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

This program applies to Commercial, GenPlus, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

OBJECTIVE

The intent of the Selective Serotonin Inverse (SSIA) prior authorization (PA) and Quantity Limit (QL) program is to appropriately select patients for therapy according to product labeling and/or clinical guidelines and according to dosing recommended in product labeling. The program requires the trial of guideline recommended clozapine and quetiapine prior to approval of the requested agent. The program allows for approval for those who are unable to use clozapine or quetiapine due to FDA labeled contraindication, intolerance, or hypersensitivity. The program will not approve for patients who have an FDA labeled contraindication to the requested agent. The program will approve for doses within the set limit. Doses above the set limit will be approved if the requested quantity is below the FDA limit and cannot be dose optimized or when the quantity is above the FDA limit and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis. Requests will be reviewed when patient specific documentation is provided.

TARGET AGENT

Nuplazid® (pimavanserin)

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

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

TARGET AGENT(S) 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 failed clozapine or quetiapine
      OR
      ii. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to clozapine or quetiapine
   OR
   b. The patient has another FDA approved indication
   AND
2. The patient does NOT have any FDA labeled contraindication(s) to the requested agent
   AND
3. ONE of the following:
   a. The quantity requested is less than or equal to the program quantity limit
   OR
   b. The quantity (dose) requested is above the program limit, less than or equal to the maximum dose recommended in FDA approved labeling and

the prescribed dose cannot be achieved using a lesser quantity of a higher strength

OR

c. The quantity (dose) requested is greater than the maximum dose recommended in FDA approved labeling and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist

Length of Approval: 12 months

This pharmacy policy is not an authorization, certification, explanation of benefits or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All pharmacy policies are based on (i) information in FDA approved package inserts (and black box warning, alerts, or other information disseminated by the FDA as applicable); (ii) research of current medical and pharmacy literature; and/or (iii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

The purpose of Blue Cross and Blue Shield of Alabama's pharmacy policies are to provide a guide to coverage. Pharmacy policies are not intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.

Neither this policy, nor the successful adjudication of a pharmacy claim, is guarantee of payment.

FDA APPROVED INDICATIONS AND DOSAGE[1]

Agent	Indication	Dosage & Administration
Nuplazid® (pimavanserin)	Treatment of hallucinations and delusions associated with Parkinson's disease psychosis	Recommended dose is 34 mg taken orally once daily, without titration

CLINICAL RATIONALE

Psychosis is a frequent complication of Parkinson's Disease (PD). It is characterized mainly by visual hallucinations and delusions. Hallucinations are the most common manifestation and can affect up to 40% of patients with PD. Psychosis maybe triggered by infection, delirium, dementia, or medications. The adverse effects of antiparkinson medications, in particular dopamine agonists, are probably the most important cause of psychosis in patients with PD.[2]

The management of psychosis in patients with PD involves identifying and treating the underlying causes and contributory factors. 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 reverse order of their potency and effectiveness if hallucinations are causing disability. The suggested sequence begins with anticholinergic drugs, followed by amantadine, monoamine oxidase type B (MAO B) inhibitors, catechol-O-methyl transferase (COMT) inhibitors, and dopamine agonists. 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]

Clozapine, quetiapine, and pimavanserin are treatments options for Parkinson's patients and psychosis.[2,3] Quetiapine is easier to use than clozapine and considered the treatment of first choice.[2] Clozapine is associated with agranulocytosis that may be fatal. The absolute neutrophil count must be monitored.[3] Pimavanserin was well tolerated and was not associated with worsening of motor symptoms or other adverse effects. However, its long-term safety and efficacy have not been established.[2] All antipsychotic drugs appear to be associated with a small increased risk of mortality when used to treat behavioral disorders in older adult patients, with dementia.

Efficacy

Pimavanserin's efficacy in hallucinations and delusions associated with Parkinson's disease psychosis 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.

Safety[1]

Pimavanserin has the following black box warnings:

- 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.

REFERENCES

1. Nuplazid prescribing information. ACADIA Pharmaceuticals Inc. November 2017.

2. Tarsy, Daniel, MD., et al. Management of nonmotor symptoms in Parkinson disease. UpToDate. Last updated: August 2017.
3. Practice Parameter: Evaluation and treatment of depression, psychosis, and dementia in Parkinson disease (an evidence-based review) Report of the Quality Standards Subcommittee of the American Academy of Neurology. American Academy of Neurology. NEUROLOGY. 2006;66:996–1002