



Parkinson's Disease

More Than Motor Symptoms

Speaker Introduction and Disclosures

Disclosures:

I am a healthcare provider presenting this program on behalf of Acadia Pharmaceuticals Inc. as a paid speaker

I will not be able to address questions about your specific situation and encourage you to speak to your doctor. I am happy to answer more general questions about hallucinations and delusions associated with Parkinson's disease, and treatment with NUPLAZID[®] (pimavanserin)

Objectives

- Introduce non-motor symptoms of Parkinson's disease (PD): hallucinations and delusions
- Describe the symptoms of PD-related hallucinations and delusions
- Explore how you can talk to your healthcare provider about your symptoms and establish a treatment plan



Non-Motor Symptoms in PD: Hallucinations and Delusions

Parkinson's Disease Is More Than Just Motor Symptoms

- Approximately 1 million people in the US have Parkinson's disease (PD)¹
- The most familiar symptoms of PD are motor symptoms, or TRAP²
 - **T**remor
 - **A**kinesia/slowness of movement
 - **R**igidity/stiffness
 - **P**ostural instability/trouble with balance



- Non-motor symptoms
 - Are experienced by the majority of people with PD²⁻⁵
 - Non-motor symptoms combined can be more troublesome than motor symptoms in terms of quality of life³



1. Parkinson's Disease Foundation. Statistics on Parkinson's.
<https://www.parkinson.org/Understanding-Parkinsons/Statistics>. Accessed January 20, 2022.

2. Olanow C, et al. In: Kasper D et al, eds. *Harrison's Principles of Internal Medicine*. 19th ed. New York, NY: McGraw-Hill; 2015.
<http://accessmedicine.mhmedical.com/content.aspx?bookid=1130&Sectionid=79755616>.

Accessed January 20, 2022.

3. Martinez-Martin P, et al. *Mov Disord*. 2011;26(3):399-406.

4. Forsaa EB, et al. *Arch Neurol*. 2010;67:996-1001.

5. Chaudhuri KR, et al. *Mov Disord*. 2006;21:916-923.

Hallucinations and Delusions

Hallucinations¹

Seeing, hearing, or otherwise
perceiving things that others
don't

Delusions¹

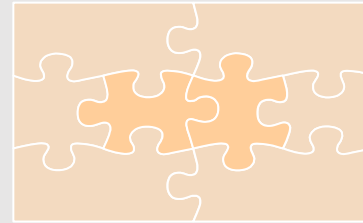
Believing things that are not true
despite evidence to the contrary

1. Ravina B, et al. *Mov Disord*. 2007;22:1061-1068.

What Can Cause Hallucinations and Delusions in PD?

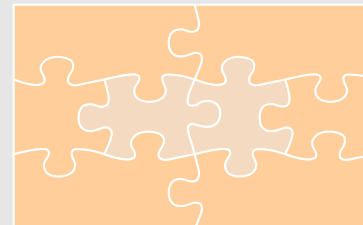
It is important for your healthcare provider to rule out causes not associated with PD

Internal Causes¹⁻³



- **PD-related**
- Dehydration
- Change in vision
- Other medical conditions
- Infection (ie, urinary tract infection or pneumonia)

External Causes¹⁻⁵



- Some PD medications (levodopa or dopamine agonists) or other medications (anticholinergics)
- Alcohol or other recreational drugs
- Dim lighting or time of day

1. Wolters ECh. *J Neural Transm Suppl.* 2006;71:31-37.
2. Goldman JG. AAN Institute; 2014.
3. National Parkinson Foundation. Hallucination/Delusions. <http://www.parkinson.org/understanding-parkinsons/non-motor-symptoms/Psychosis>. Accessed January 20, 2022.
4. Ravina B, et al. *Mov Disord.* 2007;22:1061-1068.
5. Sanchez-Ramos JR, et al. *Arch Neurol.* 1996;53:1265-1268

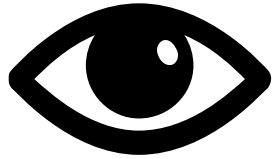


The Symptoms: PD-Related Hallucinations and Delusions

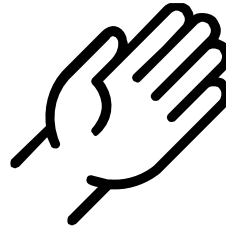
Early Symptoms



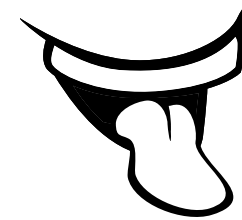
Hallucinations: Seeing, Hearing, or Experiencing Things That Others Don't



Seeing Things



Feeling Things



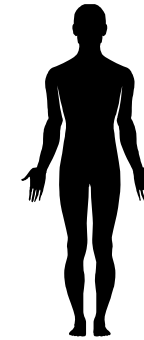
Tasting Things



Hearing Things



Smelling Things



Body Sensations

1. Fénelon G, et al. *Mov Disord*. 2010;25: 763-766.
2. Fénelon G. *CNS Spectr*. 2008;13:18-25.
3. Goetz CG, et al. *Mov Disord*. 2011;26:2196-2200.
4. Goldman JG, et al. *Curr Treat Options Neurol*. 2014;16:281.

Hallucinations



Delusions: What People With PD May Believe



Persecutory Delusions

- Impression of someone trying to harm, steal from, or deceive you

Jealousy Delusions

- Impression partner is cheating on you



Reference Delusions

- Believing a song or TV show is speaking to you directly



1. Voss T, et al. *Parkinsonism Relat Disord*. 2013;19:295-299.

2. Andreasen N. The scale for the assessment of positive symptoms (SAPS). University of Iowa; Iowa City: 1984.

Delusions



Symptoms May Worsen Over Time

Early Symptoms¹⁻³

- Insight is retained
- Illusions
- Feelings of passage or presence
- Hallucinations

In one study, symptom progression was shown to occur over a 3-year time period,² but this can vary for individual people with PD¹⁻³

Symptoms Progress²

Later Symptoms¹⁻³

- Insight is lost
- Complex hallucinations
- Delusions

1. Ravina B, et al. *Mov Disord.* 2007;22:1061-1068.
2. Goetz CG, et al. *Arch Neurol.* 2006;63:713-716.
3. Goetz CG, et al. *Mov Disord.* 2011;26:2196-2200.

What PD-Related Hallucinations and Delusions Are Not

Hallucinations and delusions are NOT dementia or Alzheimer's and are NOT vivid dreams or problems with sleep^{1,2}

- People can be unsure of what to call these symptoms and may use terminology they are more familiar with³
- Terms such as vivid dreams (to describe hallucinations) or dementia (to describe delusions) may be used incorrectly³



1. Ravina B, et al. *Mov Disord*. 2007;22:1061-1068.
2. Meral H, et al. *Clin Neuro Neurosurg*. 2007;109:862-867.
3. Data on File, Acadia Pharmaceuticals Inc, Market Research. 2014.

Who May Be at Risk and Why?

About 50% of people with PD may develop hallucinations and/or delusions at some point during the course of their disease¹

Dopamine deficiency is believed to play a major role in motor symptoms²

Serotonin is thought to play a major role in hallucinations and delusions^{3,4}

Risk Factors⁵

- Having PD
- Older age
- PD duration
- PD severity

1. Forsaa EB, et al. *Arch Neurol*. 2010;67:996-1001.

2. Olanow C, et al. In: Kasper D et al, eds. *Harrison's Principles of Internal Medicine*. 19th ed. New York, NY: McGraw-Hill; 2015.
<http://accessmedicine.mhmedical.com/content.aspx?bookid=1130&Sectionid=79755616>. Accessed January 20, 2022.

3. Ballanger B, et al. *Arch Neurol*. 2010;67(4):416-421.

4. Joutsa J, et al. *J Nucl Med*. 2015;56:1036-1041.

5. Fénelon G, et al. *Brain*. 2000;123:733-745.

What Are Potential Concerns That May Be Associated With PD-Related Hallucinations and Delusions?



In one study, motor complications and psychosis, including hallucinations and delusions, were shown to be responsible for **>50%** of hospitalizations for people with Parkinson's¹

Hallucinations and delusions in PD are associated with **increased burden and emotional distress** for caregivers^{2,3}



1. Klein C, et al. *J Neural Transm.* 2009;116:1509-1512.
2. Martinez-Martin P, et al. *Parkinsonism Relat Disord.* 2015;21:629-634.
3. Aarsland D, et al. *Int J Geri Psychiatry.* 1999;14:866-874.

Treatment and Management of PD-Related Hallucinations and Delusions

It's important to rule out other potential causes of hallucinations and delusions, such as infections or electrolyte imbalances, which can be the underlying cause of hallucinations and delusions in people with PD¹



Non-Drug Treatment Approaches

- **Self-managed coping strategies^{2,3}**
 - Cognitive techniques
 - Interactive techniques
 - Visual techniques
- **Psychotherapy techniques⁴**
 - Cognitive-behavioral therapy
 - Supportive therapy
 - Psychoeducation

Drug Treatment Approaches

- Adjusting certain antiparkinson medication may help in the management of hallucinations and delusions¹
- Drugs can be added to treat PD-related hallucinations and delusions, but prior to 2016 there were no FDA-approved treatments⁵



1. Ravina B, et al. *Mov Disord*. 2007;22:1061-1068.

2. Parkinson Foundation. Hallucinations/Delusions. <http://www.parkinson.org/understanding-parkinsons/non-motor-symptoms/Psychosis>. Accessed January 20, 2022.

3. Diederich NJ, et al. *Mov Disord*. 2003;18:831-838.

4. Zahodne LB, Fernandez HH. *Drugs Aging*. 2008;25:665-682.

5. Acadia Pharmaceuticals Inc. NUPLAZID® [package insert]. San Diego, CA; 2020. NU-1479-v7 3/23.



Establishing a Plan of Action

Report Symptoms As Soon As They Occur

Most people do not voluntarily report their hallucinations and/or delusions to their healthcare provider¹

If you sense or experience something unusual, ask your loved one if they perceived the same thing^{2,3}

If your loved one describes or interacts with something that you don't perceive, ask questions to understand what they are experiencing^{2,3}

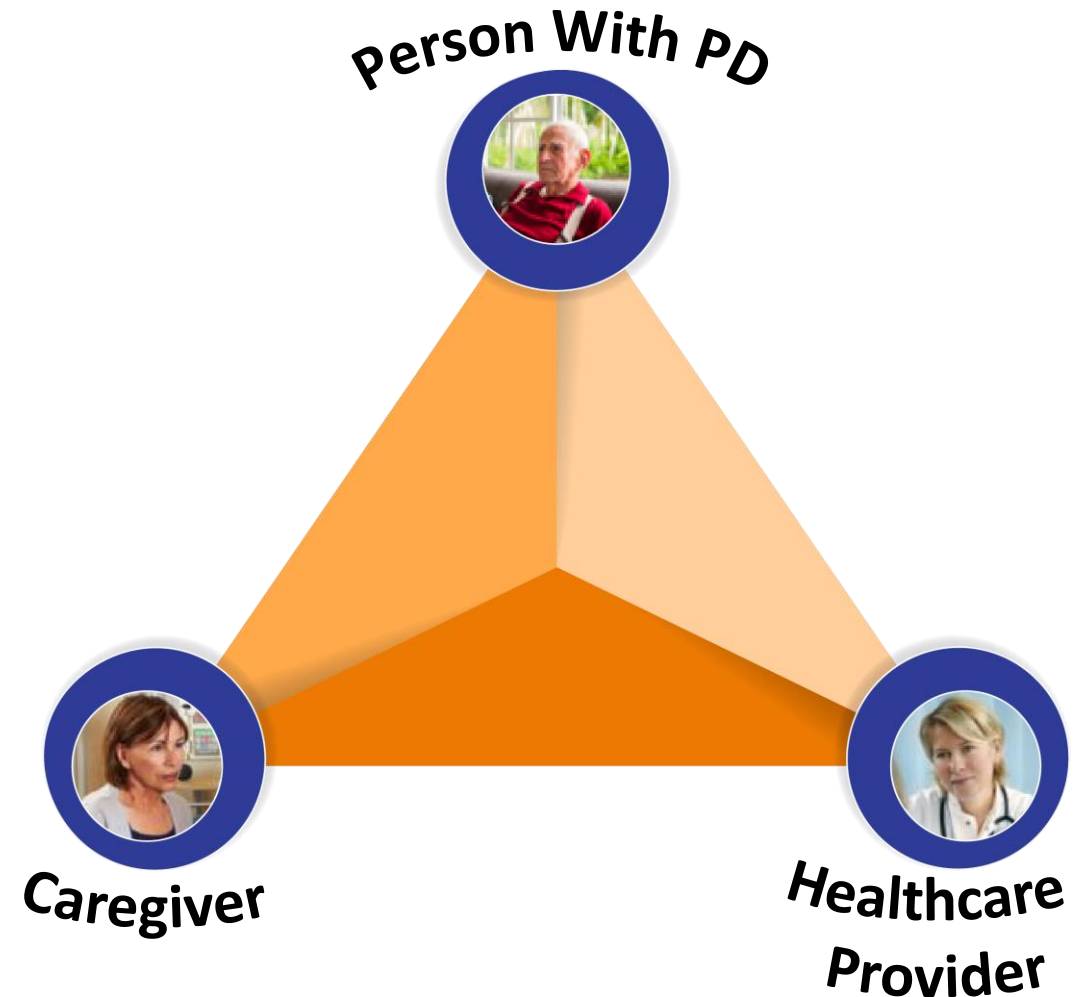
If you fear or believe that a loved one is deceiving you, speak up^{2,3}

If your loved one accuses you of deceiving them, don't stay silent, speak to your healthcare provider^{2,3}

1. Chaudhuri KR, et al. *Mov Disord.* 2010;25(6):704-709.
2. Ondo WG, et al. *J Clin Mov Disord.* 2015;2(17):1-7.
3. Ravina B, et al. *Mov Disord.* 2007;22:1061-1068.

Don't Wait to Start The Conversation

- Patients and caregivers should proactively discuss their symptoms with their healthcare provider so they can be monitored over time¹
- Describe what is seen, heard, sensed, experienced, or believed and how these symptoms affect your lives²⁻⁴



1. National Parkinson Foundation. Hallucination/Delusions. <http://www.parkinson.org/understanding-parkinsons/non-motor-symptoms/Psychosis>. Accessed March 2, 2022.

2. Ravina B, et al. *Mov Disord*. 2007;22:1061-1068.

3. Martinez-Martin P, et al. *Parkinsonism Relat Disord*. 2015;21:629-634.

4. Chaudhuri KR, et al. *Mov Disord*. 2010;25:704-709..
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Establishing a Plan of Action

Educate Yourself

About 50% of people with PD may develop hallucinations and/or delusions at some point during the course of their disease and may worsen over time^{1,2}

Talk to Your Healthcare Provider at the First Sign

Discuss symptoms with your healthcare provider and the impact they have on both of your lives.³⁻⁵ The sooner your healthcare provider knows, the sooner they can help

Get a Diagnosis and Establish a Treatment Plan

It is important for your healthcare provider to track symptoms over time and discuss your treatment options^{2,6}

1. Forsaa EB, et al. *Arch Neurol*. 2010;67(8):996-1001.

2. Goetz CG, et al. *Arch Neurol*. 2006;63(5):713-716.

3. Martinez-Martin P, et al. *Parkinsonism Relat Disord*. 2015;21:629-634.

4. Aarsland D, et al. *Int J Geri Psychiatry*. 1999;14:866-874.

5. Martinez-Martin P, et al. *Parkinsonism Relat Disord*. 2011;26(3):399-406.

6. Parkinson's Foundation. March 23, 2018. Accessed January 20, 2022.

<https://www.parkinson.org/blog/research/Hallucinations-and-Delusions-in-Parkinsons-Disease>

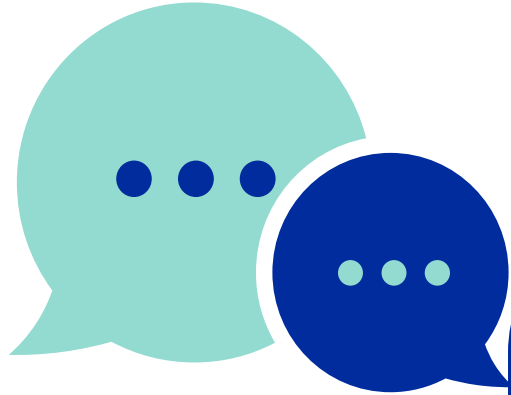
Summary

- About 50% of people with PD may develop hallucinations and/or delusions at some point during the course of their disease¹
- Visual hallucinations are the most common PD-related symptom but other types of hallucinations and delusions also occur^{2,3}
- Hallucinations and delusions may worsen over time⁴⁻⁶
- Discussing your symptoms openly and understanding what treatment options are available are critical to establishing a plan of action with your healthcare provider^{7,8}

1. Forsaa EB, et al. *Arch Neurol*. 2010;67:996-1001.
2. Fénelon G, et al. *Mov Disord*. 2010;25(6):763-766.
3. Fénelon G, Alves G. *J Neurol Sci*. 2010;289:12-17.
4. Ravina B, et al. *Mov Disord*. 2007;22:1061-1068.
5. Goetz CG, et al. *Arch Neurol*. 2006;63:713-716.
6. Goetz CG, et al. *Mov Disord*. 2011;26:2196-2200.

7. Parkinson Foundation. Hallucinations and Delusions in Parkinson's Disease. <https://www.parkinson.org/blog/research/Hallucinations-and-Delusions-in-Parkinsons-Disease>. Accessed January 20, 2022.
8. Minton L, et al. Parkinson's Foundation; 2020. Accessed March 10, 2023. <https://www.parkinson.org/library/books/psychosis>

Discussing Your Treatment Options



- What is an FDA-approved treatment option to manage this condition?
- What is the most important thing I should know about this treatment?
- What are the potential side effects?
- Can I take this treatment with Parkinson's disease medicines or other medicines?



ONCE-DAILY
NUPLAZID[®]
(pimavanserin) 34mg capsules

For the Treatment of Hallucinations and Delusions
Associated With Parkinson's Disease Psychosis

Please see Important safety Information and **Boxed WARNING** in this presentation.

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What Is the Most Important Information I Should Know About NUPLAZID®?

- Medicines like NUPLAZID can raise the risk of death in elderly people who have lost touch with reality (psychosis) due to confusion and memory loss (dementia).
- 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.

What Is NUPLAZID® Used for?



NUPLAZID is:

- the only FDA-approved prescription treatment for hallucinations and delusions associated with Parkinson's disease psychosis

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(pimavanserin) 34mg capsules

How Does NUPLAZID® Work?

- How it works is not fully understood
- It is thought to affect the activity of serotonin in the brain



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How Effective Is NUPLAZID®?

- In the clinical study,* the majority of people who took NUPLAZID experienced fewer and/or less severe hallucinations or delusions
- And some patients did not experience any hallucinations or delusions after 6 weeks
- Not everyone will respond to NUPLAZID and some may worsen



NUPLAZID may begin to reduce the frequency and/or severity of hallucinations and delusions as soon as 4 weeks, but it may take up to 6 weeks to feel the full effect.

You should speak with your healthcare provider before discontinuing NUPLAZID.

*The clinical study included 199 adults (at least 40 years of age with a mean age of 72 years)²

1. Acadia Pharmaceuticals Inc. NUPLAZID® [package insert]. San Diego, CA; 2020.
2. Cummings J, et al. *Lancet*. 2014;383:533-540.

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(pimavanserin) 34mg capsules

Will NUPLAZID® Affect My Parkinson's-Related Movement Issues?

NUPLAZID had no effect on motor symptoms

- In the clinical study, NUPLAZID did not worsen motor function compared to a placebo
- You can take NUPLAZID without adjusting the doses of carbidopa/levodopa medicines



What Are the Commonly Reported Side Effects of NUPLAZID®?

Adverse Reactions in Clinical Trials*

| | NUPLAZID 34 mg (N=202) | Placebo (N=231) |
|------------------------------|---------------------------|--------------------|
| Nausea | 7% | 4% |
| Swelling in the legs or arms | 7% | 2% |
| Feeling confused | 6% | 3% |
| Hallucinations | 5% | 3% |
| Constipation | 4% | 3% |
| Changes to normal walking | 2% | <1% |

- These are not all the possible side effects of NUPLAZID; for more information, please see the prescribing information, or ask your healthcare provider about this medicine
- You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088. You can also call Acadia Pharmaceuticals Inc. at 1-844-4ACADIA (1-844-422-2342).

*Adverse reactions reported in placebo-controlled studies of 6-week treatment duration, and reported in ≥2% of the study population and at a greater rate than seen in patients treated with placebo

Who Should Not Take NUPLAZID®?



- Do not take NUPLAZID if you are allergic to pimavanserin or any of the other ingredients in NUPLAZID

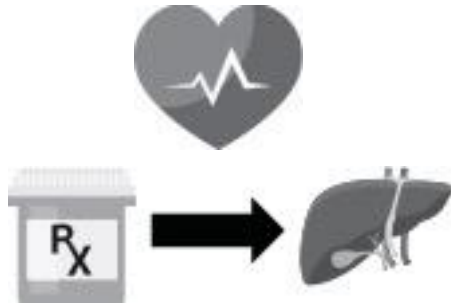


- NUPLAZID may increase the risk of certain changes to your heart rhythm. Therefore, do not take NUPLAZID if:

- You have certain heart conditions that change your heart rhythm
- You are currently taking medicines that are known to prolong the QT interval (including some medicines used to treat abnormal heart rhythms, antipsychotics, and antibiotics)



What Should I Tell My Healthcare Provider Before Taking NUPLAZID®?



Before taking NUPLAZID, tell your healthcare provider if you:

- have heart problems
- take medicines that affect the way certain liver enzymes work



Tell your healthcare provider about all the medicines that you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How Do I Take NUPLAZID®?



Not actual size

- The recommended dose of NUPLAZID is one 34 mg capsule, once per day, taken by mouth

How Do I Get NUPLAZID®?

Acadia Connect® is a free support program and, when enrolled, pairs you with a Care Coordinator. They will be your dedicated contact and offer things such as:

- Navigating your insurance coverage
- Managing costs and understanding your financial support options
- Working with your pharmacy and getting your prescription filled
- Arranging convenient prescription delivery

acadia
connect®

**Your connection to
support**

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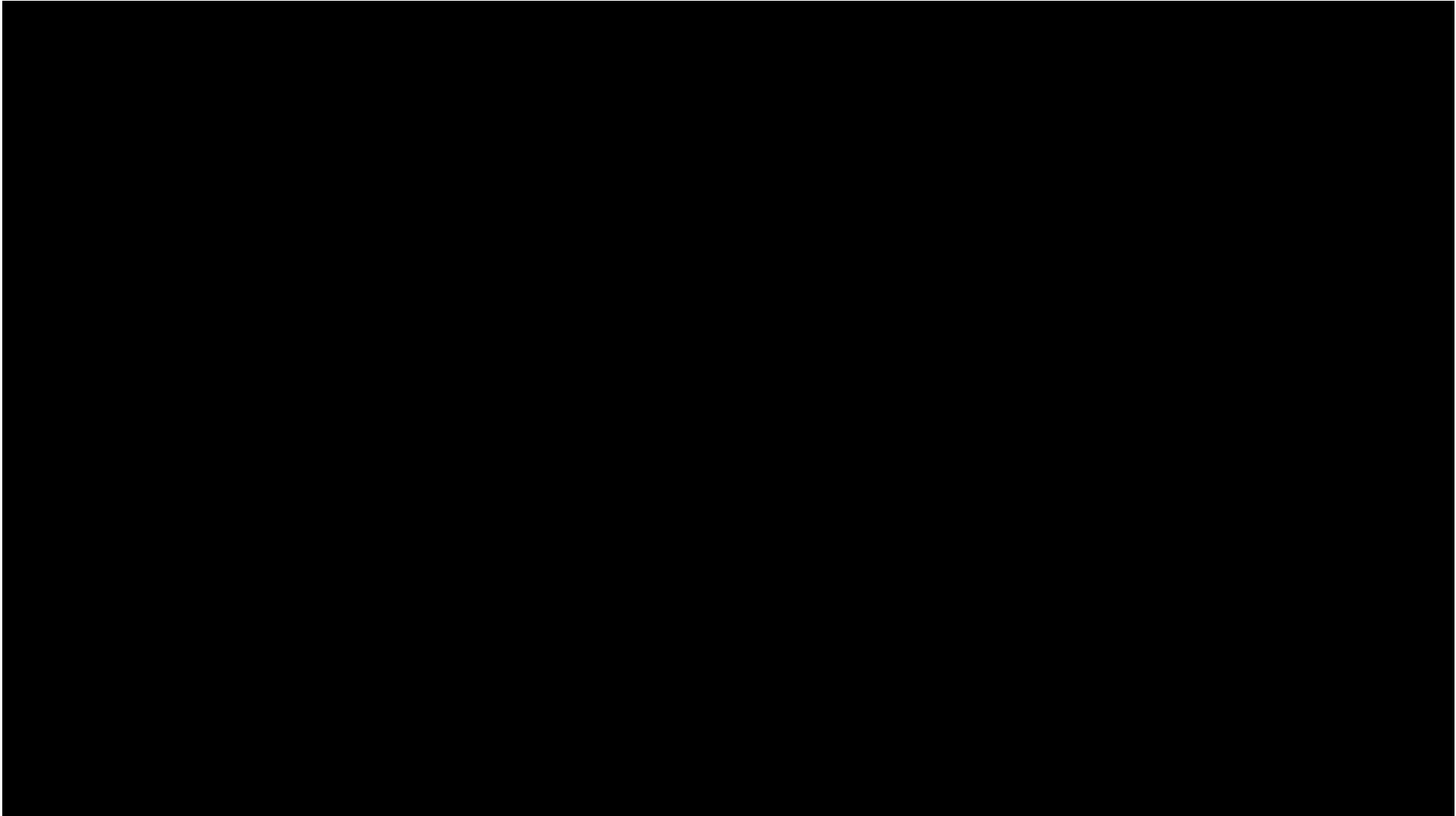
Summary of NUPLAZID®

- NUPLAZID is the only FDA-approved prescription treatment for hallucinations and delusions associated with Parkinson's disease psychosis
- In the clinical study, the majority of people who took NUPLAZID experienced fewer and/or less severe Parkinson's-related hallucinations and delusions
- In the clinical study, NUPLAZID had no effect on motor symptoms
- NUPLAZID can be taken without adjusting doses of carbidopa/levodopa medicines
- Common side effects of NUPLAZID include swelling in the legs or arms, nausea, confusion, hallucination, constipation, and changes to normal walking

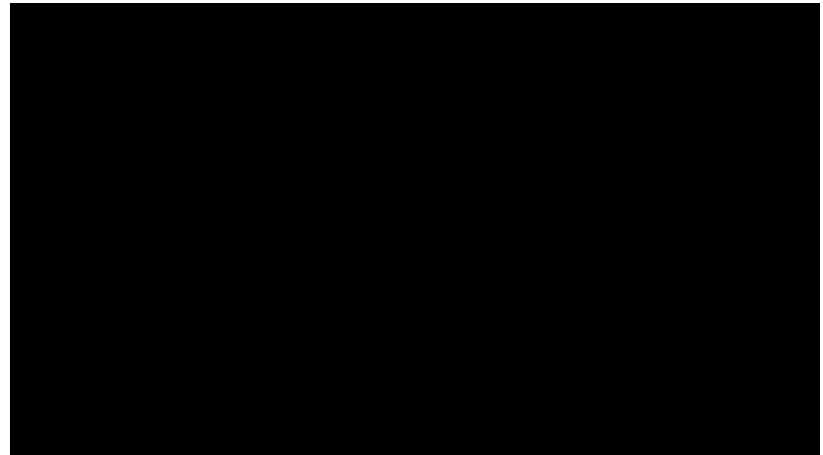
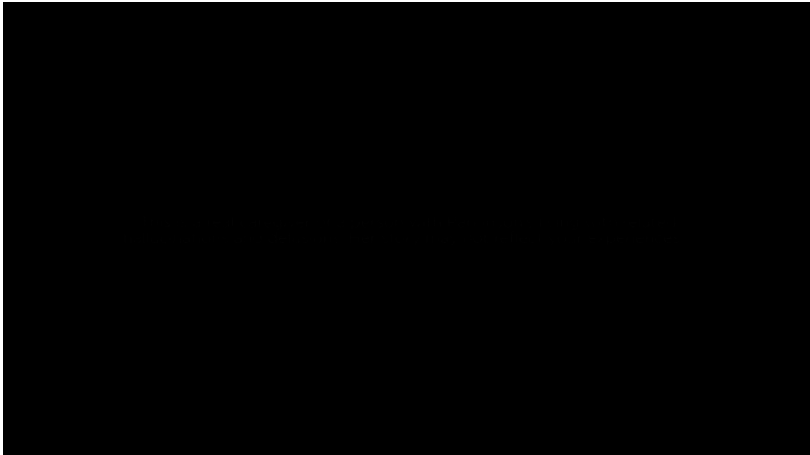
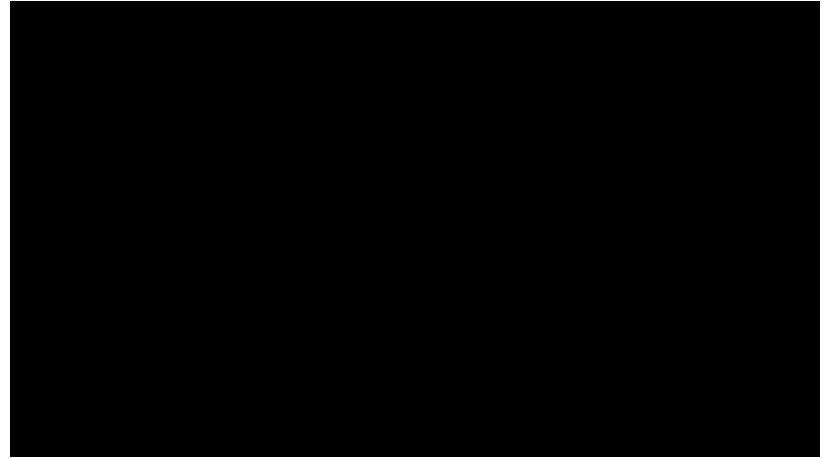
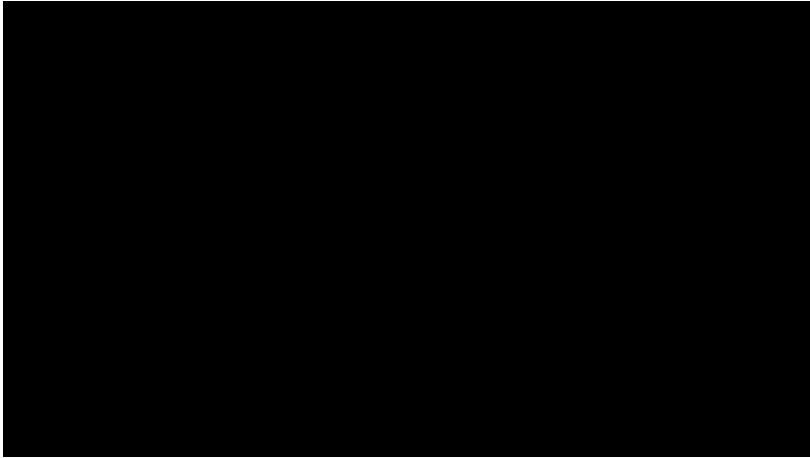
Please see full Prescribing Information including **Boxed WARNING**, available at this program, or visit [NUPLAZID.com](https://www.nuplazid.com).

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A Caregiver's Story



Caregiver Stories



Questions



Don't Wait to Start the Conversation
Parkinson's disease-related hallucinations and
delusions are treatable

For more information, please go to **NUPLAZID.com**

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