IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Pimavanserin (Nuplazid) is an atypical antipsychotic medication approved to treat Parkinson’s disease (PD) psychosis.
Policy/Criteria

I. Most contracts require prior authorization approval of pimavanserin (Nuplazid) prior to coverage. Pimavanserin (Nuplazid) may be considered medically necessary when criteria A, B, C, and D below are met.

A. A diagnosis of Parkinson’s disease psychosis (defined by illusions, a false sense of presence, hallucinations, or delusions).

AND

B. Diagnosis established by or in consultation with a neurologist.

AND

C. The psychosis is not due to other conditions. Other conditions may include, but are not limited to, another mental disorder or physiological effects of a substance.

AND

D. Treatment with clozapine has been ineffective, not tolerated, or is contraindicated.

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx considers pimavanserin (Nuplazid) to be a self-administered medication.

B. When prior authorization is approved, pimavanserin (Nuplazid) may be authorized in quantities of 60 tablets per 30 days.

C. Initial authorization shall be reviewed at 3 months to confirm that current medical necessity criteria are met and that the medication is effective in improving quality of life related to psychosis symptoms.

D. Continued authorization shall be reviewed at least annually to confirm that current medical necessity criteria are met and the medication is effective.

III. Pimavanserin (Nuplazid) is considered investigational when used for all other conditions, including but not limited to:

A. Alzheimer’s disease psychosis

B. Schizophrenia
Position Statement

Summary

- Pimavanserin (Nuplazid) is an orally administered inverse agonist/antagonist of the serotonin 2A and 2C receptors. The exact mechanism of action is unknown. [1]

- Pimavanserin (Nuplazid) is approved to treat PD psychosis, defined as illusions, a false sense of presence, hallucinations, or delusions. [2]

- Although there are no other FDA approved medications available to treat PD psychosis, evidence-based guidelines recommend treatment with clozapine. [2,3] There is no evidence that pimavanserin is safer or more effective than clozapine, but it is more costly.

- Available guidelines have not been updated since the approval of pimavanserin (Nuplazid). [4,5]

- The efficacy of pimavanserin (Nuplazid) was established by a phase 3, randomized, double-blinded, placebo-controlled trial. It failed to demonstrate efficacy in at least one previous unpublished phase 3 trial.

- The recommended dose of pimavanserin (Nuplazid) 34 mg once daily. The safety and effectiveness of higher doses have not been established.

- Long term efficacy has not been evaluated. Pimavanserin (Nuplazid) carries a boxed warning regarding the increased risk for mortality in the elderly associated with the use of atypical antipsychotics. Treatment efficacy should be periodically re-evaluated. [1]

- The safety and effectiveness of pimavanserin (Nuplazid) in conditions other than PD psychosis have not been established. There are ongoing trials in Alzheimer’s disease psychosis and schizophrenia, but no data is yet available to support use in these populations.

Clinical Efficacy

- Efficacy of pimavanserin (Nuplazid) was established by a 6-week phase 3, randomized, double-blinded, placebo-controlled trial in subjects 40 years of age or older with a score of at least 3 on the scale of assessment of positive symptoms (SAPS) hallucinations or delusions global item, and at least 3 on one other non-global item on the Parkinson’s disease-adapted SAPS scale (SAPS-PD). [6]

- Treatment with pimavanserin (Nuplazid) was associated with a 5.8 point decrease in SAPS-PD, compared to a 2.7 point decrease in the placebo group over the course of the 6 week trial. The clinical relevance of this difference is unclear. The FDA medical review recommended against approval of pimavanserin (Nuplazid) on the basis of inadequate evidence of efficacy in light of the safety concerns. [7]

- A previous unpublished phase 3 trial of pimavanserin (Nuplazid) versus placebo in PD psychosis failed to demonstrate efficacy. A second unpublished phase 3 trial was halted early. Limited details of these trials are available from the manufacturer.
**Investigational Uses**

- There are no published clinical trials evaluating the safety or efficacy of pimavanserin (Nuplazid) for the treatment of conditions other than PD psychosis.
- The clinical efficacy of clozapine in PDP has been established by multiple clinical trials comparing clozapine to placebo or other atypical antipsychotics. [8-14] Multiple evidence based guidelines based on systematic reviews of the literature recommend clozapine for the treatment of PDP. [3,4]

**Safety (optional)**

- Pimavanserin (Nuplazid) carries a boxed warning regarding the increased mortality risk in elderly patients with dementia-related psychosis. The benefit of treatment should be carefully considered in this context.
- Pimavanserin is not recommended in patients with mild to moderate renal impairment (GFR < 30 ml/min).
- Clozapine carries boxed warnings regarding an increased mortality risk in elderly patients with dementia-related psychosis; severe neutropenia; orthostatic hypotension, bradycardia, and syncope; seizures; and myocarditis and cardiomyopathy. [15] Patients treated with clozapine must participate in the clozapine registry, and frequent laboratory tests are required to monitor for side effects.

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<td>HCPCS/ J-Code</td>
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**References**

1. NUPLAZID™ (pimavanserin) tablets, for oral use [package insert]. San Diego, CA: ACADIA Pharmaceuticals Inc; April 29, 2016


15. CLOZARIL® (clozapine) tablets, for oral use. Rosemon, PA: HLS Therapeutics (USA), Inc; September 2015

Revision History

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<tr>
<th>Revision Date</th>
<th>Revision Summary</th>
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<tbody>
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<td>06/10/2016</td>
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