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Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	June 10, 2016
Subject:	Nuplazid	**Page:**	1 of 5

Last Review Date: March 7, 2025

Nuplazid

Description

Nuplazid (pimavanserin)

Background
Nuplazid is an atypical antipsychotic used in patients with psychosis due to Parkinson's disease. Parkinson's disease is a neurodegenerative brain disorder where cell death causes a reduction in the amount of dopamine being secreted. This may result in a variety of effects including motor problems as well as neuropsychiatric symptoms (1).

Regulatory Status
FDA-approved indications: Nuplazid is indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis (2).

Nuplazid has a boxed warning that 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 (2).

Nuplazid is not recommended in patients with hepatic impairment or severe renal impairment (CrCL ≥ 30 mL/min Cockcroft-Gault). Nuplazid has not been evaluated in these patient populations (2).

For patients with hallucinations or delusions despite antiparkinsonian medication adjustments, first-line options for treatment are quetiapine and clozapine (3).

Safety and effectiveness of Nuplazid in pediatric patients under 18 years of age have not been established (2).

Related policies
Inbrija, Nourianz, Tasmar

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Nuplazid may be considered **medically necessary** if the conditions indicated below are met.

Nuplazid may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Hallucinations and/or delusions associated with Parkinson's disease psychosis

AND ALL of the following:

1. Inadequate treatment response, intolerance, or contraindication to quetiapine
2. Presence of hallucinations or delusions (which may include illusions or a false sense of presence) on a recurrent or continuous basis for at least 1 month
3. Prescribing physician has attempted to adjust Parkinson's disease medications in order to reduce psychosis without worsening motor symptoms prior to requesting Nuplazid
4. Used in combination with another Parkinson's disease medication
5. **NOT** to be used to treat psychiatric symptoms attributed to Alzheimer's disease, schizophrenia, schizoaffective disorder or delusional disorder
6. Prescriber agrees to monitor for QTc prolongation

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Hallucinations and/or delusions associated with Parkinson's disease psychosis

AND ALL of the following:

1. Patient has been assessed since the last Prior Authorization (PA) and has improvement in the frequency/severity of symptoms in comparison to baseline
2. Used in combination with another Parkinson's disease medication
3. **NOT** to be used to treat psychiatric symptoms attributed to Alzheimer's disease, schizophrenia, schizoaffective disorder or delusional disorder
4. Prescriber agrees to continue to monitor for QTc prolongation

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Medication	Quantity Limit
10 mg	90 tablets per 90 days **OR**
34 mg	90 capsules per 90 days

Duration 6 months

Prior – Approval *Renewal* Limits

Quantity

Medication	Quantity Limit

10 mg	90 tablets per 90 days **OR**
34 mg	90 capsules per 90 days

Duration 12 months

Rationale

Summary

Nuplazid is an atypical antipsychotic used in patients with psychosis due to Parkinson's disease. Parkinson's disease is a neurodegenerative brain disorder where cell death causes a reduction in the amount of dopamine being secreted. This may result in a variety of effects including motor problems as well as neuropsychiatric symptoms. Psychosis such as hallucinations or delusions may be the result of excessive dopamine from Parkinson's disease medications. Safety and effectiveness of Nuplazid in pediatric patients under 18 years of age has not been established (1-2).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Nuplazid while maintaining optimal therapeutic outcomes.

References

1. National Parkinson Foundation. Understanding Parkinson's: Non-Movement Symptoms. Retrieved from: https://www.parkinson.org/Understanding-Parkinsons/Non-Movement-Symptoms.
2. Nuplazid [package Insert]. San Diego, CA: ACADIA Pharmaceuticals Inc.; September 2023.
3. UpToDate. Waltham, MA: Wolters Kluwer Health; 2019. https://www.uptodate.com/home.

Policy History

Date	Action
May 2016	Addition to PA
September 2016	Annual review Removal of Mini-Mental State Examination (MMSE) score ≥ 21 per SME Addition of used in combination with another Parkinson's disease medication, not to be used to treat Alzheimer's dementia, and patient must be assessed for QTc prolongation per SME Policy number changed from 5.59.03 to 5.60.03
December 2016	Annual review
December 2017	Annual editorial review and reference update

May 2018	Added to Managed PA Addition of the following requirements: inadequate treatment response, intolerance, or contraindication to clozapine OR quetiapine; the presence of hallucinations or delusions (which may include illusions or a false sense of presence) on a recurrent or continuous basis for at least 1 month; not to be used to treat psychiatric symptoms attributed to schizophrenia, schizoaffective disorder or delusional disorder
June 2018	Annual review
August 2018	Addition of strengths 10mg and 34mg to criteria. Revised quantity limits on 17mg
September 2018	Annual review
January 2019	Removal of Nuplazid 17 mg tablets
March 2019	Annual review and reference update. Revised QTc monitoring requirement for continuation of therapy
April 2019	Removed trial option of clozapine for initiation of therapy
June 2019	Annual review and reference update
December 2019	Annual review and reference update
January 2020	Revised QTc prolongation monitoring requirement for initiation of therapy. Changed approval durations for initiation to 6 months and renewal to 12 months
March 2020	Annual review and reference update
September 2021	Annual review and reference update
September 2022	Annual review. Revised continuation requirement for clarity: “patient has been assessed since the last PA and has improvement in the frequency/severity of symptoms in comparison to baseline”
September 2023	Annual review
December 2023	Annual review and reference update
January 2024	Per FEP, removed from Managed PA
March 2024	Annual review
December 2024	Annual review
March 2025	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.