diagnosis of mania might seem straightforward for clinicians who work in inpatient settings; however, mania might not present with classic florid symptoms among outpatients. Patients might have

a chief concern of irritability, dysphoria, anxiety, or "insomnia," which may lead clinicians to focus initially on non-bipolar conditions.<sup>2</sup>

During the interview, it is important to assess for any current DSM-5 symptoms of a manic episode, while being careful not to accept a patient's denial of symptoms. Patients with mania often have poor insight and are unaware of changes from their baseline state when manic.<sup>3</sup> Alternatively, manic patients may want you to believe that they are well and could minimize or deny all symptoms. Therefore, it is important to pay attention to mental status examination findings, such as hyperverbal speech, elated affect, psychomotor agitation, a tangential thought process, or flight of ideas.

Countertransference feelings of diagnostic confusion or frustration after long patient monologues or multiple interruptions by the patient should be incorporated into the diagnostic assessment. Family members or friends often can provide objective observations of behavioral changes necessary to secure the diagnosis.

### Treatment strategy

**Decision points.** When treating manic outpatients, assess the need for hospitalization at each visit. Advantages of the inpatient setting include:

- the possibility of rapid medication adjustments
- continuous observation to ensure the patient's safety
- keeping the patient temporarily removed from his community to prevent irreversible social and economic harms.

However, a challenge with hospitalization is third-party payers' influence on a patient's length of stay, which may lead to rapid medication changes that may not be clinically ideal.

At each outpatient visit, explore with the patient and family emerging symptoms that could justify involuntary hospitalization. Document whether you recommended inpatient hospitalization, the patient's response to the recommendation, that you are aware and have considered the risks associated with outpatient care, and that

you have discussed these risks with the patient and family.

For patients well-known to the psychiatrist, a history of dangerous mania may lead him (her) to strongly recommend hospitalization, whereas a pre-existing therapeutic alliance and no current or distant history of dangerous mania may lead the clinician to look for alternatives to inpatient care. Concomitant drug or alcohol use may increase the likelihood of mania becoming dangerous, making outpatient treatment ill-advised and riskier for everyone involved.

In exchange for agreeing to provide outpatient care for mania, it often is helpful to negotiate with the patient and family a threshold level of symptoms or behavior that will result in the patient agreeing to voluntary hospitalization (*Table 1*). Such an agreement can include stopping outpatient treatment if the patient does not improve significantly after 2 or 3 weeks or develops psychotic symptoms. The negotiation also can include partial hospitalization as an option, so long as the patient's mania continues to be non-dangerous.

Obtaining pretreatment blood work can help a clinician determine whether a medication is safe to prescribe and establish causality if laboratory abnormalities arise after treatment begins. Ideally, the psychiatrist should follow consensus guidelines developed by the International Society for Bipolar Disorders<sup>4</sup> or the American Psychiatric Association (APA)<sup>5</sup> and order appropriate laboratory tests before prescribing anti-manic medications. Determine the pregnancy status of female patients of childbearing age before prescribing a potentially teratogenic medication, especially because mania is associated with increased libido.<sup>6</sup>

Manic patients might be too disorganized to follow up with recommendations for laboratory testing, or could wait several days before completing blood work. Although not ideal, to avoid delaying treatment, a clinician might need to prescribe medication at the initial office visit, without pretreatment laboratory results. When the patient is more organized, complete the blood work. Keeping home pregnancy tests in the office can help rule out pregnancy before prescribing medication.

**Table 1**

### Possible stipulations for manic patients to receive outpatient treatment

Patient agrees to complete blood work at earliest possible time requested by the physician
Patient agrees to complete a urine pregnancy test when requested by the physician, if patient is female and of childbearing age
Family member agrees to monitor medication adherence
Family member agrees to attend all visits to provide objective reporting
Patient agrees not to drive
Patient agree to voluntary hospitalization <i>if</i> any of the following occur: <ul style="list-style-type: none"><li>• An incident involving police</li><li>• Any abuse of alcohol or drugs</li><li>• Any reckless or dangerous behavior</li><li>• Development of any psychotic symptoms</li></ul>
Note: Clinicians can choose from these or other stipulations based on the situation and their experience with the patient

**Medication.** Meta-analyses have established the efficacy of mood stabilizers and antipsychotics for treating mania,<sup>7,8</sup> and several consensus guidelines have incorporated these findings into treatment algorithms.<sup>9</sup>

For a patient already taking medications recommended by the guidelines, assess treatment adherence during the initial interview by questioning the patient and family. When the logistics of phlebotomy permit, obtaining the blood level of psychotropics can show the presence of any detectable drug concentration, which demonstrates that the patient has taken the medication recently.

If there is no evidence of nonadherence, an initial step might be to increase the dosage of the antipsychotic or mood stabilizer that the patient is already taking, ensuring that the dosage is optimized based on FDA indications and clinical trials data. The recommended rate of dosage adjustments differs among medications; however, optimal dosing should be reached quickly because a World Federation of Societies of Biological Psychiatry task force recommends that a mania treatment trial not exceed 2 weeks.<sup>10</sup>

continued

### Clinical Point

Concomitant drug or alcohol use might increase the likelihood of mania becoming dangerous, making outpatient treatment ill-advised



## Outpatient mania

### Clinical Point

SGAs should be dosed moderately and lower than if the patient were hospitalized to avoid intolerable side effects

Table 2

## FDA-approved agents for treating acute mania in adults

Class	Agent
First-generation antipsychotic	Chlorpromazine
Second-generation antipsychotics	Aripiprazole
	Asenapine
	Olanzapine
	Quetiapine
	Risperidone
Ziprasidone	
Mood stabilizers	Carbamazepine (extended-release)
	Divalproex
	Lithium

Dosage increases can be made at weekly visits or sooner, based on treatment response and tolerability. If there is no benefit after optimizing the dosage, the next step would be to add a mood stabilizer to a second-generation antipsychotic (SGA), or vice versa to promote additive or synergistic medication effects.<sup>11</sup> Switching one medication for the other should be avoided unless there are tolerability concerns.

For a patient who is not taking any medications, select a treatment that balances rapid stabilization with long-term efficacy and tolerability. *Table 2* lists FDA-approved treatments for mania. Lamotrigine provides prophylactic efficacy with few associated risks, but it has no anti-manic effects and would be a poor choice for most actively manic patients. Most studies indicate that antipsychotics work faster than lithium at the 1-week mark; however, this may be a function of the lithium titration schedule followed in the protocols, the severity of mania among enrolled patients, the inclusion of typically non-responsive manic patients (eg, mixed) in the analysis, and the antipsychotic's sedative potential relative to lithium. Although the anti-manic and prophylactic potential of lithium and valproate might make them an ideal first-line option, antipsychotics could stabilize a manic patient faster, especially if agitation is present.<sup>12,13</sup>

Breaking mania quickly is important when treating patients in the outpatient setting. In these situations, a reasonable choice is to prescribe a SGA, because of their rapid onset of effect, low potential for switch to depression, and utility in treating classic, mixed, or psychotic mania.<sup>10</sup> Oral loading of valproate (20 mg/kg) is another option. An inpatient study that used an oral-loading strategy demonstrated a similar time to response as olanzapine,<sup>14</sup> in contrast to an inpatient<sup>15</sup> and an outpatient study<sup>16</sup> that employed a standard starting dosage for each patient and led to slower improvement compared with olanzapine.

SGAs should be dosed moderately and lower than if the patient were hospitalized, to avoid alienating the patient from treatment by causing intolerable side effects. In particular, patients and their families should be warned about immediate risks, such as orthostasis or extrapyramidal symptoms. Although treatment guidelines recommend combination therapy as a possible first-line option,<sup>9</sup> in the outpatient setting, monotherapy with an optimally dosed, rapid-acting agent is preferred to promote medication adherence and avoid potentially dangerous sedation. Manic patients experience increased distractibility and verbal memory and executive function impairments that can interfere with medication adherence.<sup>17</sup> Therefore, patients are more likely to follow a simpler regimen. If SGA or valproate monotherapy does not control mania, begin combination treatment with a mood stabilizer and SGA. If the patient experiences remission with SGA monotherapy, the risks and benefits of maintaining the SGA vs switching to a mood stabilizer can be discussed.

Provide medication “as needed” for agitation—additional SGA dosing or a benzodiazepine—and explain to family members when their use is warranted. Benzodiazepines can provide short-term benefits for manic patients: anxiety relief, sedation, and anti-manic efficacy as monotherapy<sup>18-20</sup> and in combination with other medications.<sup>21</sup> Studies showing monotherapy efficacy employed high dosages of benzodiazepines (lorazepam mean dosage, 14 mg/d; clonazepam mean dosage,

13 mg/d)<sup>19</sup> and high dosages of antipsychotics as needed,<sup>18,20</sup> and often were associated with excessive sedation and ataxia.<sup>18,19</sup> This makes benzodiazepine monotherapy a potentially dangerous approach for outpatient treatment of mania. IM lorazepam treated manic agitation less quickly than IM olanzapine, suggesting that SGAs are preferable in the outpatient setting because rapid control of agitation is crucial.<sup>22</sup> If prescribed, a trusted family member should dispense benzodiazepines to the patient to minimize misuse because of impulsivity, distractibility, desperation to sleep, or pleasure seeking.

SGAs have the benefit of sedation but occasionally additional sleep medications are required. Benzodiazepine receptor agonists (BzRAs), such as zolpidem, eszopiclone, and zaleplon, should be used with caution. Although these medicines are effective in treating insomnia in individuals with primary insomnia<sup>23</sup> and major depression,<sup>24</sup> they have not been studied in manic patients. The decreased need for sleep in mania is phenomenologically<sup>25</sup> and perhaps biologically different than insomnia in major depression.<sup>26</sup> Therefore, mania-associated sleep disturbance might not respond to BZRAs. BZRAs also might induce somnambulism and other parasomnias,<sup>27</sup> especially when used in combination with psychotropics, such as valproate<sup>28</sup>; it is unclear if the manic state itself increases this risk further. Sedating antihistamines with anticholinergic blockade, such as diphenhydramine and low dosages (<100 mg/d) of quetiapine, are best used only in combination with anti-manic medications because of putative link between anticholinergic blockade and manic induction.<sup>29</sup> Less studied but safer options include novel anticonvulsants (gabapentin, pregabalin), melatonin, and melatonin receptor agonists. Sedating antidepressants, such as mirtazapine and trazodone, should be avoided.<sup>25</sup>

Important adjunctive treatment steps include discontinuing all pro-manic agents, including antidepressants, stimulants, and steroids, and discouraging use of caffeine, energy drinks, illicit drugs, and alcohol. The patient should return for office visits at

Table 3

### Teaching points for families of manic patients

A psychiatric hospital is the ideal setting for rapid and safe recovery from mania
Several episodes of untreated mania can be neurotoxic and can result in serious social and economic harms
Consistent medication adherence will reduce the time to recovery and the likelihood of relapse
Mania can cause a patient to act or speak to family members in uncharacteristic, hurtful ways that the patient might later regret
Manic patients often lack insight and judgment
Family support is crucial for recovery

least weekly, and possibly more frequently, depending on severity. Telephone check-in calls between scheduled visits may be necessary until the mania is broken.

**Psychotherapy.** Other than supportive therapy and psychoeducation, other forms of psychotherapy during mania are not indicated. Psychotherapy trials in bipolar disorder do not inform anti-manic efficacy because few have enrolled acutely manic patients and most report long-term benefits rather than short-term efficacy for the index manic episode.<sup>30</sup> Educate patients about the importance of maintaining regular social rhythms and taking medication as prescribed. Manic patients might not be aware that they are acting differently during manic episodes, therefore efforts to improve the patient's insight are unlikely to succeed. More time should be spent emphasizing the importance of adherence to treatment and taking anti-manic medications as prescribed. This discussion can be enhanced by focusing on the medication's potential to reduce the unpleasant symptoms of mania, including irritability, insomnia, anxiety, and racing thoughts. At the first visit, discuss setting boundaries with the patient to reduce mania-driven, intrusive phone calls. A patient might develop insight after mania has resolved and he (she) can appreciate social or economic harm that occurred while manic. This discussion might fos-

### Clinical Point

**Patients might not be aware that they are acting differently during manic episodes; efforts to improve insight are unlikely to succeed**



## Outpatient mania

### Clinical Point

**Encourage the family to engage in mania harm-reduction techniques to the extent that the patient will allow**

**Table 4**

### Mania: Harm-reduction techniques

Ensure that a trusted friend or family member controls the patient's credit cards to prevent excessive spending
Take away the patient's cell phone to prevent intrusive calling
Lock up the patient's car keys to prevent traffic accidents and violations
Change the patient's password to social networking sites to prevent the patient from posting messages that he (she) might regret
Remove alcohol, drugs, and firearms from the home
Relieve the patient of child-care responsibilities

ter adherence to maintenance treatment. Advise your patient to limit activities that may increase stimulation and perpetuate the mania, such as exercise, parties, concerts, or crowded shopping malls. Also, recommend that your patient stop working temporarily, to reduce stress and prevent any manic-driven interactions that could result in job loss.

If your patient has an established relationship with a psychotherapist, discuss with the therapist the plan to initiate mania treatment in the outpatient setting and work as a collaborative team, assuming that the patient has granted permission to share information. Encourage the therapist to increase the frequency of sessions with the patient to enable greater monitoring of changes in patient's manic symptoms.

### Family involvement

Family support is crucial when treating mania in the outpatient setting. Lacking insight and organization, manic patients require the "auxiliary" judgment of trusted family members to ensure treatment success. The family should identify a single person to act as the liaison between the family and the psychiatrist. The psychiatrist should instruct this individual to accompany the patient to each clinic visit and provide regular updates on the patient's adherence to treatment, changes in symptoms, and any new behaviors that would

justify involuntary hospitalization. The treatment plan should be clearly communicated to this individual to ensure that it is implemented correctly. Ideally, this individual would be someone who understands that bipolar disorder is a mental illness, who can tolerate the patient's potential resentment of them for taking on this role, and who can influence the patient and the other family members to adhere to the treatment plan. This family member also should watch the patient take medication to rule out nonadherence if the patient's condition does not improve.

Provide extensive psychoeducation to the family (*Table 3, page 43*). Discuss these teaching points and their implications at length during the first visit and reinforce them at subsequent visits. Advise spouses that the acute manic period is not the time to make major decisions about their marriage or to engage in couple's therapy. These options are better explored after the patient recovers from the manic episode.

Encourage the family to engage in mania harm-reduction techniques to the extent that the patient will allow (*Table 4*). In particular, they should hold onto their loved one's credit cards and checkbook, and discourage the patient from making any major financial decisions until the mania has resolved. Additionally, patients should be relieved of childcare responsibilities during this period. If there are any child welfare safety concerns, the clinician will need to report this to authorities as required by local laws.

Advise family members or roommates to call emergency services and request a crisis intervention team, or to take the patient to an emergency room if he (she) makes verbal threats to harm themselves or others, is violent, or demonstrates behaviors that indicate that he is no longer able to care for himself. The psychiatrist should assist with completing Family and Medical Leave Act paperwork for family members who will monitor the patient at home, a work-excuse letter for the patient so he does not lose his job, and short-term disability paperwork to ensure income for the patient during the manic period.

These interventions can be challenging for the entire family system because they

place family members in a paternalistic role and reduce the patient's autonomy within the family. This is problematic when these role changes occur between spouses or between a patient-parent and his (her) children. Such changes typically need to be reversed over time and may require the help of a family or couple's therapist. To support the psychological health of the patient's family, refer them to the National Alliance on Mental Illness for family support groups or to individual psychotherapists.

### Outpatient management can be rewarding

For "non-dangerous" manic patients who cannot be hospitalized involuntarily and refuse full or partial hospitalization, a psychiatrist must choose between beginning treatment in the clinic and referring the patient to another provider. The latter option is consistent with the APA's ethical guidelines,<sup>31</sup> but must be done appropriately to avoid legal liability.<sup>32</sup> This decision may disappoint a family desperate to see their loved one recover quickly and may leave them feeling betrayed by the mental health system. On the other hand, choosing to treat mania in the outpatient setting can be rewarding when resolution of mania restores the family's homeostasis.

To achieve this outcome, the outpatient psychiatrist must engage the patient's family to ensure that the patient adheres to the treatment plan and monitor for potentially dangerous behavior. The psychiatrist also must use his knowledge of mood symptoms, cognitive impairments, and the psychological experience of manic patients to create a safe and effective treatment strategy that the patient and family can implement.

## Bottom Line

Treating mania in the outpatient setting is risky but can be accomplished in select patients with the help of the patient's family and a strategy that integrates evidence-based pharmacotherapeutic and psychotherapeutic strategies. Because manic patients could display dangerous behavior, be familiar with your state's laws regarding involuntary commitment, patient abandonment, and mandatory reporting.

### Related Resources

- National Alliance on Mental Illness. [www.NAMI.org](http://www.NAMI.org).
- Depression and Bipolar Support Alliance. [www.DBSAAlliance.org](http://www.DBSAAlliance.org).

### Drug Brand Names

Aripiprazole • Abilify	Lorazepam • Ativan
Asenapine • Saphris	Mirtazapine • Remeron
Carbamazepine •	Olanzapine • Zyprexa
Equetro, Tegretol	Pregabalin • Lyrica
Chlorpromazine • Thorazine	Quetiapine • Seroquel
Clonazepam • Klonopin	Risperidone • Risperdal
Diphenhydramine • Benadryl	Trazodone • Desyrel
Eszopiclone • Lunesta	Valproate • Divalproex
Gabapentin • Neurontin	Zaleplon • Sonata
Lamotrigine • Lamictal	Ziprasidone • Geodon
Lithium • Eskalith, Lithobid	Zolpidem • Ambien

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Because of mania's unpredictability and destructive potential, psychiatrists who agree to treat manic patients as outpatients should be familiar with their state's statutes and case law that pertain to the refusal to accept a new patient, patient abandonment, involuntary hospitalization, confidentiality, and mandatory reporting. They also should seek clinical or legal consultation if they feel overwhelmed or uncertain about the safest and most legally sound approach.

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### Clinical Point

**Advise spouses that the acute manic period is not the time to make major decisions about their marriage or engage in couple's therapy**





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### Clinical Point

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