
PIMAVANSERIN (Nuplazid) Fact Sheet

Bottom Line:

Pimavanserin is the only antipsychotic with virtually no effect on dopamine receptors. It is the only approved medication for psychosis in Parkinson's disease, but we do not yet know if it has any efficacy advantages over quetiapine, which has generally been the go-to antipsychotic for this syndrome. Its lack of weight gain is a side effect advantage, but there are some concerns about increases in hospitalization and higher mortality in patients with Parkinson's disease psychosis.

FDA Indications:

Hallucinations and delusions associated with Parkinson's disease psychosis.

Off-Label Uses:

Depression.

Dosage Forms:

- **Tablets:** 10 mg.
- **Capsules:** 34 mg.

Dosage Guidance:

Start and continue with 34 mg once daily (no titration). Use 10 mg tablet in patients taking concurrent CYP3A4 inhibitors.

Monitoring: Fasting glucose, lipids.

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

Side Effects:

- Most common: Nausea, peripheral edema, confusion.
- Serious but rare: QT prolongation (dose related; mean prolongation of 5–8 msec at usual dose); class warning regarding increased mortality in elderly.
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Second-generation antipsychotic with combination of inverse agonist and antagonist activity at 5-HT_{2A} and, less so, at 5-HT_{2C} receptors.
- Metabolized by CYP3A4 and CYP3A5; t_{1/2}: 57 hours (200 hours for active metabolite).
- Caution with potent inhibitors or inducers of CYP3A4 (adjust dose per above). Avoid use with other medications that may increase QT interval.

Clinical Pearls:

- FDA approval based on a six-week placebo-controlled outpatient study of 185 patients that showed only modest (but statistically significant) improvement in hallucinations and delusions compared to placebo.
- The study didn't find any difference (improvement or worsening) in motor function between those who received Nuplazid or placebo.
- All in all, though, pimavanserin did not show statistically significant benefit in three out of four pre-approval clinical studies.
- Reports of post-marketing deaths in patients who had taken Nuplazid have sparked investigation and controversy, though we still don't know if it's any more dangerous than clozapine or quetiapine use in Parkinson's.
- Preliminary data have shown antidepressant efficacy when pimavanserin is added to an SSRI or SNRI in patients with inadequate response.

Fun Fact:

The FDA rejected an indication bid for dementia-related psychosis—twice—due to lack of significantly meaningful effect in some subgroups of patients.