BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

NUPLAZID® (pimavanserin tartrate) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Nuplazid (pimavanserin tartrate) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Neurologist or Psychiatrist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of hallucinations and delusions associated with Parkinson disease psychosis with **ALL** of the following:
    a. Hallucinations or delusions have been present for at least 1 month
    b. Hallucinations or delusions occur at least once weekly

c. Hallucinations or delusions are severe and frequent enough to warrant treatment with an antipsychotic
d. Symptoms of psychosis developed after the Parkinson's disease diagnosis

4. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for quetiapine or clozapine

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual **does not have any** of the following:
   a. Dementia-related psychosis unrelated to the hallucinations and delusions associated with Parkinson's disease
   b. QT Interval prolongation
   c. History of cardiac arrhythmias, symptomatic bradycardia, hypokalemia, or hypomagnesemia

7. There are no significant interacting drugs such as:
   a. Medications that prolong the QT interval such as:
      i. Class 1A antiarrhythmics such as quinidine, procainamide, other
      ii. Class 3 antiarrhythmics such as amiodarone, sotalol, other
      iii. Antipsychotics such as ziprasidone, chlorpromazine, thioridazine, other
      iv. Antibiotics such as gatifloxacin, moxifloxacin, other
   b. Strong or moderate CYP3A4 inducers (such as, carbamazepine, St. John's wort, phenytoin, rifampin, modafinil, thioridazine, efavirenz, nafcillin, other)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Nuplazid (pimavanserin tartrate) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy):**

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist or Psychiatrist

2. Individual's condition has responded while on therapy with response defined as a decrease in hallucinations or delusions

3. Individual has been adherent with the medication

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any significant adverse drug effects that may exclude continued use such as QT Interval prolongation

6. There are no significant interacting drugs such as:
    a. Medications that prolong the QT interval such as:
        i. Class 1A antiarrhythmics such as quinidine, procainamide, other
        ii. Class 3 antiarrhythmics such as amiodarone, sotalol, other
        iii. Antipsychotics such as ziprasidone, chlorpromazine, thioridazine, other
        iv. Antibiotics such as gatifloxacin, moxifloxacin, other

    b. Strong or moderate CYP3A4 inducers (such as, carbamazepine, St. John's wort, phenytoin, rifampin, modafinil, thioridazine, efavirenz, nafcillin)

7. Individual does not have dementia-related psychosis unrelated to the hallucinations and delusions associated with Parkinson's disease

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Nuplazid (pimavanserin tartrate) is an atypical antipsychotic indicated for the treatment of hallucinations and delusions associated with Parkinson's disease (PD) psychosis. It is not approved for the treatment of patients with dementia-related psychosis unrelated to the hallucinations and delusions associated with Parkinson's disease psychosis. Nuplazid (pimavanserin tartrate) package label includes a Boxed Warning regarding elderly patients treated with antipsychotic drugs and an increased risk of death. Nuplazid (pimavanserin tartrate) mechanism of action is unclear, but the effect may be mediated through a combination of inverse agonist and antagonist activity at serotonin 5-HT_{2A} receptors and to a lesser extent at serotonin 5-HT_{2C} receptors.

Parkinson's disease (PD) is a progressive neurodegenerative disease with the primary motor features of tremor, bradykinesia, and rigidity. The treatment primarily resolves around enhancing effects of dopamine or inhibiting the effects of acetylcholine. However, almost all individuals with PD also report non-motor manifestations. Nonmotor symptoms include cognitive dysfunction and dementia, psychosis and hallucinations, mood disorders, sleep disturbances, fatigue, and autonomic dysfunction. The treatment of non-motor symptoms is targeted at each individual symptom.

Psychosis is a frequent non-motor symptom and may affect up to 40% of individuals with PD, particularly those with advanced stages. The most important cause of psychosis in PD is antiparkinsonian medications, in particular, dopamine agonists. Underlying dementia also predisposes patients to hallucinations and delusions. Psychosis is primarily characterized as visual hallucinations and delusions, but auditory, olfactory, and tactile hallucinations can also occur. Psychosis is associated with increased caregiver burden and is the greatest risk factor for nursing home patients with PD.

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The management of psychosis in PD involves both treating contributing causes such as infections and decreasing medications when able. While it is not possible to stop all antiparkinsonian drugs, reducing or stopping some may balance benefit while reducing harm. For hallucinations and delusions refractory to dose reductions, antipsychotic medications may be necessary. Quetiapine, clozapine and pimavanserin have been studied for PD associated psychosis. Clozapine is largely effective but the need for laboratory monitoring and hematologic risks limits its use.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Resources:

Nuplazid (pimavanserin) capsule and tablet product information, revised by Acadia Pharmaceuticals Inc. 09-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 11, 2024.

Rodnitzky RL. Cognitive impairment and dementia in Parkinson disease. In: UpToDate, DeKosky ST, Wilterdink JL (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through June 2024. Topic last updated November 02, 2022. Accessed July 11, 2024.

Chahine L. Management of nonmotor symptoms in Parkinson disease. In: UpToDate, Hurtig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through June 2024. Topic last updated May 23, 2024. Accessed July 11, 2024.

Chou KL. Clinical manifestations of Parkinson disease. In: UpToDate, Hutig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through June 2024. Topic last updated March 14, 2024. Accessed July 11, 2024.

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