

# 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
<b>Benzodiazepines</b>	<ul style="list-style-type: none"> <li>• Wide range of half-lives</li> <li>• 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</li> </ul>	<ul style="list-style-type: none"> <li>• Abuse potential, tolerance, and withdrawal</li> <li>• Daytime sedation</li> <li>• Motor/cognitive impairment</li> </ul>
<b>Benzodiazepine receptor agonists (BzRAs)</b>	<ul style="list-style-type: none"> <li>• Like traditional benzodiazepines but more specific to GABA<sub>A</sub> receptors</li> <li>• Short to intermediate half-life, with the potential to reduce daytime sleepiness</li> </ul>	<ul style="list-style-type: none"> <li>• Potential for tolerance and withdrawal</li> </ul>
<b>Sedating antidepressants</b>	<ul style="list-style-type: none"> <li>• Most commonly prescribed agents for chronic insomnia at low doses</li> <li>• Less concern about long-term use than benzodiazepines and BzRAs</li> <li>• Access widely available</li> </ul>	<ul style="list-style-type: none"> <li>• Trazodone and antidepressants (specifically tricyclics) are known to have to ability to induce mania in bipolar patients</li> <li>• Should be used with caution in patients with bipolar disorder</li> </ul>
<b>Sedating antipsychotics</b>	<ul style="list-style-type: none"> <li>• Can be used as monotherapy to improve sleep and as maintenance treatment of bipolar disorder</li> </ul>	<ul style="list-style-type: none"> <li>• Unfavorable side effect profile (metabolic abnormalities, daytime sedation, extrapyramidal symptoms, etc.)</li> <li>• May induce or worsen sleep-related movement disorders</li> </ul>
<b>Anticonvulsants</b>	<ul style="list-style-type: none"> <li>• Agents not approved for bipolar treatment (gabapentin, topiramate, and tiagabine) are sometimes used as hypnotics in patients with bipolar disorder</li> <li>• Sedating and not associated with manic switching</li> <li>• Some have demonstrated mood stabilizing properties</li> </ul>	<ul style="list-style-type: none"> <li>• Probably less effective than benzodiazepines and BzRAs in insomnia</li> <li>• Possible side effects of cognitive impairment and daytime sedation</li> </ul>
<b>Melatonin receptor agonists</b>	<ul style="list-style-type: none"> <li>• May be useful in patients with comorbid substance use, as these agents are not associated with abuse</li> <li>• Melatonin has shown some promise in treatment-refractory mania in rapid-cycling patients</li> </ul>	<ul style="list-style-type: none"> <li>• Have not been carefully studied in maintenance treatment of bipolar disorder</li> <li>• 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</li> </ul>

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

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