April 1, 2019

ACADIA Pharmaceuticals Responds to False and Misleading Claims about NUPLAZID

ACADIA is aware of recent media reports that have repeated old and discredited claims containing false and misleading information about NUPLAZID® (pimavanserin). There is no new safety information from the U.S. Food and Drug Administration (FDA) about NUPLAZID and its benefit/risk profile. Reporting information that is not factual and balanced risks negatively affecting patient care. At ACADIA, our top priority is patient safety. We are focused on making a meaningful difference in the lives of patients and their caregivers and stand by the established efficacy and safety profile of NUPLAZID as described in the FDA-approved labeling.

Facts you should know about NUPLAZID and Parkinson's Disease Psychosis (PDP):

- NUPLAZID is the only drug approved by the FDA to treat hallucinations and delusions associated with PDP. NUPLAZID was approved based on data from a pivotal Phase 3 clinical study that demonstrated clinically robust and highly statistically significant efficacy combined with data from other supportive clinical studies.

- The FDA is the regulatory body in the U.S. responsible for approving drugs as well as continuously reviewing evolving scientific data for approved drugs. The NUPLAZID benefit/risk profile has been thoroughly assessed by the FDA on at least two occasions, including at time of approval in 2016 and following a 2018 Tracked Safety Issue (TSI) evaluation. Key documents from this evaluation are available on the ACADIA website and provide detailed information on the NUPLAZID safety data assessment, internal review, and analyses conducted by the FDA. Based on all available evidence, the FDA issued a public statement on September 20, 2018 stating they did not identify any new or unexpected safety findings and the benefits of NUPLAZID treatment outweigh the risks when used according to the FDA-approved label.

- The FDA statement also included specific language to address the use of concomitant medications with NUPLAZID that can increase the risk of QT interval prolongation and reminded healthcare providers to be aware of the risks as described in the current label of NUPLAZID.

- The NUPLAZID label, including the Boxed Warning, applies to all patients who take NUPLAZID. The Boxed Warning has always been a part of the FDA-approved NUPLAZID label. The Boxed Warning and other important safety information from the NUPLAZID label are included with all promotional communications to the public, including physicians, patients, and their families when NUPLAZID is mentioned.

- The International Parkinson and Movement Disorder Society (MDS) recently published an update to their recommendations for "Treatments for Non-Motor Symptoms of Parkinson's Disease." MDS treatment recommendations provide guidance on the standard of care for appropriate treatment of PDP. According to the 2019 MDS Evidence-Based Medicine Review, NUPLAZID is recognized as an efficacious and clinically useful treatment option for PDP.

- Hallucinations (seeing, hearing, or experiencing things that others don't) and delusions (believing things that aren't true) are non-motor symptoms of Parkinson's disease (PD). Together they are known as PDP and may affect around half of people living with PD over the course of their disease.[1,2] People who develop non-motor symptoms of PD like hallucinations or delusions often have to deal with a broader set of challenges that can be more troublesome than motor symptoms in terms of quality of life.[3] These non-motor symptoms may come with additional challenges including increased caregiver distress and burden and nursing home placement.[4,5,6] Additional information about PDP can be found at www.MoretoParkinsons.com.

Important Safety Information and Indication 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 CYP3A4 inducers may reduce NUPLAZID exposure. Monitor patients for reduced efficacy and an increase in NUPLAZID dosage may be needed.

Pediatric Use: Safety and efficacy have not been established in pediatric patients.

Dosage and Administration: Recommended dose: 34 mg taken orally once daily, without titration.

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

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).

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

Please see the full Prescribing Information including **Boxed WARNING** for NUPLAZID at https://www.nuplazid.com/pdf/NUPLAZID_Prescribing_Information.pdf.

---

[1] 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.
[2] 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.
[3] Martinez-Martin P, Rodriguez-Blazquez C, Kurtis MM, Chaudhuri KR, Group NV. The impact of non-motor symptoms on health-related quality of life of patients with Parkinson's disease. *Mov Disord.* 2011;26(3):399-406.
[4] Aarsland D, Larsen JP, Karlsen K, Lim NG, Tandberg E. Mental symptoms in Parkinson's disease are important contributors to caregiver distress. *Int J Geriatr Psychiatry.* 1999;14(10):866-874.
[5] Martinez-Martin, Rodriguez-Blazquez, Forjaz, et al. Neuropsychiatric symptoms and caregiver's burden in Parkinson's disease. *Parkinsonism and Related Disorders.* 2015;21(6):629-634.
[6] Goetz CG, Stebbins GT. Risk factors for nursing home placement in advanced Parkinson's disease. Neurology. 1993;43(11):2227-2229.