09-J2000-66

Original Effective Date: 09/15/16

Reviewed: 11/09/22

Revised: 12/15/22

Subject: Pimavanserin (Nuplazid®)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

The Food and Drug Administration (FDA) approved pimavanserin (Nuplazid®) in April 2016 for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis (PDP). Pimavanserin (Nuplazid®) is an atypical antipsychotic that works as an inverse agonist and antagonist at serotonin 5-HT2A receptors and to a lesser extent at serotonin 5-HT2C receptors. Pimavanserin has no binding affinity for dopamine receptors.

Pimavanserin was evaluated in a 6-week randomized, placebo-controlled study. Study participants were aged 40 years or older and had a diagnosis of Parkinson's disease (PD) established at least 1 year prior to study entry. The participants were on stable PD medications and were required to have a Mini-Mental State Examination (MMSE) score greater than or equal to 21. Participants had severe psychotic symptoms (hallucinations and/or delusions) severe enough to warrant treatment that began after diagnosis of PD. The primary efficacy endpoint of the study was assessed using the Scale for the Assessment of Positive Symptoms adapted for PD (SAPS-PD). Pimavanserin significantly reduced the frequency and/or severity of hallucinations and delusions as compared to placebo in participants with PDP (difference -3.06, p=0.001). Pimavanserin did not show an effect on motor function.

POSITION STATEMENT:

Initiation of pimavanserin (Nuplazid) **meets the definition of medical necessity** when **ALL** of the following are met:

1. Member has a diagnosis of Parkinson's disease
2. Use is for the treatment of hallucinations or delusions associated with Parkinson's disease psychosis

3. Symptoms of psychosis (hallucinations or delusions) have been present for at least one month and developed after the diagnosis of Parkinson's disease
4. Other causes of psychosis have been ruled out (e.g., infection, electrolyte disturbances)
5. The member is not receiving treatment with an additional antipsychotic
6. Dose does not exceed **ONE** of the following:
    a. Capsules: 34 mg daily using the fewest number of capsules per day
    b. Tablets: 10 mg daily using the fewest number of tablets per day

Approval duration: 6 months

Continuation of pimavanserin (Nuplazid) **meets the definition of medical necessity** when **ALL** of the following are met:

1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years, **OR** the member has previously met all indication-specific criteria
2. Use is for the treatment of hallucinations or delusions associated with Parkinson's disease psychosis
3. Member has demonstrated a beneficial response to therapy (e.g., improvement in hallucinations or delusions)
4. The member is not receiving treatment with an additional antipsychotic
5. Dose does not exceed **ONE** of the following:
    a. Capsules: 34 mg daily using the fewest number of capsules per day
    b. Tablets: 10 mg daily using the fewest number of tablets per day

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

Pimavanserin is indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis. The recommended dose is 34 mg, taken orally once daily, without titration, and can be taken with or without food. The capsules can be taken whole, or opened and the entire contents sprinkled over a tablespoon (15 mL) of applesauce, yogurt, pudding, or liquid nutritional supplement.

Dose Adjustments

Severe renal impairment: Pimavanserin should be used with caution in patients with severe renal impairment (CrCl < 30 ml/min) and end stage renal disease.

Strong CYP3A4 Inhibitors (e.g., ketoconazole, clarithromycin, itraconazole): Reduce dose to 10 mg once daily.

Strong or moderate CYP3A4 Inducers (e.g., rifampin, carbamazepine, phenytoin): Avoid use.

Drug Availability

- 34 mg capsules
- 10 mg tablets

PRECAUTIONS:

Boxed Warning

- **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. Pimavanserin is not approved for the treatment of patients with dementia –related psychosis unrelated to the hallucinations and delusions associated with Parkinson's disease psychosis.

Contraindications

- Known hypersensitivity to pimavanserin or any of its components.

Precautions/Warnings

- **QT Interval Prolongation:** Increases in QT interval; avoid use with drugs that also increase the QT interval and in patients with risk factors for prolonged QT interval.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not otherwise specified

ICD-10 Diagnoses Codes That Support Medical Necessity

G20	Parkinson's disease

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the guideline creation.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. AHFS Drug Information. Bethesda (MD): American Society of Health-System Pharmacists, Inc; 2016 [cited 2016-07-25]. In: STAT!Ref Online Electronic Medical Library [Internet]. Available from: http://online.statref.com/.
2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2022 [cited 2022-Oct-24]. Available from: http://www.clinicalpharmacology.com/.
3. Cummings J, Isaacson S, Mills R et al. Pimavanserin for patients with Parkinson's disease psychosis: a randomized, placebo-controlled phase 3 trial. *Lancet* 2014; 383: 533-40.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2022-Oct-24]. Available from: www.micromedexsolutions.com/
5. Nuplazid® (pimavanserin) [package insert]. Acadia Pharmaceuticals Inc. San Diego, CA. November 2020.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/09/22.

GUIDELINE UPDATE INFORMATION:

09/15/16	New Medical Coverage Guideline.
09/15/17	Review and revision to guideline; including updating references.
07/15/18	Review and revision to guideline; consisting of updating position statement and references.
10/15/19	Review and revision to guideline; consisting of updating position statement dosing and references.
10/15/20	Review and revision to references.
12/15/22	Review and revision to guideline; consisting of updating dosing and references.