pimavanserin (Nuplazid®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO053

Description

Pimavanserin (Nuplazid) is an orally administered is an atypical antipsychotic that works as a selective serotonin inverse agonist with an unknown mechanism of action.

Length of Authorization

- Initial: six months
- Renewal: 12 months

Quantity limits

Product Name	Indication	Dosage Form	Quantity Limit
pimavanserin (Nuplazid)	Parkinson's disease psychosis	34 mg capsules	30 capsules/30 days
		10 mg tablets	30 tablets/ 30 days

Initial Evaluation

I. **Pimavanserin (Nuplazid)** may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. The medication is prescribed by or in consultation with a neurologist; **AND**
   C. A diagnosis of **Parkinson's disease psychosis** with symptoms of hallucinations and delusions when the following are met:
      1. Symptoms of hallucinations and delusions have continued after reductions in current medications for Parkinson's disease or reductions in medications are not possible based on provider attestation; **AND**
      2. Treatment with clozapine or quetiapine has been ineffective or intolerable, unless both are contraindicated

II. Pimavanserin (Nuplazid) is considered investigational when used for all other conditions, including but not limited to the diagnosis of:
   A. Alzheimer's disease psychosis
   B. Schizophrenia
   C. Dementia related psychosis

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**

II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has experienced a reduction in delusions and hallucinations.

Supporting Evidence

I. There is a lack of safety and efficacy in the use of pimavanserin (Nuplazid) for those under the age of 18.
II. Due to the complexity around the diagnosis of Parkinson's disease (PD) and the treatment options, therapy should be prescribed by, or in consultation with, a neurologist.
III. Psychosis is a frequent complication of PD, occurring in up to 40% of patients, particularly those in the advanced stages of the disease due to the adverse effects of antiparkinsonian medications over time; mainly, the dopamine agonists. There is a recommended algorithm by the Movement Disorder Society to approaching treatment in these patients. Firstly, ruling out if psychosis is from an underlaying infection, and then assessing if the patient's psychosis is bothersome enough to warrant treatment. Treatment first begins with simply reducing or stopping PD medications if possible; if this is not possible or the symptoms continue, then initiating therapy with antipsychotic therapy (pimavanserin, quetiapine or clozapine) occurs.
IV. Pimavanserin (Nuplazid) was studied in a 6-week, randomized, placebo-controlled, parallel-group study in 199 patients with a diagnosis (PD) and psychotic symptoms (hallucinations and/or delusions) severe and frequent enough to warrant antipsychotic treatment. Patients were all 40 years or older with a documented PD history of at least one year; the majority of patients were on PD medications at the study start and were on stable doses at least 30 days prior to the start of the study.
V. The primary efficacy outcome was the change from baseline to week 6 in a PD-adapted scale for the assessment of positive symptoms (SAPS-PD). SAPS-PD is a 9-item scale adapted for PD from the Hallucinations and Delusions domains of the SAPS scale for schizophrenia. The SAPS-PD total score can range from 0 to 45 with higher scores reflecting greater severity of illness. A negative change in score indicates improvement.
VI. A positive effect was seen on both hallucination and delusion components of the SAPS-PD for pimavanserin (n=95) versus placebo (n=90) [-3.06 (95% CI -4.91, -1.2)]. No difference in motor function was observed between pimavanserin and placebo. Although statistically significant, the clinical relevance of this result is unclear.
VII. Pimavanserin (Nuplazid) also had an open-label extension (OLE) for patients completing one of the three double-blind, placebo-controlled studies. All patients received pimavanserin 34mg once daily for an additional four weeks of treatment. Efficacy results once again looked at SAPS-PD. Of 459 patients able to start the OLE, 424 patients continued in the trial for the four additional weeks. The SAPS-PD continued to show improvement during this four-week period,

and those who originally were on placebo and switched over to pimavanserin showed the most positive effects during the OLE, having mean scores improving to the same level as the study arm group receiving pimavanserin during the double-blind trial.

VIII. In 2022, a long-term outcomes review was reported for pimavanserin for psychosis in clinical practice. A retrospective chart review was conducted at the Movement Disorders practice in Providence, Rhode Island between 2016-2021 where 53 patients were identified as initiating pimavanserin, 45 of these patients had PD, and patients were on pimavanserin an average of 26 weeks. Initial improvement was seen in 47% of the group (25 of 53 patients). Due to inadequate control of symptoms with pimavanserin, an addition of another antipsychotic was needed to maintain a positive response for 10 of those 25 patients; whereas eight of the 25 patients were able to continue on pimavanserin for monotherapy.

IX. There are not head-to-head trials of the antipsychotic agents used in PD psychosis. Multiple systemic reviews and meta-analyses have been completed to address this. One in 2023, reviewed 19 studies evaluating atypical antipsychotics in a total of 1,242 patients with PD psychosis. Based on the Clinical Global Impression Scale for Severity, pimavanserin with a standardized mean difference (SMD) of -4.81 (95% CI -5.39,-4.24) and clozapine with a SMD of -4.25 (95% CI, -5.24, -3.26) both significantly improved symptoms compared to placebo.

X. The 2019 American Geriatrics Society Beers Panel recommends to generally avoid all antipsychotic medications in older patients with PD, with exceptions made for quetiapine, clozapine, and pimavanserin. The Movement Disorder Society rated clozapine as more efficacious compared to quetiapine, which was deemed to have insufficient evidence, and does not make any recommendation on pimavanserin (Nuplazid). An update was added one year later in 2019, discussing change in practice implications to the data on quetiapine, noting it was similarly efficacious to clozapine in a clozapine-controlled trial which did not have a placebo arm; updating quetiapine to possibly useful in PD-psychosis. There were no new comments to clozapine or pimavanserin regarding favoring one or the other.

Investigational or Not Medically Necessary Uses

I. Pimavanserin (Nuplazid) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   - A. Alzheimer's disease psychosis
     - i. The use in AD psychosis remains experimental at this time. In August of 2022, the FDA issued a complete response letter noting it could not approve the new indication at this time and recommended an additional trial in this space.
   - B. Schizophrenia
     - i. The use of pimavanserin in schizophrenia remains experimental at this time while a phase III trial continues.
   - C. Dementia related psychosis

i. A complete response letter was issued in April 2021 that "cited a lack of statistical significance in some of the subgroups of dementia and insufficient numbers of patients with certain less common dementia subtypes as lack of substantial evidence of effectiveness to support approval."

References

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11. Pahwa, R., Isaacson, S.H., Small, G.W. et al. Screening, Diagnosis, and Management of Parkinson's Disease Psychosis: Recommendations From an Expert Panel. Neurol Ther 11, 1571–1582 (2022). https://doi.org/10.1007/s40120-022-00388-y

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
istradefylline_Nourianz	Parkinson's Disease
levodopa_Inbrija	
apomorphine_Apokyn_Kynmobi	

Policy Implementation/Update:

Action and Summary of Changes	Date
Annual review; reformatted indication table, added in related policies, general formatting updates. Updated policy requirements to align with updated guidelines, addition of option to trial quetiapine OR clozapine. Updated supporting evidence to strengthen policy requirements.	11/2023
Transition from criteria to policy: Included requirements to attempt dose reduction in Parkinson's medications and specified what members must try and fail.	9/2019