

North Dakota Medicaid Pharmacy Program

Pharmacotherapy for Insomnia in Members with Bipolar Disorder

- Studies suggest that patients with bipolar disorder may experience more manic episodes in response to poor sleep.
 - The correlation between impaired sleep and relapse in patients with bipolar disorder has made pharmacotherapy for insomnia a part of their treatment regimen.
- Currently, there is no medication specifically approved for the management of insomnia in patients with bipolar disorder.
- Providers should consider patient-specific benefit risk ratios when choosing empiric treatment with benzodiazepines, benzodiazepine agonists, sedating antidepressants, sedating antipsychotics, anticonvulsants, and melatonin agonists.

Medication Class	Pros	Cons
Benzodiazepines	<ul style="list-style-type: none">• Wide range of half-lives• Clonazepam was found to be effective as a replacement for neuroleptics used adjunctively with lithium in the maintenance treatment of bipolar disorder in an uncontrolled retrospective chart review and a prospective open trial	<ul style="list-style-type: none">• Abuse potential, tolerance, and withdrawal• Daytime sedation• Motor/cognitive impairment
Benzodiazepine receptor agonists (BzRAs)	<ul style="list-style-type: none">• Like traditional benzodiazepines but more specific to GABA_A receptors• Short to intermediate half-life, with the potential to reduce daytime sleepiness	<ul style="list-style-type: none">• Potential for tolerance and withdrawal
Sedating antidepressants	<ul style="list-style-type: none">• Most commonly prescribed agents for chronic insomnia at low doses• Less concern about long-term use than benzodiazepines and BzRAs• Access widely available	<ul style="list-style-type: none">• Trazodone and antidepressants (specifically tricyclics) are known to have to ability to induce mania in bipolar patients• Should be used with caution in patients with bipolar disorder
Sedating antipsychotics	<ul style="list-style-type: none">• Can be used as monotherapy to improve sleep and as maintenance treatment of bipolar disorder	<ul style="list-style-type: none">• Unfavorable side effect profile (metabolic abnormalities, daytime sedation, extrapyramidal symptoms, etc.)• May induce or worsen sleep-related movement disorders
Anticonvulsants	<ul style="list-style-type: none">• Agents not approved for bipolar treatment (gabapentin, topiramate, and tiagabine) are sometimes used as hypnotics in patients with bipolar disorder• Sedating and not associated with manic switching• Some have demonstrated mood stabilizing properties	<ul style="list-style-type: none">• Probably less effective than benzodiazepines and BzRAs in insomnia• Possible side effects of cognitive impairment and daytime sedation
Melatonin receptor agonists	<ul style="list-style-type: none">• May be useful in patients with comorbid substance use, as these agents are not associated with abuse• Melatonin has shown some promise in treatment-refractory mania in rapid-cycling patients	<ul style="list-style-type: none">• Have not been carefully studied in maintenance treatment of bipolar disorder• A case series of five rapid-cycling patients suggested that melatonin has little effect on mood and sleep, and melatonin withdrawal delayed sleep onset time and may have mild mood-elevating effects

Plante, David, M.D. and Winkelman, John, M.D., Ph.D. Sleep Disturbance in Bipolar Disorder: Therapeutic Implications | American Journal of Psychiatry (psychiatryonline.org)

<http://www.hidesigns.com/ndmedicaid> for information on prior authorization. Helpful links include PA Forms, PA Criteria, and NDC Drug Lookup.