ONCE-DAILY
NUPLAZID®
(pimavanserin) 34mg capsules

Recognizing and Managing Parkinson's Disease Psychosis in Long-Term Care Facilities

Indication
NUPLAZID is indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis.

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.
- 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.

See additional Important Safety Information including **Boxed WARNING** on last page. Please read the full Prescribing Information.

During the course of their disease, around 50% of people with Parkinson's may experience hallucinations or delusions.[1]

Parkinson's disease (PD), a neurodegenerative disorder with associated motor disturbances, has a multifaceted clinical presentation.[2] One aspect of PD—PD psychosis—can be overshadowed by more visible motor symptoms and may go unrecognized and underreported.[3-5] Importantly, PD psychosis should be considered when a patient who previously has been diagnosed with PD has experienced recurrent or continuous delusions or hallucinations for 1 month that cannot be attributed to another cause.[6]

Important symptoms of PD psychosis[6,7]:

DELUSIONS

- Firmly held false beliefs (e.g., believing that a spouse is being unfaithful)

HALLUCINATIONS

- Perceiving something that others don't
- Visual hallucinations are the most common
- Auditory, tactile, and olfactory hallucinations may occur in combination with the visual hallucination, or more rarely, in isolation

ILLUSIONS

- Misidentification of actual stimuli, for example, believing that a belt is actually a snake

FALSE SENSE OF PRESENCE

- Experience that someone is present when nobody is actually there

Prior to initiating NUPLAZID® (pimavanserin) 34 mg, the resident's symptoms must be clearly identified and documented.[8]

Document a diagnosis of PD psychosis

- Section I of the Minimum Data Set (MDS) captures a resident's active diagnoses[9]
- Coding must be to the highest level of specificity and all coding decisions are ultimately the responsibility of each prescribing health care professional
- ICD-10-CM coding combinations that are recognized for PD psychosis include diagnosis code G20 (PD) plus one of the following[10]:
  - **F06.0**—Psychotic disorder with hallucinations due to known physiological condition
  - **F06.2**—Psychotic disorder with delusions due to known physiological condition

Monitor and document the resident's PD psychosis symptoms and response to therapy

- Section E0100 of the MDS also provides a place to document the presence of delusions and hallucinations[9]

Per Centers for Medicare & Medicaid Services (CMS) guidelines, gradual dose reduction (GDR) may be clinically contraindicated for psychotropics used to treat enduring and progressive conditions such as PD psychosis.[11]

F758 in the CMS *State Operations Manual* for long-term care facilities outlines the requirements for appropriate use of psychotropic medications in nursing facilities, including patient monitoring, documentation of symptoms, and GDR. CMS specifically notes the following[11]:

- Residents with specific progressive and enduring conditions [such as PD psychosis] may need psychotropic medications indefinitely
- GDR of a psychotropic medication may be clinically contraindicated if continued use is in accordance with relevant current standards and the physician has documented that a GDR is not appropriate

CMS guidelines include PD psychosis in the list of enduring and progressive conditions[11]

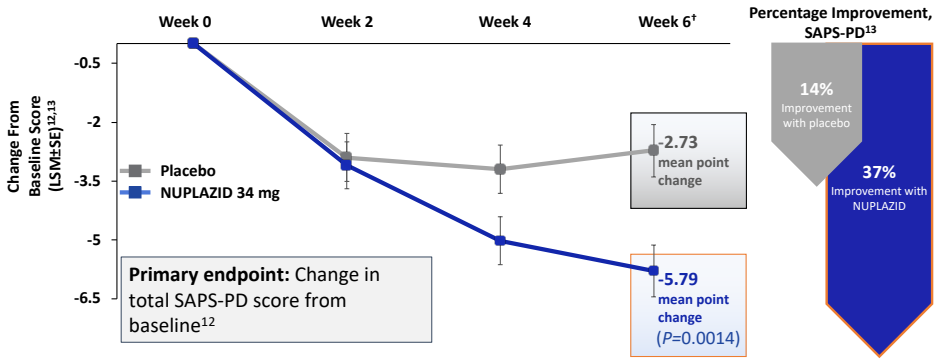
NUPLAZID 34 mg is the only FDA-approved therapy proven to reduce delusions and hallucinations associated with PD psychosis in elderly patients[12]

A GDR may be clinically contraindicated for enduring and progressive conditions[11]

Under these guidelines, treatment for PD psychosis may not require a GDR. Document appropriately. Review the CMS *State Operations Manual* for long-term care facilities for complete information on psychotropic prescribing, monitoring, and documentation in long-term care facilities.[11]

NUPLAZID® (pimavanserin) 34 mg is the first and only FDA-approved therapy proven to reduce the symptoms of delusions and hallucinations associated with PD psychosis.[12]

NUPLAZID 34 mg reduced the frequency and/or severity of PD psychosis, with continued improvement over 6 weeks[12,13*]

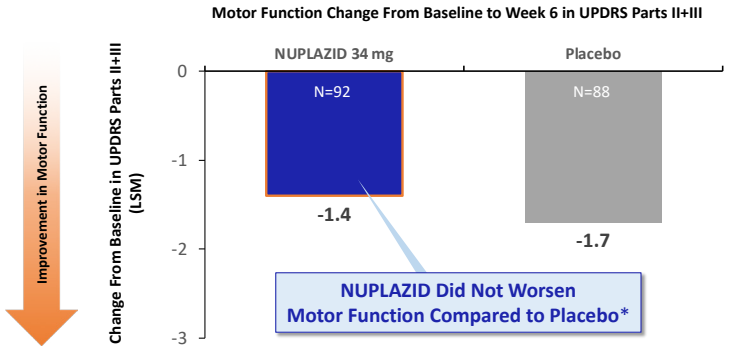


*Mean SAPS-PD baseline score was 15.9 for NUPLAZID and 14.7 for placebo.
†Difference in change at Week 6 between the two arms was 3.06 points.

The mean age was 72.4 years for both the NUPLAZID 34 mg (n=95) and placebo (n=90) groups.[13]

- In a placebo-controlled, randomized, parallel-group study of 185 patients with PD psychosis, NUPLAZID 34 mg (n=95) was statistically superior to placebo (n=90) in decreasing the frequency and/or severity of delusions and hallucinations as measured by central, independent, and blinded raters using the SAPS-PD scale[12]

Secondary endpoint: NUPLAZID 34 mg did not worsen motor function compared to placebo[12,13*]



*PD medications remained stable.

- NUPLAZID 34 mg did not worsen motor function compared to placebo, as measured using the UPDRS Parts II+III; a negative change in score indicates improvement in motor function[12]

FDA, US Food and Drug Administration; LSM, least-squares mean; SAPS-PD, Scale for the Assessment of Positive Symptoms-Parkinson's Disease; SE, standard error; UPDRS, Unified Parkinson's Disease Rating Scale.

Percentage of patients reporting adverse reactions at an incidence of ≥2% and >placebo[12*]

	NUPLAZID 34 mg N=202	Placebo N=231
Nausea	7%	4%
Peripheral edema	7%	2%
Confusional state	6%	3%
Hallucination	5%	3%
Constipation	4%	3%
Gait disturbance	2%	<1%

* Based on 6-week placebo-controlled studies.

- Discontinuation rates due to adverse reactions were low[12*]
  - 8% with NUPLAZID® (pimavanserin) vs 4% with placebo
  - The adverse reactions that occurred in more than one patient and with an incidence at least twice that of placebo were hallucination (2% NUPLAZID vs <1% placebo), urinary tract infection (1% NUPLAZID vs <1% placebo), and fatigue (1% NUPLAZID vs 0% placebo)
- No events of neuroleptic malignant syndrome, tardive dyskinesia, or serotonin syndrome were reported with NUPLAZID 34 mg[14,15*]

Achieve the proven efficacy of NUPLAZID by starting residents on once-daily 34 mg without titration[12]

Dosing and administration considerations[12]:

- For patients taking a strong CYP3A4 inhibitor, reduce the dosage of NUPLAZID to 10 mg once daily
- Avoid concomitant use of strong or moderate CYP3A4 inducers with NUPLAZID
- Avoid the use of NUPLAZID in patients with known QT prolongation or in combination with other drugs known to prolong QT interval
- NUPLAZID does not require a dosage adjustment in elderly patients, in patients with mild to severe renal impairment or end stage renal disease (ESRD), or in patients with hepatic impairment[†]
- No dosage adjustment of carbidopa/levodopa is required when administered concomitantly with NUPLAZID

[†] Increased exposure (C_{max} and AUC) to NUPLAZID occurred in patients with severe renal impairment (CrCl <30 mL/min, Cockcroft-Gault) in a renal impairment study. NUPLAZID should be used with caution in patients with severe renal impairment and ESRD.[12]

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Important Safety Information for NUPLAZID (pimavanserin)

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.**
- **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.**

- **Contraindication:** NUPLAZID is contraindicated in patients with a history of a hypersensitivity reaction to pimavanserin or any of its components. Rash, urticaria, and reactions consistent with angioedema (e.g., tongue swelling, circumoral edema, throat tightness, and dyspnea) have been reported.
- **QT Interval Prolongation:** NUPLAZID prolongs the QT interval.
  - The use of NUPLAZID should be avoided in patients with known QT prolongation or in combination with other drugs known to prolong QT interval including Class 1A antiarrhythmics or Class 3 antiarrhythmics, certain antipsychotic medications, and certain antibiotics.
  - NUPLAZID should also be avoided in patients with a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of torsade de pointes and/or sudden death, including symptomatic bradycardia, hypokalemia or hypomagnesemia, and presence of congenital prolongation of the QT interval.
- **Adverse Reactions:** The most common adverse reactions (≥2% for NUPLAZID and greater than placebo) were peripheral edema (7% vs 2%), nausea (7% vs 4%), confusional state (6% vs 3%), hallucination (5% vs 3%), constipation (4% vs 3%), and gait disturbance (2% vs <1%).
- **Drug Interactions:**
  - Coadministration with strong CYP3A4 inhibitors (e.g., ketoconazole) increases NUPLAZID exposure. Reduce NUPLAZID dose to 10 mg taken orally as one tablet once daily.
  - Coadministration with strong or moderate CYP3A4 inducers reduces NUPLAZID exposure. Avoid concomitant use of strong or moderate CYP3A4 inducers with NUPLAZID.

Please read the accompanying Prescribing Information, also available at NUPLAZIDhcp.com

References: 1. Forsaa EB, Larsen JP, Wentzel-Larsen T, et al. A 12-year population-based study of psychosis in Parkinson disease. *Arch Neurol*. 2010;67(8):996-1001. **2.** Olanow CW, Schapira HV. Parkinson's disease and other movement disorders. In: *Harrison's Principles of Internal Medicine*. 18th ed. New York, NY: The McGraw-Hill Companies; 2012. **3.** Fénelon G, Mahieux F, Huon R, Ziégler M. Hallucinations in Parkinson's disease: prevalence, phenomenology and risk factors. *Brain*. 2000;123(pt 4):733-745. **4.** Holroyd S, Currie L, Wooten GF. Prospective study of hallucinations and delusions in Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 2001;70(6):734-738. **5.** Chaudhuri KR, Prieto-Jurcynska C, Naidu Y, et al. The nondeclaration of nonmotor symptoms of Parkinson's disease to health care professionals: an international study using the nonmotor symptoms questionnaire. *Mov Disord*. 2010;25(6):704-709. **6.** Ravina B, Marder K, Fernandez HH, et al. Diagnostic criteria for psychosis in Parkinson's disease: report of an NINDS, NIMH work group. *Mov Disord*. 2007;22(8):1061-1068. **7.** Fenelon G, Soulas T, Zenasni F, Cleret de Langavant L. The changing face of Parkinson's disease-associated psychosis: a cross-sectional study based on the new NINDS-NIMH criteria. *Mov Disord*. 2010;25(6):763-766. **8.** Centers for Medicare & Medicaid Services. Long-Term Care Facility Resident Assessment Instrument 3.0 User's Manual. Version 1.13. https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/NursingHomeQualityInits/Downloads/MDS-30-RAI-Manual-V113.pdf. Published October 2015. Accessed September 26, 2018. **9.** Centers for Medicare & Medicaid Services. Minimum Data Set (MDS) 3.0 RAI Manual. Download 4: MDS Forms (Item Sets). https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/NursinghomeQualityInits/MDS30RAIManual.html. Updated October 1, 2015. Accessed September 26, 2018. **10.** World Health Organization. International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10)-2015-WHO Online Version for 2015. WHO website. http://apps.who.int/classifications/icd10/browse/2015/en. Accessed September 26, 2018. **11.** Centers for Medicare & Medicaid Services. State Operations Manual Pub. 100-07. Appendix PP – Guidance to Surveyors for Long Term Care Facilities. Baltimore, MD: US Dept of Health and Human Services; 2018. **12.** ACADIA Pharmaceuticals Inc. NUPLAZID® [package insert]. San Diego, CA; 2019. **13.** Cummings J, Isaacson S, Mills R, et al. Pimavanserin for patients with Parkinson's disease psychosis: a randomised, placebo-controlled phase 3 trial. *Lancet*. 2014;383(9916):533-540. **14.** Data on File, ACADIA Pharmaceuticals Inc. **15.** ACADIA Pharmaceuticals Inc. NUPLAZID Advisory Committee Briefing Document. San Diego, CA: Sponsor Background Information for a Meeting of the Psychopharmacologic Drugs Advisory Committee; March 29, 2016. https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/DrugsPsychopharmacologicDrugsAdvisoryCommittee/UCM492453.pdf. Accessed September 26, 2018.

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