How you choose to treat Parkinson's disease (PD) psychosis matters

NUPLAZID® CAN MAKE A DIFFERENCE

The first and only treatment approved for hallucinations and delusions associated with PD psychosis.[1]

ONCE-DAILY
NUPLAZID®
(pimavanserin) 34mg capsules

Indication

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

Important Safety Information

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

See additional Important Safety Information located throughout. Please read the full **Prescribing Information**, including **Boxed WARNING**, available at **NUPLAZIDhcp.com**.

ACADIA®

Effects of antipsychotics may be a product of their individual actions at multiple receptor sites

Selected potential side effects of antipsychotics[2,3]

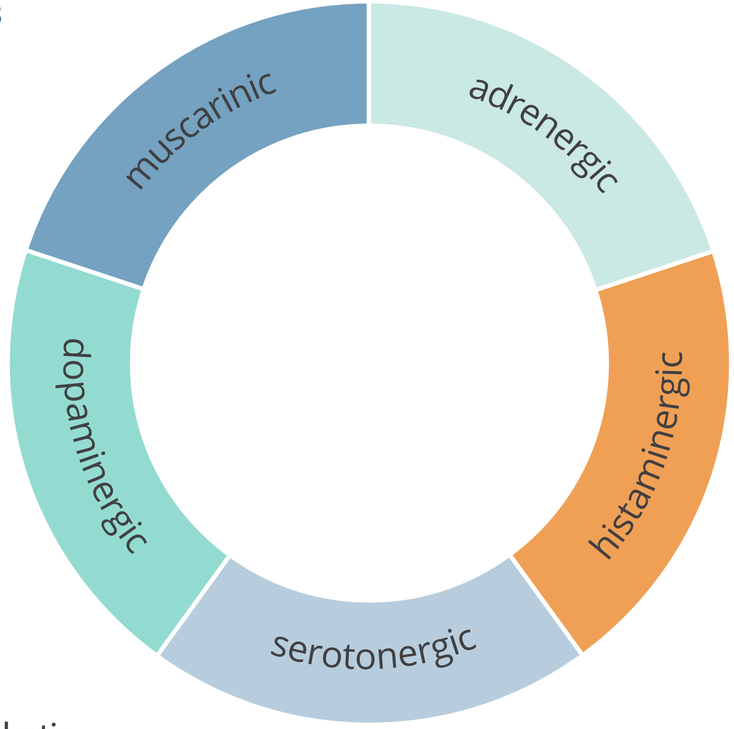
Muscarinic:
cognitive blunting,
dry mouth,
constipation,
urinary retention,
blurred vision

Alpha adrenergic:
orthostatic hypotension,
drowsiness,
dizziness,
syncope

Histaminergic:
sedation,
weight gain

Serotonergic:
increased appetite,
weight gain

Dopaminergic:
extrapyramidal symptoms,
tardive dyskinesia,
prolactin elevation



Receptor affinities and binding effects may vary by dosage of any given antipsychotic.

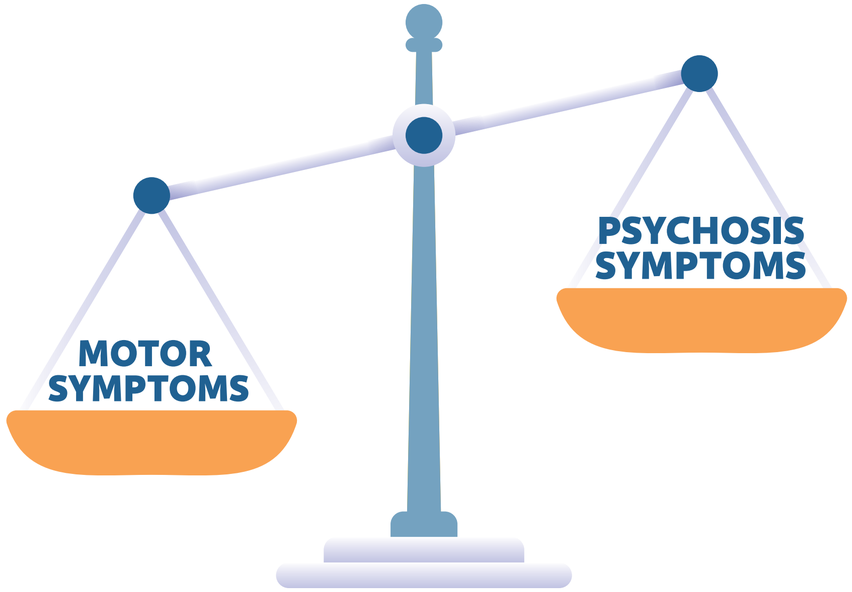
Note: The clinical relevance of this information is unknown, and it is not intended to make safety comparisons between antipsychotics based on the receptor activity. Please review the full Prescribing Information for list of all side effects associated with the use of antipsychotics.

ACADIA

Unwinding the therapeutic bind in Parkinson's disease psychosis

When treating Parkinson's disease (PD) motor symptoms, dopaminergic medications can create a therapeutic bind when a patient has PD psychosis[4,5]

- Attempting to manage psychosis in patients with PD by decreasing dopamine replacement therapy can exacerbate motor symptoms and may not be effective
- As PD progresses and motor symptoms become harder to manage, dopaminergic PD medications are often increased, which could exacerbate psychosis

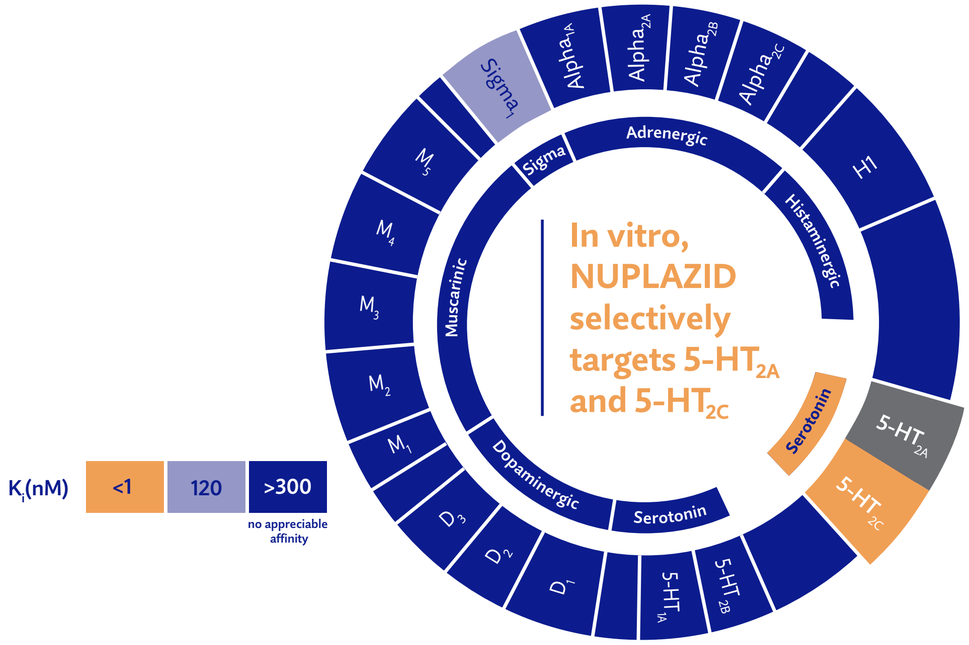


Antipsychotics with greater D_2 blockade may worsen motor symptoms in patients with PD

PREVIOUS | NEXT

ACADIA

NUPLAZID® is designed to selectively target key serotonin receptors[6]



- The effect of NUPLAZID could be mediated through a combination of inverse agonist and antagonist activity at 5-HT$_{2A}$ receptors and, to a lesser extent, at 5-HT$_{2C}$ receptors*
- NUPLAZID has no appreciable affinity† for dopaminergic, histaminergic, muscarinic, or adrenergic receptors
- The precise mechanism of action of NUPLAZID in the treatment of hallucinations and delusions associated with Parkinson's disease psychosis is unclear

*Serotonin 5-HT$_{2A}$ receptors: Ki value 0.087 nM; serotonin 5-HT$_{2C}$ receptors: Ki value 0.44 nM.[6] Lower Ki numbers indicate a greater binding affinity, and thus, a smaller amount of the drug is needed to block activity.[7]

†Ki value >300 nM.[6]

PREVIOUS | NEXT

Indication

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

Important Safety Information

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

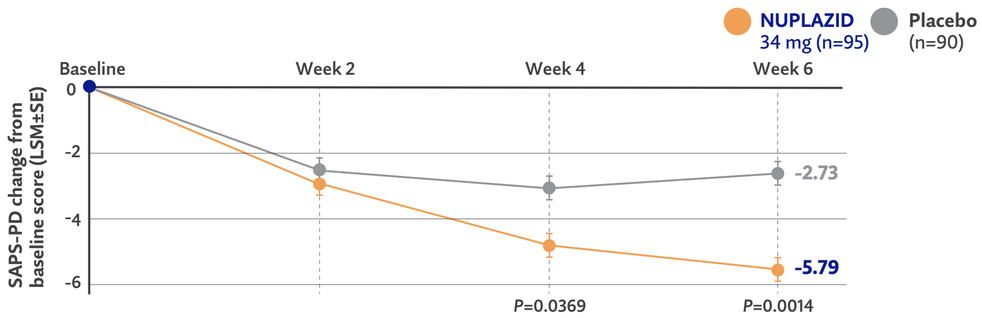
- **Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.**
- **NUPLAZID is not approved for the treatment of patients with dementia who experience psychosis unless their hallucinations and delusions are related to Parkinson's disease.**

See additional Important Safety Information located throughout. Please read the full **Prescribing Information**, including **Boxed WARNING**, available at **NUPLAZIDhcp.com**.

ONCE-DAILY NUPLAZID® (pimavanserin) 34mg capsules

NUPLAZID® significantly reduced the frequency and/or severity of hallucinations and delusions associated with Parkinson's disease (PD) psychosis[6]

SAPS-PD CHANGE FROM BASELINE THROUGH WEEK 6 vs PLACEBO (PRIMARY ENDPOINT)[6,8]



NUPLAZID worked without impacting motor function or activities of daily living vs placebo at Week 6 (key secondary endpoint)[6,8]

The mean change from baseline was -1.4 for NUPLAZID (n=92) and -1.7 for placebo (n=88) as measured by the UPDRS Parts II+III.† The placebo-subtracted difference was 0.3 [95% CI: -2.1, 2.7]).[6,8‡§]

*SAPS-PD is a 9-item scale derived from SAPS that evaluates hallucinations and delusions in patients with PD psychosis. Each item is scored on a scale of 0 (none) to 5 (severe and frequent symptoms), for a maximum score of 45.[6,9]

†The mean UPDRS II+III baseline score in the secondary endpoint was 51.5 for NUPLAZID and 52.6 for placebo.[8]

‡Difference (drug minus placebo) in LSM.[6]

§Noninferiority criteria required that the upper bound of the 95% CI not exceed 5.[8]

CI=confidence interval; **LSM**=least squares mean; **SAPS-PD**=Scale for the Assessment of Positive Symptoms adapted for Parkinson's disease; **SD**=standard deviation; **SE**=standard error; **UPDRS II+III**=Unified Parkinson's Disease Rating Scale Parts II and III.

NUPLAZID has been studied in patients with Parkinson's disease (PD)–related hallucinations and/or delusions with or without dementia[6]

Study design

A Phase 3, randomized, double-blind, placebo-controlled, parallel-group study of patients with hallucinations and delusions associated with PD psychosis (N=199).[6] Primary efficacy was evaluated based on change from baseline to Week 6 in the 9-item SAPS-PD total score.[6,8]* The mean age of patients enrolled in the clinical study with NUPLAZID was 72 years and patients had MMSE scores ≥21.[8] At screening, 20% of patients (40/198) had a history of dementia per medical history, and 37% of patients (69/185) were taking anti-dementia medications at baseline.[10,11] The mean (SD) SAPS-PD baseline score was 15.9 (6.12) for NUPLAZID and 14.7 (5.55) for placebo.[6,8] The majority of patients were on PD medications at entry; these medications were required to be stable for at least 30 days prior to study start and throughout the study.[6]

Study results

The LSM change from baseline (SE) for NUPLAZID was -5.79 (0.66) and -2.73 (0.67) for placebo; placebo-subtracted difference (drug minus placebo) for NUPLAZID was -3.06 (95% CI: -4.91, -1.20).[6,8]

Important Safety Information (cont'd)

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.

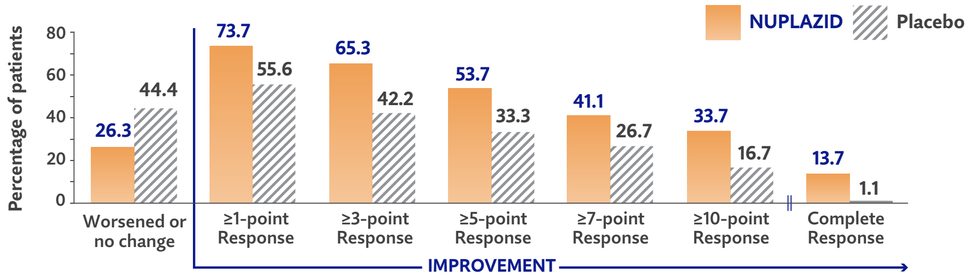
See additional Important Safety Information located throughout. Please read the full **Prescribing Information**, including **Boxed WARNING**, available at **NUPLAZIDhcp.com**.

PREVIOUS | NEXT

Real improvement for the majority of your PD psychosis patients

About 65% of NUPLAZID®-treated patients experienced a clinically meaningful ≥3-point response vs 42.2% for placebo[6]*

PROPORTION OF PATIENTS (RESPONDERS) WITH SAPS-PD SCORE IMPROVEMENT AT END OF WEEK 6 (N=185)[6]



13.7% of NUPLAZID-treated patients experienced complete resolution of symptoms (SAPS-PD score reduced to 0 from baseline) vs 1.1% for placebo.[6]

26.3% of NUPLAZID-treated patients experienced a worsening of, or no change in their SAPS-PD scores vs 44.4% for placebo.[6]

Note: Complete response=SAPS-PD scores reduced to 0 from baseline value. Patients with missing values were counted as nonresponders.[6]

*Based on regression analysis, a clinically meaningful 1-unit change in the CGI-I scale was associated with a 2.33-point change in SAPS-PD.[9]

SAPS-PD=Scale for the Assessment of Positive Symptoms adapted for Parkinson's disease; CGI-I=Clinical Global Impression-Improvement scale.

The SAPS-PD scale

SAPS-PD is a 9-item scale derived from SAPS that evaluates hallucinations and delusions in patients with PD psychosis.[9] The types of hallucinations measured were auditory, voices conversing, somatic or tactile, and visual as well as a global rating of severity.[9] The types of delusions measured were persecutory, jealousy, and reference, as well as a global rating of severity.[9] Each item is scored on a scale of 0 (none) to 5 (severe and frequent symptoms), for a maximum score of 45.[6] Below is a representation of one item of the full SAPS-PD scale.

EXAMPLE SAPS ITEM: GLOBAL HALLUCINATIONS[12]

Scale	Severity	Patient response
0	None	
1	Questionable	
2	Mild	Hallucinations definitely present, but occur infrequently; at times, the patient may question their existence
3	Moderate	Hallucinations are vivid and occur occasionally; they may bother the patient to some extent
4	Marked	Hallucinations are quite vivid, occur frequently, and pervade the patient's life
5	Severe	Hallucinations are almost daily and are sometimes unusual or bizarre; they are very vivid and extremely troubling

A 2.33-point change in the SAPS-PD is associated with clinically meaningful improvement—equivalent to a 1-point change in CGI-I[9]

PREVIOUS | NEXT

Important Safety Information (cont'd)

Warnings and Precautions: 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 (e.g., Class 1A antiarrhythmics, Class 3 antiarrhythmics, certain antipsychotics or 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.

See additional Important Safety Information located throughout. Please read the full **Prescribing Information**, including **Boxed WARNING**, available at **NUPLAZIDhcp.com**.

ONCE-DAILY NUPLAZID® (pimavanserin) 34mg capsules

Demonstrated safety in patients with Parkinson's disease psychosis[6]

ADVERSE DRUG REACTIONS REPORTED IN ≥2% AND GREATER THAN PLACEBO IN 6-WEEK PLACEBO-CONTROLLED STUDIES[6]

	NUPLAZID® n=202	Placebo n=231
GASTROINTESTINAL DISORDERS		
Nausea	**7%**	**4%**
Constipation	**4%**	**3%**
GENERAL DISORDERS		
Peripheral edema	**7%**	**2%**
Gait disturbance	**2%**	**<1%**
PSYCHIATRIC DISORDERS		
Hallucination	**5%**	**3%**
Confusional state	**6%**	**3%**

Low rates of discontinuation due to adverse reactions[6]

In the 6-week placebo-controlled studies, 8% (n=16) of patients treated with NUPLAZID discontinued due to adverse reactions vs 4% (n=10) with placebo.[6] The adverse reactions that occurred in more than 1 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).[6]

PREVIOUS | NEXT

Important Safety Information (cont'd)

Drug Interactions:

- Coadministration with strong CYP3A4 inhibitors 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.

See additional Important Safety Information located throughout. Please read the full **Prescribing Information**, including **Boxed WARNING**, available at **NUPLAZIDhcp.com**.

Demonstrated safety in patients with Parkinson's disease psychosis[6] (cont'd)

SEDATION-RELATED AND ORTHOSTATIC HYPOTENSION–RELATED EVENTS[13]

	NUPLAZID® n=202	Placebo n=231
Sedation-related events	6.4%	5.2%
Orthostatic hypotension–related events	6.9%	10.4%

- There are no warnings or precautions in the Prescribing Information for sedation or orthostatic hypotension[6]
- Sedation-related events included sedation, somnolence, fatigue, asthenia, lethargy, and hypersomnia[13]
- Orthostatic hypotension–related events included dizziness, hypotension, orthostatic hypotension, orthostatic intolerance, syncope, vertigo positional, postural orthostatic tachycardia syndrome, and vertigo[13]

PREVIOUS | NEXT

Important Safety Information (cont'd)

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

Warnings and Precautions: 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 (e.g., Class 1A antiarrhythmics, Class 3 antiarrhythmics, certain antipsychotics or 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.

Drug Interactions:

- Coadministration with strong CYP3A4 inhibitors 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.

See additional Important Safety Information located throughout. Please read the full **Prescribing Information**, including **Boxed WARNING**, available at **NUPLAZIDhcp.com**.

ONCE-DAILY NUPLAZID® (pimavanserin) 34mg capsules

Indication

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

Important Safety Information

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 who experience psychosis unless their hallucinations and delusions are related to Parkinson's disease.**
- **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.
- **Warnings and Precautions**: 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 (e.g., Class 1A antiarrhythmics, Class 3 antiarrhythmics, certain antipsychotics or 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 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 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.

Dosage and Administration

Recommended dose: 34 mg capsule taken orally once daily, without titration, with or without food.

NUPLAZID is available as 34 mg capsules and 10 mg tablets.

Please read the full **Prescribing Information**, including **Boxed WARNING**, available at **NUPLAZIDhcp.com**.

References: 1. U.S. Food and Drug Administration. FDA approves first drug to treat hallucinations and delusions associated with Parkinson's disease. April 29, 2016. Accessed May 5, 2023. https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-treat-hallucinations-and-delusions-associated-parkinsons-disease. **2.** Correll CU. From receptor pharmacology to improved outcomes: individualising the selection, dosing, and switching of antipsychotics. *Eur Psychiatry*. 2010;25(suppl 2):S12-S21. **3.** Stahl SM. *Stahl's Essential Psychopharmacology*. 4th ed. Cambridge University Press; 2013. **4.** Goldman JG, Holden S. Treatment of psychosis and dementia in Parkinson's disease. *Curr Treat Options Neurol*. 2014;16(3):281. doi: 10.1007/s11940-013-0281-2 **5.** Friedman JH. Pharmacological interventions for psychosis in Parkinson's disease patients. *Expert Opin Pharmacother*. 2018;19(5):499-505. **6.** Acadia Pharmaceuticals Inc. NUPLAZID® [package insert]. San Diego, CA; 2023. **7.** Shim J, Hong ZY, Sohn I, Hwang C. Prediction of drug–target binding affinity using similarity-based convolutional neural network. *Sci Rep*. 2021;11(1):4416. doi: 10.1038/s41598-021-83679-y **8.** 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. **9.** Voss T, Bahr D, Cummings J, Mills R, Ravina B, Williams H. Performance of a shortened scale for assessment of positive symptoms for Parkinson's disease psychosis. *Parkinsonism Relat Disord*. 2013;19(3):295-299. **10.** Data on File_ACP-103-020 posthoc demographics_July2020. **11.** Espay AJ, Guskey MT, Norton C, et al. Pimavanserin for Parkinson's disease psychosis: effects stratified by baseline cognition and use of cognitive-enhancing medications. *Mov Disord*. 2018;33(11):769-1776. **12.** Andreasen NC. Scale for the Assessment of Positive Symptoms (SAPS). Iowa City, IA: University of Iowa; 1984. **13.** 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. **14.** Seppi K, Chaudhuri KR, Coelho M, et al; on behalf of Movement Disorders Society Evidence-Based Medicine Committee. Update on Treatments for Nonmotor Symptoms of Parkinson's Disease-An evidence-based medicine review. *Mov Disord*. 2019;34(2):180-198. **15.** Fredericks D, Norton JC, Atchison C, Schoenhaus R, Pill MW. Parkinson's disease and Parkinson's disease psychosis: a perspective on the challenges, treatments, and economic burden. *Am J Manag Care*. 2017;23(5 suppl):S83-S92. **16.** 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. **17.** Fabbri M, Barbosa R, Rascol O. Off-time treatment options for Parkinson's disease. *Neurol Ther*. 2023;12(2):391-424. **18.** Weiss HD, Marsh L. Impulse control disorders and compulsive behaviors associated with dopaminergic therapies in Parkinson disease. *Neurol Clin Pract*. 2012;2(4):267-274.

PREVIOUS | NEXT

ONCE-DAILY
NUPLAZID®
(pimavanserin) 34mg capsules

ONCE-DAILY
NUPLAZID®
(pimavanserin) 34mg capsules

Choose NUPLAZID® as your first-line prescription for hallucinations and delusions associated with Parkinson's disease (PD) psychosis

NUPLAZID is recognized by the **Movement Disorder Society (MDS)** as being efficacious and clinically useful for the treatment of PD psychosis.[14]

Physicians are paid consultants for Acadia Pharmaceuticals Inc.

"It's unfair to patients when we don't fully recognize the impact Parkinson's-related hallucinations and delusions have on therapeutic strategies to treat motor symptoms." [4,5, 15-18]

— Stuart Isaacson, MD, movement disorder specialist

Watch videos of specialists discussing the symptoms, diagnosis, and treatment of PD-related hallucinations and delusions.

Important Safety Information (cont'd)

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

See additional Important Safety Information located throughout. Please read the full **Prescribing Information**, including **Boxed WARNING**, available at **NUPLAZIDhcp.com**.

ACADIA®