
LURASIDONE (Latuda) Fact Sheet

BOTTOM LINE:

This drug offers some advantages, including no need for titration, once-daily dosing, relatively low-moderate metabolic profile, and relatively low QT prolongation risk. However, its use is limited by the need to administer with ≥ 350 calories of food, potential for drug interactions, and side effects including sedation, akathisia, and EPS, not to mention relatively minimal data (and certainly no long-term data) in kids.

PEDIATRIC FDA INDICATIONS:

Schizophrenia (13–17 years); **bipolar I depression** (as monotherapy and adjunct, 10–17 years).

ADULT FDA INDICATIONS:

Schizophrenia; bipolar I depression (as monotherapy and adjunct).

OFF-LABEL USES:

Mixed depression; treatment-resistant depression; impulse control disorders.

DOSAGE FORMS:

Tablets: 20 mg, 40 mg, 60 mg, 80 mg, 120 mg.

PEDIATRIC DOSAGE GUIDANCE:

Start 40 mg QD, with food (at least 350 calories); no titration required. Usual dose 40–80 mg/day. Max dose 80 mg/day for adolescents vs 160 mg/day in adults.

MONITORING: Weight, waist circumference, glucose, lipids, BP/P, abnormal movements.

COST: \$\$\$\$

SIDE EFFECTS:

- Most common: Somnolence (dose related), EPS, akathisia (dose related), nausea and vomiting, weight gain.
- Serious but rare: Orthostatic hypotension and syncope reported (rarely).

MECHANISM, PHARMACOKINETICS, AND DRUG INTERACTIONS:

- Dopamine D2 and serotonin 5HT2A and 5HT7 antagonist; serotonin 5HT1A partial agonist.
- Metabolized primarily through CYP3A4; $t_{1/2}$: 18 hours.
- Avoid use with medications that cause orthostasis, potent 3A4 inhibitors (eg, ketoconazole, clarithromycin), or inducers (eg, rifampin, St. John's wort, carbamazepine). Exercise caution/monitor when using in combination with moderate 3A4 inhibitors (eg, diltiazem); decrease lurasidone dose by 50% in patients taking moderate 3A4 inhibitors.

EVIDENCE AND CLINICAL PEARLS:

- Newest indication of bipolar depression in kids is based on a six-week randomized double-blind placebo-controlled study of 347 kids receiving lurasidone 20–80 mg/day or placebo. Lurasidone-treated patients had a statistically significant larger improvement in symptoms of bipolar depression, with an effect size of 0.45 (as measured by Children's Depression Rating Scale, Revised).
- A placebo-controlled study of lurasidone in irritability associated with autism found it no better than placebo, and 13 out of 18 kids ages 6–12 years experienced vomiting.
- While using lurasidone in bipolar depression has not been associated with an increase in the development of mania, its efficacy in treating manic episodes has not been established, so its use should be reserved for depressive episodes.
- Administration with food (at least 350 calories) increases bioavailability two-fold and peak serum levels roughly three-fold; fat content of meal is not important.
- Appears to be relatively weight-neutral and to have little effect on cardiometabolic parameters in company-sponsored trials, although post-marketing observations have been limited, particularly in kids.

FUN FACT:

One unique feature of Latuda is its high affinity for the 5HT7 receptor, which has been linked to depression, learning/memory, cognition, anxiety, and pain. Unfortunately, to date, Latuda has shown no clear benefit over other second-generation antipsychotics on these measures.