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## ILOPERIDONE (Fanapt) Fact Sheet

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### Bottom Line:

Iloperidone is not recommended as a first-choice agent due to twice-daily dosing, need for titration, QT prolongation (comparable to ziprasidone), dizziness, moderate weight gain, and increases in blood sugar; and because it appears less efficacious than other antipsychotics.

### FDA Indications:

**Schizophrenia.**

### Off-Label Uses:

Bipolar disorder; major depression; behavioral disturbances; impulse control disorders.

### Dosage Forms:

**Tablets:** 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, 12 mg.

### Dosage Guidance:

Start 1 mg BID; ↑ to 2 mg BID on day two and then daily by 4 mg/day to a target dose of 6–12 mg BID daily; max 12 mg BID.

**Monitoring:** Fasting glucose, lipids.

**Cost:** \$\$\$\$\$

### Side Effects:

- Most common: Dizziness (dose-related), dry mouth, fatigue, nasal congestion, orthostatic hypotension (can minimize by gradual dose titration), somnolence, tachycardia (dose-related), moderate weight gain.
- Serious but rare: Relatively moderate to high risk of QT prolongation (risk is increased in patients taking potent CYP2D6 or CYP3A4 inhibitors, or at higher doses); avoid use in patients with bradycardia, history of MI, hypokalemia, hypomagnesemia, or concomitant use of other drugs that prolong QT. Priapism reported rarely.
- Pregnancy/breastfeeding: Not enough data to recommend.

### Mechanism, Pharmacokinetics, and Drug Interactions:

- Dopamine D2 and serotonin 5-HT<sub>2A</sub> receptor antagonist.
- Metabolized primarily through CYP2D6, also CYP3A4; t<sub>1/2</sub>: 18 hours (33 hours in poor metabolizers).
- Avoid concomitant use of other drugs known to prolong the QT interval.
- Potent inhibitors of CYP2D6 (eg, fluoxetine, paroxetine, quinidine) or CYP3A4 (eg, clarithromycin, ketoconazole) may increase iloperidone levels; in such cases, decrease iloperidone dose by 50%.

### Clinical Pearls:

- Must follow initial titration schedule if treatment has been interrupted for more than three days.
- Minimal data regarding long-term use in schizophrenia and uses other than schizophrenia.
- Avoid use in patients with severe hepatic impairment due to potential for elevated levels leading to QT interval prolongation.
- A network meta-analysis of 212 studies involving more than 43,000 patients found that olanzapine and risperidone improved core symptoms more than other second-generation antipsychotics, and that paliperidone improved core illness symptoms more than lurasidone and iloperidone (*American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia*, September 2020).

### Fun Fact:

Iloperidone was initially on track for FDA approval in 2002, but its approval was delayed to 2009 due to multiple company mergers and out-licensing deals as well as the FDA's request for more data.