VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Parkinson's Disease – Nuplazid® (pimavanserin capsules and tablets – Acadia)

TAC APPROVAL DATE: 07/31/2019

OVERVIEW

Nuplazid is a selective serotonin 5-HT_{2A} inverse agonist indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis.[1] Nuplazid activity is thought to be mediated through a combination of inverse agonist and antagonist activity at serotonin 5-HT2A receptors and to a lesser extent at serotonin 5-HT_{2C} receptors. Nuplazid does not have activity at the dopamine receptors which differs from typical and atypical antipsychotics. Common adverse events occurring in the clinical trials were peripheral edema and confusional state.

Disease Overview

Parkinson's disease is the second most common neurodegenerative disease.[2] Characterized by the cardinal signs of bradykinesia, rigidity, tremor at rest, and abnormalities of balance, posture, and gait, the etiology of Parkinson's disease remains unknown in most patients. Nonmotor symptoms in Parkinson's disease, an increasingly recognized intrinsic feature of Parkinson's disease, may affect three domains: autonomic, neuropsychiatric, and sensory, including pain. The prevalence of nonmotor symptoms is high. Psychosis can occur in as many as 50% of patients with Parkinson's disease at some time during the course of their illness.[3] The nonmotor features of Parkinson's disease such as dementia, depression, and psychosis may result in significant disability; however, recognition of these clinical features is low.[2] Furthermore, many Parkinson's disease symptoms overlap with features of depression and dementia including symptoms of withdrawal, lack of motivation, flattened affect, decreased physical activity, or bradyphrenia, thus confounding the identification of these behavioral and cognitive disorders.

The spectrum of psychotic symptoms in Parkinson's disease is wide-ranging from mild visual illusions to fully formed hallucinations and delusions.[4] Diagnostic criteria for PDP require the presence of at least one of the following: hallucinations, delusions, illusions, or false sense of presence. Psychosis is associated with poorer quality of life, increased morbidity and mortality, increased caregiver burden, and increased nursing home placement.

Guidelines

According to the **American Academy of Neurology (AAN) practice parameter on the evaluation and treatment of depression, psychosis, and dementia in Parkinson disease (2006)**, for patients with Parkinson's disease and psychosis, treatment with clozapine should be considered (Level B), treatment with quetiapine may be considered (Level C), and treatment with olanzapine should not be routinely considered (Level B).[2] Clozapine use is associated with agranulocytosis that may be fatal, and the patient's absolute neutrophil count must be monitored. Guidelines note that there is a concern that all atypical neuroleptics have a small increased risk of mortality particularly in elderly patients with dementia who are treated for behavioral disorders, and this must be balanced by the high morbidity and mortality associated with Parkinson's disease psychosis. Nuplazid is not mentioned in the guideline. The **Movement Disorder Society** has also published a review on treatments for the non-motor symptoms of Parkinson's disease (2019).[5] The conclusions reached on drugs to treat Parkinson's disease psychosis mirrored those published by AAN with the addition of implications for Nuplazid:

clozapine is clinically useful, Nuplazid is clinically useful, quetiapine is possibly useful, and olanzapine is not useful.

Safety

As with other antipsychotic medications, Nuplazid has a Boxed Warning regarding increased mortality in elderly patients with dementia-related psychosis.[1] 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. Nuplazid also prolongs the QT interval; clozapine and quetiapine have a similar Warning.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Nuplazid. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Nuplazid as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Nuplazid to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Nuplazid is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Parkinson's Disease Psychosis.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
   - **A)** Patient has hallucinations and delusions associated with Parkinson's disease pychosis; AND
   - **B)** Patient does not have dementia-related psychosis unrelated to the hallucinations and delusions associated with Parkinson's disease psychosis; AND
   - **C)** Nuplazid is prescribed by or in consultation with a neurologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Nuplazid has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Dementia-Related Psychosis.** Nuplazid prescribing information has a Boxed Warning regarding increased mortality in elderly patients with dementia-related psychosis.[1] Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Nuplazid® tablets and capsules [prescribing information]. San Diego, CA: Acadia Pharmaceuticals Inc.; May 2019.
2. Miyasaki JM, Shannon K, Voon V, et al. Practice parameter: evaluation and treatment of depression, psychosis, and dementia in Parkinson disease (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2006;66(7):996-1002. Available at: http://www.neurology.org/content/66/7/996.full.pdf+html. Accessed on July 25, 2019.
3. FDA approves first drug to treat hallucinations and delusions associated with Parkinson's disease. U.S. Food and Drug Administration Web site. Page last updated: May 2, 2016. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm498442.htm. Accessed on July 25, 2019.
4. Goldman JG, Holden S. Treatment of psychosis and dementia in Parkinson's disease. *Curr Treat Options Neurol*. 2014;16(3):281.
5. Seppi K, Ray Chaudhuri K, Coelho M, et al. Update on treatments for nonmotor symptoms of Parkinson's disease-an evidence-based medicine review. *Mov Disord*. 2019;34(2):180-198..

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
New Policy	--	07/18/2018
DEU revision	1/16/2019: Addition of "Parkinson's Disease" to title of policy.	--
Annual revision	No change to criteria.	07/31/2019

* For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; TAC – Therapeutic Assessment Committe.