

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/or 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.
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Medical Necessity Requirements for **NUPLAZID** (pimavanserin tartrate)

Criteria for Initial Therapy:

Prescriber Qualifications

- Prescribed by a Neurologist or Psychiatrist, or in consultation with a Neurologist or Psychiatrist

Indication

- Diagnosis of hallucinations and delusions associated with Parkinson disease psychosis

Age Requirement

- 18 years or older

ORIGINAL EFFECTIVE DATE: 08/19/2021 | ARCHIVE DATE: | LAST REVIEW DATE: 08/21/2025 | LAST CRITERIA REVISION DATE: 08/15/2024

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Baseline Clinical Evaluation

- **ALL** of the following:
 - Hallucinations or delusions have been present for at least one month
 - Hallucinations or delusions occur at least once weekly
 - Symptoms are severe and frequent enough to require antipsychotic treatment
 - Psychosis symptoms developed after Parkinson disease diagnosis

Alternative Therapies

- Failure (trial for at least three months duration), contraindication, intolerance to **ONE** of the following:
 - Quetiapine
 - Clozapine

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the U.S. Food and Drug Administration (FDA) (see Definitions section)

Safety

- **NONE** of the following:
 - Dementia related psychosis unrelated to Parkinson disease
 - QT interval prolongation
 - History of cardiac arrhythmias, symptomatic bradycardia, hypokalemia, or hypomagnesemia
- No concomitant use of significant interacting drugs such as:
 - Medications that prolong QT interval:
 1. Class 1A antiarrhythmics (e.g., quinidine, procainamide)
 2. Class 3 antiarrhythmics (e.g., amiodarone, sotalol)
 3. Antipsychotics (e.g., ziprasidone, chlorpromazine, thioridazine)
 4. Antibiotics (e.g., gatifloxacin, moxifloxacin)
 - Strong or moderate CYP3A4 inducers (e.g., carbamazepine, St. John's wort, phenytoin, rifampin, modafinil, thioridazine, efavirenz, nafcillin, etc.)

Documentation Requirements

- A completed request form must be submitted, including:
 - Chart notes
 - Lab results
 - Supporting clinical documentation

Initial Therapy Criteria Approval Duration:

- 6 months OR end of plan year

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Criteria for Continuation of Therapy (renewal therapy)

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications

- Continues to be seen by a Neurologist or Psychiatrist, or is in consultation with a Neurologist or Psychiatrist

Clinical Response

- Positive clinical response documented as a decrease in hallucinations or delusions

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- Does **NOT** have dementia related psychosis unrelated to Parkinson disease
- No concomitant use of significant interacting drugs such as:
 - Medications that prolong QT interval:
 1. Class 1A antiarrhythmics (e.g., quinidine, procainamide)
 2. Class 3 antiarrhythmics (e.g., amiodarone, sotalol)
 3. Antipsychotics (e.g., ziprasidone, chlorpromazine, thioridazine)
 4. Antibiotics (e.g., gatifloxacin, moxifloxacin)
 - Strong or moderate CYP3A4 inducers (e.g., carbamazepine, St. John's wort, phenytoin, rifampin, modafinil, thioridazine, efavirenz, nafcillin, etc.)

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

Continuation Therapy Criteria Approval Duration:

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

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:

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

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. 01-2025. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed May 01, 2025.



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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 May 2025. Topic last updated May 23, 2024. Accessed June 16, 2025.

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 May 2025. Topic last updated May 22, 2025. Accessed June 16, 2025.

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