LURASIDONE (Latuda) Fact Sheet [G]

Bottom Line:
Lurasidone offers some advantages, including no need for titration, once-daily dosing, relatively low-moderate metabolic profile, and relatively low QT prolongation risk. It is also one of five antipsychotics approved for bipolar depression (along with cariprazine, lumateperone, olanzapine/fluoxetine, and quetiapine). However, its use is limited by the need to administer with at least 350 calories of food, potential for drug interactions, and side effects including sedation, akathisia, and EPS. In clinical practice, you might lump lurasidone with the other second-generation antipsychotics that cause little weight gain, such as aripiprazole and ziprasidone.

FDA Indications:
Schizophrenia (adults, adolescents 13–17); **bipolar I depression** (as monotherapy and adjunct; adults, children 10–17).

Off-Label Uses:
Mixed depression; treatment-resistant depression; impulse control disorders.

Dosage Forms:
Tablets (G): 20 mg, 40 mg, 60 mg, 80 mg, 120 mg.

Dosage Guidance:
- Schizophrenia (adolescents and adults): Start 40 mg QD, with food (at least 350 calories); no titration required. Usual dose 40–120 mg/day. Max dose 160 mg QD (80 mg/day for adolescents).
- Bipolar depression (adults and children): Start 20 mg QD, with food (at least 350 calories); no titration required. Usual dose 20–120 mg/day (20–40 mg/day in kids). Max dose 120 mg QD (80 mg/day in kids), although doses >80 mg/day rarely more effective.

Monitoring: Fasting glucose, lipids.

Cost: $

Side Effects:
- Most common: Sedation (dose-related), akathisia (dose-related), nausea, parkinsonism, agitation.
- Serious but rare: Orthostatic hypotension and syncope reported (rarely).
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:
- Dopamine D2 and serotonin 5-HT2A and 5-HT7 antagonist; serotonin 5-HT1A partial agonist.
- Metabolized primarily through CYP3A4; t ½: 18 hours.
- Avoid use with medications that cause orthostasis, potent CYP3A4 inhibitors (eg, clarithromycin, ketoconazole), or inducers (eg, carbamazepine, rifampin, St. John's wort). Exercise caution/monitor when using in combination with moderate 3A4 inhibitors (eg, diltiazem); decrease lurasidone dose by 50% in patients taking moderate 3A4 inhibitors.

Clinical Pearls:
- 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 cardiometabolic parameters were little affected in company-sponsored trials, although post-marketing observations have been limited. In kids, weight gain was a common side effect in studies.
- A network meta-analysis of 10 RCTs with 3,336 adults with schizophrenia found that 40 mg, 80 mg, 120 mg, and 160 mg of lurasidone were effective but not 20 mg. The 160 mg dose was best for PANSS score reduction. Side effects, especially sedation and EPS, increased as dose went up. A good target may be 80 mg, which produced efficacy in 50% of patients. If patients still symptomatic but tolerating, increase to 120–160 mg.
- While using lurasidone in bipolar depression has not been associated with 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.

Fun Fact:
One unique feature of Latuda is its high affinity for the 5-HT7 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.