
PALIPERIDONE (Invega) Fact Sheet [G]

Bottom Line:

Paliperidone is the active metabolite of risperidone. In comparison with its parent compound, paliperidone has the advantages of no drug-drug interactions, an easy transition to several long-acting injectable formulations, and a unique FDA indication for schizoaffective disorder. Disadvantages include more QT interval prolongation than risperidone, more tachycardia, possibly more EPS, and the same amount of hyperprolactinemia.

FDA Indications:

Schizophrenia in adults and children ≥ 12 years; **schizoaffective disorder**.

Off-Label Uses:

Bipolar disorder; behavioral disturbances; impulse control disorders.

Dosage Forms (see LAI fact sheet and table for long-acting injections):

- **Controlled-release tablets (G):** 1.5 mg, 3 mg, 6 mg, 9 mg (not breakable).
- **Long-acting injection: Invega Sustenna:** 39 mg, 78 mg, 117 mg, 156 mg, 234 mg; **Invega Trinza:** 273 mg, 410 mg, 546 mg, 819 mg; **Invega Hafyera:** 1,092 mg, 1,560 mg (see LAI fact sheet and table).

Dosage Guidance:

- Schizophrenia/schizoaffective disorder (adults): Start 6 mg QAM, which may be the effective dose; if required, may \uparrow by 3 mg/day at intervals of greater than five days to max 12 mg/day.
- Schizophrenia (adolescents): Start 3 mg QAM, \uparrow by 3 mg/day at intervals of >5 days to max 6 mg/day (<51 kg) or 12 mg/day (≥ 51 kg).
- Paliperidone 3 mg, 6 mg, 9 mg, and 12 mg roughly equivalent to 1–2 mg, 2–4 mg, 4–6 mg, and 6–8 mg risperidone, respectively.
- Dose timing: The manufacturer recommends taking it in the morning; however, some patients experience drowsiness and should try nighttime dosing.
- Long-acting injection: See LAI fact sheet and table.

Monitoring: Fasting glucose, lipids; prolactin if symptoms.

Cost: \$\$

Side Effects:

- Most common: Akathisia, EPS (dose-related), tremor, tachycardia, insomnia, somnolence (especially adolescents), weight gain, orthostatic hypotension, headache, prolactin elevation.
- Serious but rare: Modest increase in QT interval. Orthostatic hypotension and syncope reported. Rarely, controlled-release tablet may get caught in GI tract and cause obstructive symptoms in patients with known strictures; avoid use in patients with severe, preexisting GI narrowing (either pathologic or iatrogenic). Esophageal dysmotility and aspiration possible; use caution in patients at risk for aspiration pneumonia (eg, those with advanced Alzheimer's dementia).
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Dopamine D2 and serotonin 5-HT_{2A} receptor antagonist.
- Not metabolized by liver; $t_{1/2}$: 23 hours.
- Avoid use with drugs known to prolong the QT interval or to cause orthostasis. Paliperidone is the principal active metabolite of risperidone; therefore, avoid use with risperidone. Minimal drug interactions.

Clinical Pearls:

- Warn your patients that they may find what looks like intact capsules in their stool. These are actually empty "ghost pills." They appear because Invega is an extended-release tablet based on the OROS osmotic delivery system (as is Concerta; see fact sheet in ADHD chapter). Water from the GI tract enters through a semipermeable membrane coating the tablet, causing the drug to be expelled through laser-drilled holes in the coating. The shell is nonabsorbable and will be expelled in the stool, but the drug itself is absorbed.
- Swallow whole, with fluids; do not chew, divide, or crush.
- Adjust dose in patients with renal impairment.
- Studies suggest paliperidone is not highly effective in acute mania, either as monotherapy or in combination with lithium or valproate.
- Along with risperidone, causes the most EPS and hyperprolactinemia of all the second-generation antipsychotics.

Fun Fact:

First drug with FDA approval for schizoaffective disorder, allowing Janssen to carve out a marketing niche and separate this drug from its competitors (at least from a commercial and marketing perspective).