Original Effective Date: 05/13/2018
Current Effective Date: 06/28/2025
Last P&T Approval/Version: 04/30/2025
Next Review Due By: 04/2026
Policy Number: C12066-A

Nuplazid (pimavanserin)

PRODUCTS AFFECTED

Nuplazid (pimavanserin)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Hallucinations and/or delusions associated with Parkinson's disease

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. PARKINSON'S DISEASE HALLUCINATIONS:
1. Documented diagnosis of Parkinson's disease psychosis (defined by illusions, a false sense of presence, hallucinations, or delusions).

AND

2. Prescribing physician has attempted to adjust Parkinson's disease medications in order to reduce psychosis without worsening motor symptoms PRIOR to requesting Nuplazid
AND
3. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Nuplazid (pimavanserin) include: Known hypersensitivity to Nuplazid or any of its components, avoid concomitant use of Strong or Moderate CYP3A4 Inducers, avoid use with drugs that also increase the QT interval, avoid in patients with risk factors for prolonged QT interval.]

CONTINUATION OF THERAPY:

A. PARKINSON'S DISEASE HALLUCINATIONS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms

DURATION OF APPROVAL:

Initial authorization: 12 months Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified neurologist or psychiatrist [If prescribed in consultation, consultation notes must be submitted within initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

Maximum 34 mg/day

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral

DRUG CLASS:

Antipsychotics – Misc

FDA-APPROVED USES:
Indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Psychosis is a frequent complication of Parkinson's Disease (PD). It is characterized by visual hallucinations and delusions, which are often paranoid in content. Hallucinations are the most common manifestation, affecting up to 40% of patients with PD, particularly those at an advanced stage of illness.
The adverse effects of antiparkinson medications, the dopamine agonists in particular, are probably the most important cause of psychosis in patients with PD. Psychosis may also be triggered by infection, delirium, dementia, or medications. Underlying dementia predisposes to hallucinations and delusions, and psychosis is a risk factor for nursing home placement and mortality. Management of psychosis in patients with PD involves identifying and treating the underlying causes and contributing factors, including general measures similar to the treatment of delirium. Psychosis can be triggered by systemic conditions such as infection (e.g., pneumonia or urinary tract infection), which should be managed, if found Anticholinergics can contribute to confusion and exacerbate psychosis in PD. Psychoactive medications, including sedatives, anxiolytics, and antidepressants, are potential causes and should be reduced or stopped if possible. If the trigger is the antiparkinsonian medication, stopping all potential offenders is usually not an option, although dose reduction may positively impact psychosis with little loss of efficacy.

Pimavanserin is a second-generation antipsychotic drug that acts as a selective serotonin 5-HT2A receptor inverse agonist. Efficacy and safety of Nuplazid was established in a six week, randomized, placebo-controlled trial of 199 patients with PD-related psychosis. Compared with placebo, pimavanserin at 40 mg daily led to a 3-point greater reduction in scores on a 45-point PD-adapted scale for assessment of positive symptoms (PD-SAPS) from baseline to day 43. Treatment was not associated with worsening of motor symptoms. More patients discontinued therapy due to an adverse effect in the pimavanserin group (10 versus 2 patients), but the rate and type of individual adverse effects were otherwise balanced between treatment groups. The most common side effects are peripheral edema, nausea, and constipation. Rare but serious adverse effects include syncope, hypotension, and bradycardia. Like other antipsychotic drugs, pimavanserin is associated with QT prolongation.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Nuplazid (pimavanserin) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Nuplazid (pimavanserin) include: Known hypersensitivity to Nuplazid or any of its components, avoid concomitant use of Strong or Moderate CYP3A4 Inducers, avoid use with drugs that increase the QT interval and in patients with risk factors for prolonged QT interval.

Exclusions/Discontinuation:
Underlying conditions that may contribute to hallucinations and/or delusions should be ruled out (other conditions may include, but are not limited to, another mental disorder or physiological effects of a substance).

OTHER SPECIAL CONSIDERATIONS:
Nuplazid (pimavanserin) has a black box warning for increased mortality in elderly patients with dementia-related psychosis. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Nuplazid (pimavanserin) is not approved for the treatment of

patients with dementia who experience psychosis unless their hallucinations and delusions are related to Parkinson's disease.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Nuplazid CAPS 34MG
Nuplazid TABS 10MG

REFERENCES

1. Nuplazid (pimavanserin) capsules, for oral use; tablets, for oral use [prescribing information]. San Diego, CA: Acadia Pharmaceuticals Inc; January 2025.
2. Miyasaki JM, Shannon K, Voon V, et al. 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. Neurology. 2006;66(7):996-1002.Available at: http://www.neurology.org/content/66/7/996.full.pdf+html.
3. Goldman JG, Holden S. Treatment of psychosis and dementia in Parkinson's disease. CurrTreat Options Neurol. 2014; 16(3):281.
4. Seppi K, Weintraub D, Coelho M, et al. The Movement Disorder Society evidence-based medicine review update: treatments for the non-motor symptoms of Parkinson's disease. Mov Disord.2011;26(Suppl 3):S42-S80.
5. Seppi K, Chahine L, Chaudhuri RK, et al. (2019). Update on treatments for nonmotor symptoms of Parkinson's disease—an evidence-based medicine review. Movement Disorders, 34(2), 180–198. https://doi.org/10.1002/mds.27602

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION-Notable revisions: Required Medical Information Duration of Approval Background Contraindications/Exclusions/Discontinuation References	Q2 2025

REVISION-Notable revisions: Required Medical Information Contraindications/Exclusions/ Discontinuation References	Q2 2024
REVISION-Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q2 2023
REVISION-Notable revisions: Duration of Approval Prescriber Requirements Available Dosage Forms References	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file