

# ZIPRASIDONE (Geodon) Fact Sheet [G]

## **BOTTOM LINE:**

Growing body of research supports both efficacy and safety in kids. However, the disadvantages—including twice-daily dosing, need to administer with food, and relatively great QT prolongation—give us some pause in our pediatric patients.

## **PEDIATRIC FDA INDICATIONS:**

None.

## **ADULT FDA INDICATIONS:**

Schizophrenia; bipolar disorder, acute treatment of manic/mixed episode; maintenance treatment of bipolar disorder, as adjunct; acute agitation in patients with schizophrenia (IM only).

## **OFF-LABEL USES:**

Bipolar disorder; behavioral disturbances; impulse control disorders; Tourette's disorder.

## **DOSAGE FORMS:**

- **Capsules (G):** 20 mg, 40 mg, 60 mg, 80 mg.
- **Injection (G):** 20 mg/mL.

## **PEDIATRIC DOSAGE GUIDANCE:**

- No guidance on dosing in children and adolescents.
- Schizophrenia, bipolar disorder: Start 20 mg BID (40 mg BID for acute mania) with meals for two to three days; ↑ by 40 mg/day increments; can usually ↑ rather quickly to target dose 60–80 mg BID. Max approved dose is 160 mg/day, though can go higher in some patients; there are some safety data for doses up to 320 mg/day.
- Schizophrenia, acute agitation (IM injection): 10 mg Q2 hours or 20 mg Q4 hours; max 40 mg/day. Replace with oral therapy as soon as possible.

**MONITORING:** Weight, waist circumference, glucose, lipids; ECG, abnormal movements.

**COST:** \$

## **SIDE EFFECTS:**

- Most common: Somnolence, dizziness, akathisia, rash (5%), weight gain, EPS, abnormal movements.
- Serious but rare: May result in minor QTc prolongation (dose related; 10 msec at 160 mg/day). Clinically relevant prolongation (>500 msec) rare (0.06%) and less than placebo (0.23%). Significant QTc prolongation has been associated with the development of malignant ventricular arrhythmias (torsades de pointes) and sudden death. Avoid in patients receiving other drugs that prolong QTc, or who have hypokalemia, hypomagnesemia, bradycardia, or persistent QTc > 500 msec. Patients with symptoms of dizziness, palpitations, or syncope should receive further cardiac evaluation. Drug reaction with eosinophilia and systemic symptoms (DRESS) has been reported with ziprasidone exposure. DRESS begins as a rash that can spread all over the body; it may include swollen lymph nodes, fever, and damage to organs such as the heart, liver, pancreas, or kidneys, and is sometimes fatal. Discontinue ziprasidone if DRESS is suspected.

## **MECHANISM, PHARMACOKINETICS, AND DRUG INTERACTIONS:**

- Dopamine D2 and serotonin 5HT2A receptor antagonist.
- Metabolized in liver principally by aldehyde oxidase; less than 1/3 of clearance mediated by CYP450: CYP3A4 (major), and CYP1A2 (minor); t<sub>1/2</sub>: 7 hours.
- Avoid use with other drugs that prolong QT interval.

## **EVIDENCE AND CLINICAL PEARLS:**

- One six-week (with 26-week open-label extension) placebo-controlled randomized trial in adolescents with schizophrenia failed to show separation between ziprasidone and placebo in efficacy measures.
- A four-week randomized trial in 237 children and adolescents (ages 10–17) found significantly greater symptom reduction and response rates with ziprasidone compared to placebo.
- Only limited data with ziprasidone in autistic kids or kids with Tourette's.
- Administer twice daily, ideally with meals; ingestion of several hundred calories is necessary to increase absorption up to two-fold.
- Causes less weight gain than clozapine, olanzapine, quetiapine, or risperidone.
- Average increase in QTc greater than any other second-generation antipsychotics, although not much more than for quetiapine. Post-marketing surveillance has shown one or two instances of torsades de pointes possibly related to ziprasidone use.

## **FUN FACT:**

The brand name Geodon has been suggested to bring to mind the phrase “down (don) to earth (geo),” referring to the goals of the medication.