BLONANSERIN

THERAPEUTICS

Brands • Lonasen
see index for additional brand names

Generic? No

Class

- Atypical antipsychotic (serotonin dopamine antagonist; second-generation antipsychotic; also a potential mood stabilizer)

Commonly Prescribed for

(bold for FDA approved)

- Schizophrenia
- Acute mania/mixed mania
- Other psychotic disorders
- Bipolar maintenance
- Bipolar depression
- Treatment-resistant depression
- Behavioral disturbances in dementia
- Behavioral disturbances in children and adolescents
- Disorders associated with problems with impulse control

How the Drug Works

- Blocks dopamine 2 receptors, reducing positive symptoms of psychosis and stabilizing affective symptoms
- Blocks serotonin 2A receptors, causing enhancement of dopamine release in certain brain regions and thus reducing motor side effects and possibly improving cognition and affective symptoms
- Actions at dopamine 3 receptors could theoretically contribute to blonanserin's efficacy

How Long Until It Works

- Psychotic symptoms can improve within 1 week, but it may take several weeks for full effect on behavior as well as on cognition
- Classically recommended to wait at least 4–6 weeks to determine efficacy of drug, but in practice some patients may require up to 16–20 weeks to show a good response, especially on cognitive impairment and functional outcome

If It Works

- Most often reduces positive symptoms but does not eliminate them
- Can improve negative symptoms, as well as aggressive, cognitive, and affective symptoms in schizophrenia
- Most schizophrenia patients do not have a total remission of symptoms but rather a reduction of symptoms by about a third
- Perhaps 5–15% of schizophrenia patients can experience an overall improvement of greater than 50–60%, especially when receiving stable treatment for more than a year
- Such patients are considered super-responders or "awakeners" since they may be well enough to be employed, live independently, and sustain long-term relationships
- Continue treatment until reaching a plateau of improvement
- After reaching a satisfactory plateau, continue treatment for at least a year after first episode of psychosis
- For second and subsequent episodes of psychosis, treatment may need to be indefinite
- Even for first episodes of psychosis, it may be preferable to continue treatment

If It Doesn't Work

- Try one of the other atypical antipsychotics (risperidone, olanzapine, quetiapine, ziprasidone, aripiprazole, paliperidone, asenapine, iloperidone, lurasidone, amisulpride)
- If 2 or more antipsychotic monotherapies do not work, consider clozapine
- Some patients may require treatment with a conventional antipsychotic
- If no first-line atypical antipsychotic is effective, consider higher doses or augmentation with valproate or lamotrigine
- Consider noncompliance and switch to another antipsychotic with fewer side effects or to an antipsychotic that can be given by depot injection
- Consider initiating rehabilitation and psychotherapy such as cognitive remediation
- Consider presence of concomitant drug abuse

Best Augmenting Combos for Partial Response or Treatment Resistance

- Valproic acid (valproate, divalproex, divalproex ER)
- Mood stabilizing anticonvulsants (carbamazepine, oxcarbazepine, lamotrigine)
- Lithium
- Benzodiazepines

Tests

Before starting any atypical antipsychotic

- ✻ Weigh all patients and track BMI during treatment
- Get baseline personal and family history of diabetes, obesity, dyslipidemia, hypertension, and cardiovascular disease
- ✻ Get waist circumference (at umbilicus), blood pressure, fasting plasma glucose, and fasting lipid profile
- Determine if the patient is
  - overweight (BMI 25.0–29.9)
  - obese (BMI >30)
  - has pre-diabetes (fasting plasma glucose 100–125 mg/dl)
  - has diabetes (fasting plasma glucose >126 mg/dl)
  - has hypertension (BP >140/90 mm Hg)
  - has dyslipidemia (increased total cholesterol, LDL cholesterol, and triglycerides; decreased HDL cholesterol)
- Treat or refer such patients for treatment, including nutrition and weight management, physical activity counseling, smoking cessation, and medical management

Monitoring after starting any atypical antipsychotic

- ✻ BMI monthly for 3 months, then quarterly
- ✻ Consider monitoring fasting triglycerides monthly for several months in patients at high risk for metabolic complications and when initiating or switching antipsychotics
- ✻ Blood pressure, fasting plasma glucose, fasting lipids within 3 months and then annually, but earlier and more frequently for patients with diabetes or who have gained >5% of initial weight
- Treat or refer for treatment and consider switching to another atypical antipsychotic for patients who become overweight, obese, pre-diabetic, diabetic, hypertensive, or dyslipidemic while receiving an atypical antipsychotic
- ✻ Even in patients without known diabetes, be vigilant for the rare but life-threatening onset of diabetic ketoacidosis, which always requires immediate treatment, by monitoring for the rapid onset of polyuria, polydipsia, weight loss, nausea, vomiting, dehydration, rapid respiration, weakness and clouding of sensorium, even coma
- Patients with low white blood cell count (WBC) or history of drug-induced leucopenia/neutropenia should have complete blood count (CBC) monitored frequently during the first few months, and blonanserin should be discontinued at the first sign of decline in WBC in the absence of other causative factors

SIDE EFFECTS

How Drug Causes Side Effects

- By blocking dopamine 2 receptors in the striatum, it can cause motor side effects
- By blocking dopamine 2 receptors in the pituitary, it can cause elevations in prolactin
- Mechanism of weight gain and increased incidence of diabetes and dyslipidemia with atypical antipsychotics is unknown

Notable Side Effects

- Akathisia, EPS
- Insomnia, anxiety, sedation
- Urinary retention
- Theoretical risk of tardive dyskinesia

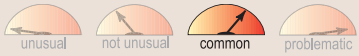
Life-Threatening or Dangerous Side Effects

- Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients taking atypical antipsychotics
- Increased risk of death and cerebrovascular events in elderly patients with dementia-related psychosis
- Rare neuroleptic malignant syndrome (much reduced risk compared to conventional antipsychotics)
- Rare seizures

Weight Gain

- Reported but not expected

Sedation



- Many experience and/or can be significant in amount

What to Do About Side Effects

- Wait
- Wait
- Wait
- Anticholinergics may reduce motor side effects when present
- Weight loss, exercise programs, and medical management for high BMIs, diabetes, dyslipidemia
- Switch to another atypical antipsychotic

Best Augmenting Agents for Side Effects

- Benztropine or trihexyphenidyl for motor side effects
- Beta blockers or benzodiazepines may reduce akathisia when present
- Many side effects cannot be improved with an augmenting agent

DOSING AND USE

Usual Dosage Range

- 8–16 mg/day divided in 2 doses

Dosage Forms

- Tablet 2 mg, 4 mg, 8 mg
- Powder 20 mg per 1 g powder

How to Dose

- Initial 8 mg/day divided in 2 doses; maintenance dose 8–16 mg/day divided in 2 doses; maximum dose 24 mg/day
- Blonanserin should be taken after a meal, as maximum concentrations are increased in the fed state; however, because the increase in systemic exposure continues until at least 4 hours after food intake, blonanserin can be taken before bedtime

Dosing Tips

- Start with twice daily dosing; once stabilized, some patients do well with 1 dose given at night

Overdose

- Limited data

Long-Term Use

- Not extensively studied past 56 weeks, but long-term maintenance treatment is often necessary for schizophrenia
- Should periodically reevaluate long-term usefulness in individual patients, but treatment may need to continue for many years in patients with schizophrenia

Habit Forming

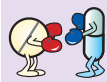
- No

How to Stop

- Down-titration, especially when simultaneously beginning a new antipsychotic while switching (i.e., cross-titration)
- Rapid discontinuation could theoretically lead to rebound psychosis and worsening of symptoms

Pharmacokinetics

- Elimination half-life 10–16 hours after single dose
- Metabolized by CYP450 3A4



Drug Interactions

- CYP450 3A4 inducers, such as carbamazepine, can lower the plasma levels of blonanserin
- CYP450 3A4 inhibitors, such as ketoconazole, nefazodone, fluvoxamine, and fluoxetine, can increase plasma levels of blonanserin
- May increase effects of antihypertensive agents
- May antagonize levodopa, dopamine agonists

Other Warnings/ Precautions

- Use with caution in patients with conditions that predispose to hypotension (dehydration, overheating)
- Dysphagia has been associated with antipsychotic use, and blonanserin should be used cautiously in patients at risk for aspiration pneumonia

Do Not Use

- In conjunction with adrenaline/epinephrine
- If patient is taking ketoconazole
- If there is a proven allergy to blonanserin

SPECIAL POPULATIONS

Renal Impairment

- Not studied

Hepatic Impairment

- Use with caution; may need to lower dose

Cardiac Impairment

- Use in patients with cardiac impairment has not been studied, so use with caution

Elderly

- Some patients may tolerate lower doses better
- Although atypical antipsychotics are commonly used for behavioral disturbances in dementia, no agent has been approved for treatment of elderly patients with dementia-related psychosis
- Elderly patients with dementia-related psychosis treated with atypical antipsychotics are at an increased risk of death compared to placebo and also have an increased risk of cerebrovascular events

Children and Adolescents

- Safety and efficacy have not been established
- Children and adolescents using blonanserin may need to be monitored more often than adults

Pregnancy

- Controlled studies have not been conducted in pregnant women
- Psychotic symptoms may worsen during pregnancy, and some form of treatment may be necessary

Breast Feeding

- Unknown if blonanserin is secreted in human breast milk, but all psychotropics assumed to be secreted in breast milk
- ✻ Recommended either to discontinue drug or bottle feed unless the potential benefit to the mother justifies the potential risk to the child
- Infants of women who choose to breast feed while on blonanserin should be monitored for possible adverse effects

THE ART OF PSYCHOPHARMACOLOGY

Potential Advantages

- May be useful when other antipsychotics have failed to provide adequate response or have not been tolerated

Potential Disadvantages

- Patients who require once daily dosing from the initiation of treatment
- Patients who require intramuscular administration

Primary Target Symptoms

- Positive symptoms of psychosis
- Negative symptoms of psychosis
- Cognitive symptoms
- Unstable mood (both depression and mania)
- Aggressive symptoms

Pearls

- Relatively selective binding profile
- Not approved for mania, but almost all atypical antipsychotics approved for acute treatment of schizophrenia have proven effective in the acute treatment of mania as well

Suggested Reading

Deeks ED, Keating GM. Blonanserin. A review of its use in the management of schizophrenia. CNS Drugs 2010;24(1):65–84.

Hida H, Mouri A, Mori K, et al. Blonanserin ameliorates phencyclidine-induced visual-recognition memory deficits: the complex mechanism of blonanserin action involving D3-5-HT2A and D1-NMDA receptors in the mPFC. Neuropsychopharmacology 2015;40(3):601–13.

Kishi T, Matsuda Y, Nakamura H, Iwata N. Blonanserin for schizophrenia: a systematic review and meta-analysis of double-blind, randomized, controlled trials. J Psychiatr Res 2013;47(2):149–54.

Yang J, Bahk WM, Cho HS, et al. Efficacy and tolerability of blonanserin in the patients with schizophrenia: a randomized, double-blind, risperidone-compared trial. Clin Neuropharmacol 2010;33(4):169–75.