## THERAPEUTICS

**Brands** • Nuplazid

See index for additional brand names

**Generic?** No

**Class**

- Atypical antipsychotic; serotonin 2A/2C antagonist/inverse agonist

**Commonly Prescribed for**

(Bold for FDA approved)

- Hallucinations and delusions associated with Parkinson’s disease psychosis

**How the Drug Works**

- Antagonism/inverse agonism at 5HT2A receptors
- Pimavanserin is also an antagonist/inverse agonist at 5HT2C receptors (activity is very low compared to that at 5HT2A receptors)

**How Long Until It Works**

- In clinical trials psychotic symptom improvement reached significance within 1 month

**If It Works**

- Most often reduces hallucinations and delusions without worsening parkinsonism

**If It Doesn’t Work**

- Try reducing the dose of antiparkinsonian dopaminergic therapies
- Try low-dose quetiapine
- Try low-dose clozapine
- Do not try any other atypical or conventional antipsychotic

**Best Augmenting Combos for Partial Response or Treatment Resistance**

- None known
- Theoretically, might be possible to combine with low-dose quetiapine, especially during prolonged cross-titration when switching from one to the other

**Tests**

- None

## SIDE EFFECTS

**How Drug Causes Side Effects**

- Mechanism of peripheral edema, confusional state, and nausea unknown

**Notable Side Effects**

- Peripheral edema
- Confusional state
- Nausea

**Life Threatening or Dangerous Side Effects**

- QTc prolongation
- Increased risk of death and cerebrovascular events in elderly patients with dementia-related psychosis has occurred with antipsychotic use

**Weight Gain**

- Reported but not expected

**Sedation**

- Reported but not expected

**What to Do About Side Effects**

- Wait
- Wait
- Wait
- Discontinue if side effects are intolerable

**Best Augmenting Agents for Side Effects**

- Many side effects cannot be improved with an augmenting agent

## DOSING AND USE

**Usual Dosage Range**

- 34 mg once daily

**Dosage Forms**

- Tablet 17 mg

**How to Dose**

- 34 mg/day taken once daily; no titration required
**SPECIAL POPULATIONS**

### Renal Impairment
- Dose adjustment not necessary in patients with mild-to-moderate impairment
- Not studied in patients with severe impairment; not recommended in patients with severe renal impairment (creatinine clearance < 30 mL/min)

### Hepatic Impairment
- Not studied; not recommend in patients with hepatic impairment

### Cardiac Impairment
- Pimavanserin can cause QTc prolongation and should be avoided in patients with known QT prolongation or in combination with drugs that are known to prolong QT interval
- Pimavanserin should be avoided in patients with a history of cardiac arrhythmias, symptomatic bradycardia, hypokalemia or hypomagnesemia, or presence of congenital prolongation of the QT interval

### Elderly
- Dose adjustment not necessary
- Pimavanserin is not approved for the treatment of dementia-related psychosis UNRELATED to the hallucinations and delusions associated with Parkinson's disease psychosis, such as the behavioral symptoms of comorbid Alzheimer dementia
- However, pimavanserin is not contraindicated for patients with dementia RELATED to Parkinson's disease who have hallucinations and delusions of Parkinson's disease psychosis

### Children and Adolescents
- Safety and efficacy have not been established

### Pregnancy
- Effective June 30, 2015, the US FDA requires changes to the content and format of pregnancy and lactation information in prescription drug labels, including the elimination of the pregnancy letter categories; the Pregnancy and Lactation Labeling Rule (PLLRR or final rule) applies
Only to prescription drugs and will be phased in gradually for drugs approved on or after June 30, 2001

- Controlled studies have not been conducted in pregnant women
- In rat and rabbit studies, pimavanserin did not demonstrate teratogenicity at doses up to 10 times the maximum recommended human dose
- In rat studies, doses 2 times the maximum recommended daily dose in humans based on area under the curve (AUC) resulted in maternal toxicity, including mortality and reduced body weight and food consumption, with corresponding decreases in pup survival, reduced litter size, and reduced pup body weight

Breast Feeding
- Unknown if pimavanserin is secreted in human breast milk, but all psychotropics assumed to be secreted in breast milk

★ Recommended to either discontinue drug or bottle feed unless the potential benefit to the mother justifies the potential risk to the child
- Infants of women who choose to breast feed while on pimavanserin should be monitored for possible adverse effects

Potential Advantages
- Does not worsen motor symptoms of Parkinson’s disease

- Not associated with the metabolic side effects of quetiapine and clozapine, including weight gain, dyslipidemia, and diabetes mellitus
- Not associated with the sedation sometimes caused by quetiapine and clozapine
- Does not require dose reduction of antiparkinsonian dopaminergic therapy given concomitantly

Potential Disadvantages
- Expensive

Primary Target Symptoms
- Hallucinations and delusions associated with Parkinson’s disease

Pearls
- Trials are underway for the use of pimavanserin to treat Alzheimer’s disease psychosis
- Theoretically should be effective for the hallucinations associated with Lewy Body psychosis
- Enhances slow wave sleep and may have hypnotic properties
- May enhance the antipsychotic action of atypical antipsychotics in patients with schizophrenia
- May be effective in other types of psychosis but based on theory and not on large randomized trials

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THE ART OF PSYCHOPHARMACOLOGY

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PIMAVANSERIN (continued)

**Suggested Reading**


