



## Selective Serotonin Inverse Agonist (SSIA) Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Open, FlexRx Closed, GenRx Open, GenRx Closed, Health Insurance Marketplace, FocusRx and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

### FDA APPROVED INDICATIONS AND DOSAGE<sup>1</sup>

Agent	Indication	Dosage
<b>Nuplazid</b> <sup>®</sup> (pimavanserin)  capsules tablets	Treatment of hallucinations and delusions associated with Parkinson's disease psychosis	34 mg taken orally once daily, without titration

### CLINICAL RATIONALE

Parkinson's disease (PD) is a chronic, progressive, neurodegenerative disease characterized by bradykinesia, hypokinesia, rest tremor, and/or rigidity. In addition to these typical motor features, patients with PD may experience nonmotor symptoms related to the disease itself or to the medications used to treat it. A frequent nonmotor complication of PD is psychosis, characterized mainly by visual hallucinations and delusions which are often paranoid in nature. Hallucinations are the most common manifestation and can affect up to 40% of patients with PD, particularly those at an advanced stage of illness. Underlying dementia predisposes to hallucinations and delusions, and psychosis is a risk factor for nursing home placement and mortality.<sup>2-4</sup>

Management of PD psychosis (PDP) involves identifying and treating the underlying causes and contributory factors, thus requiring a multidisciplinary team to be involved (e.g., psychiatrists and other mental health professionals, neurologists).<sup>3</sup> Psychosis may be triggered by infection, delirium, dementia, or medications. Anticholinergics can contribute to confusion and exacerbate psychosis in PD. Psychoactive medications, including sedatives, anxiolytics, and antidepressants, are potential culprits and should be reduced or stopped if possible. The adverse effects of antiparkinsonian medications, the dopamine agonists in particular, are probably the most important cause of psychosis in patients with PD. Stopping all potentially offending antiparkinsonian drugs is usually not an option, although dose reduction can frequently be accomplished with the amelioration of hallucinations and little loss of drug-related benefit. Antiparkinsonian drugs may be reduced or stopped in an order that balances their potency and their likelihood of exacerbating disabling hallucinations. The suggested sequence begins with anticholinergic drugs, followed by amantadine, dopamine agonists, monoamine oxidase type B (MAO B) inhibitors, and catechol-O-methyl transferase (COMT) inhibitors. Levodopa, usually combined with a peripheral decarboxylase inhibitor (e.g., carbidopa-levodopa), should be the last of a drug combination to be reduced, since it is the most effective antiparkinsonian agent and least likely to cause psychosis.<sup>2-4</sup>

For refractory hallucinations or delusions treatment options are scarce, in part because many antipsychotics are known to worsen motor symptoms or are not effective.<sup>3</sup>

Quetiapine is the most widely prescribed despite evidence of efficacy in PD patients being mixed. Clozapine has demonstrated the highest efficacy of the second-generation antipsychotics in this setting, but is underutilized because of the burdensome requirement of hematologic monitoring (agranulocytosis).<sup>2-4</sup>

### **Efficacy<sup>1</sup>**

In 2016, pimavanserin (Nuplazid) became the first antipsychotic FDA-approved to treat PDP. Pimavanserin is a second-generation antipsychotic that acts as a selective serotonin 5-HT<sub>2A</sub> receptor inverse agonist. Pimavanserin's efficacy in hallucinations and delusions associated with PDP was studied in a 6-week, randomized, placebo-controlled, parallel-group study with 199 patients. Pimavanserin was statistically significantly superior to placebo in decreasing the frequency and/or severity of hallucinations and delusions in patients with PDP as measured by central, independent, and blinded raters using the PD-adapted Scale for the Assessment of Positive Symptoms (SAPS-PD) scale. An effect was seen on both the hallucinations and delusions components of the SAPS-PD scale. Notably, pimavanserin did not negatively impact motor function, as measured by the Unified Parkinson's Disease Rating Scale (UPDRS).

### **Safety**

Pimavanserin has the following boxed warnings:<sup>1</sup>

- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.
- Nuplazid is not approved for the treatment of patients with dementia-related psychosis unrelated to the hallucinations and delusions associated with Parkinson's disease psychosis.

All antipsychotic drugs appear to be associated with a small increase in all-cause mortality and cardiovascular events when used to treat behavioral disorders in older adults with dementia. However, these risks must be balanced with the high morbidity and mortality of untreated psychosis.<sup>2,4</sup>

### **REFERENCES**

1. Nuplazid prescribing information. ACADIA Pharmaceuticals Inc. May 2019.
2. Chahine L, Tarsy D, et al. Management of nonmotor symptoms in Parkinson disease. UpToDate. Last updated May 2019. Literature review current through October 2019. Accessed November 21, 2019.
3. Taddei RN, Cankaya S, Dhaliwal S, Chaudhuri KR. Management of Psychosis in Parkinson's Disease: Emphasizing Clinical Subtypes and Pathophysiological Mechanisms of the Condition. *J Parkinsons Dis* 2017;2017:3256542. Available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5613459/>. Accessed on November 25, 2019.
4. Chen JJ. Treatment of Psychotic Symptoms in Patients with Parkinson Disease. *Ment Health Clin* 2017;7(6):262-270. Available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6007727/>. Accessed on November 25, 2019.

## Selective Serotonin Inverse Agonist (SSIA) Prior Authorization with Quantity Limit

### TARGET AGENT

**Nuplazid®** (pimavanserin)

Brand (generic)	GPI	Multisource Code	Quantity Limit Per Day
<b>Nuplazid (pimavanserin)</b>			
10 mg tablet	59400028200310	M, N, O, or Y	1 tablet
17 mg tablet	59400028200320	M, N, O, or Y	2 tablets
34 mg capsule	59400028200120	M, N, O, or Y	1 capsule

### PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

**Target Agent** will be approved when ALL of the following are met:

1. ONE of the following:
  - a. The patient has a diagnosis of hallucinations or delusions associated with Parkinson's disease psychosis **AND** ONE of the following:
    - i. The patient has tried and had an inadequate response to clozapine or quetiapine  
**OR**
    - ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to BOTH clozapine and quetiapine  
**OR**
    - iii. The patient is currently being treated with the requested agent as indicated by ALL of the following:
      - a. A statement by the prescriber that the patient is currently taking the requested agent  
**AND**
      - b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent  
**AND**
      - c. The prescriber states that a change in therapy is expected to be ineffective or cause harm  
**OR**
    - iv. The prescriber has provided documentation that BOTH clozapine and quetiapine cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm  
**OR**
  - b. The patient has another FDA approved indication for the requested agent  
**AND**
2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., neurologist, psychiatrist or other mental health professional) or the prescriber has consulted with a specialist in the area of the patient's diagnosis  
**AND**
3. The patient does NOT have any FDA labeled contraindications to the requested agent  
**AND**
4. ONE of the following:

- a. The requested quantity (dose) does NOT exceed the program quantity limit  
**OR**
- b. ALL of the following:
  - i. The requested quantity (dose) is greater than the program quantity limit  
**AND**
  - ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication  
**AND**
  - iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit**OR**
- c. ALL of the following:
  - i. The requested quantity (dose) is greater than the program quantity limit  
**AND**
  - ii. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication  
**AND**
  - iii. The prescriber has provided information in support of therapy with a higher dose for the requested indication

**Length of Approval:** 12 months