
ZIPRASIDONE (Geodon) Fact Sheet [G]

Bottom Line:

Ziprasidone has an appealing weight and metabolic profile, but many clinicians get scared off by its reputation for lengthening the QT interval. This risk is overblown, and it should probably be prescribed more.

FDA Indications:

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

Off-Label Uses:

Behavioral disturbances; impulse control disorders.

Dosage Forms:

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

Dosage Guidance:

- 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: Fasting glucose, lipids; ECG if cardiac disease.

Cost: \$

Side Effects:

- Most common: Somnolence, dizziness, akathisia, rash (5%).
- 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%). Avoid in patients with hypokalemia, hypomagnesemia, bradycardia, or persistent QTc intervals >500 msec, as well as in patients receiving other drugs that prolong QT interval. 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 also 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.
- Pregnancy/breastfeeding: Limited data suggest relative safety.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Dopamine D2 and serotonin 5-HT2A receptor antagonist.
- Metabolized in liver principally by aldehyde oxidase; less than one-third of clearance mediated by CYP3A4 and CYP1A2; $t_{1/2}$: 7 hours.
- Avoid use with other drugs that prolong QT interval.

Clinical Pearls:

- 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 is 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.