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

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

POLICY REVIEW CYCLE

Effective Date	Date of Origin
07-01-2024	07-01-2018

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Nuplazid® (pimavanserin) Capsule Tablet	Treatment of hallucinations and delusions associated with Parkinson's disease psychosis		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Parkinson's Disease	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.(2-4) 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).(3) 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.(2-4) For refractory hallucinations or delusions treatment options are scarce, in part because many antipsychotics are known to worsen motor symptoms or are not effective. 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).(2-4)
Efficacy	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-HT2A 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). Initial concerns of higher rates of mortality were shown to be no higher than those in this already frail patient group.(1,4)
Safety	Pimavanserin has the following boxed warnings:(1) • 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. And has the following contraindication:(1) • Known hypersensitivity to Nuplazid or any of its components. 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.

REFERENCES

Number	Reference
1	Nuplazid prescribing information. Acadia Pharmaceuticals Inc. September 2023.
2	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/.
3	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/.
4	Weil RS, Reeves S. Hallucinations in Parkinson's disease: new insights into mechanisms and treatments. Adv Clin Neurosci Rehabil. 2020;19(4):ONNS5189. Published 2020 Jul 13. doi:10.47795/ONNS5189.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Nuplazid	pimavanserin tartrate cap	34 MG	M ; N ; O ; Y	N		
Nuplazid	pimavanserin tartrate tab	10 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Nuplazid	Pimavanserin Tartrate Cap 34 MG (Base Equivalent)	34 MG	30	Capsules	30	DAYS			
Nuplazid	Pimavanserin Tartrate Tab 10 MG (Base Equivalent)	10 MG	30	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Nuplazid	pimavanserin tartrate cap	34 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Nuplazid	pimavanserin tartrate tab	10 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Nuplazid	Pimavanserin Tartrate Cap 34 MG (Base Equivalent)	34 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
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PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	**Target Agent(s)** will be approved when ALL of the following are met:

Module	Clinical Criteria for Approval
	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: 1. The patient has tried and had an inadequate response to clozapine or quetiapine **OR** 2. The patient has an intolerance or hypersensitivity to clozapine or quetiapine **OR** 3. The patient has an FDA labeled contraindication to BOTH clozapine and quetiapine **OR** 4. 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** 5. 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 labeled indication for the requested agent **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within the FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 3. 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 for the requested indication **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Quantity limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** C. There is support of therapy with a higher dose for the requested indication **Length of Approval**: up to 12 months