istradefylline (Nourianz™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO084

Description

Istradefylline (Nourianz) is an orally administered adenosine receptor antagonist.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Indication	Dosage Form	Quantity Limit
istradefylline (Nourianz)	Parkinson's disease	20 mg tablets	30 tablets/30 days
		40 mg tablets	30 tablets/30 days

Initial Evaluation

I. **Istradefylline (Nourianz)** may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years or older; **AND**
   B. Prescribed by, or in consultation with, a neurologist; **AND**
   C. A diagnosis of **Parkinson's Disease** when the following are met:
      1. Treatment with one the following has been ineffective, contraindicated or not tolerated:
         i. Carbidopa/levodopa IR up to five times a day; **OR**
         ii. Carbidopa/levodopa XR/CR/ER; **AND**
      2. Current or previous treatment with at least TWO of the following agents used as adjunctive treatment to levodopa/carbidopa has been ineffective, contraindicated, or not tolerated:
         i. Dopamine agonist (e.g., ropinirole, pramipexole)
         ii. COMT inhibitor (e.g,. entacapone, tolcapone)
         iii. MAO-B inhibitor (e.g., rasagiline, safinamide, selegiline); **AND**
      3. Provider attests that the member is experiencing OFF time after trial of first line Parkinson's medications (i.e., Carbidopa/levodopa at four times a day, add on therapy of dopamine agonist); **AND**
      4. Prescriber attests that member will be using istradefylline (Nourianz) in combination with carbidopa/levodopa

II. Istradefylline (Nourianz) is considered investigational when used for all other conditions, including but not limited to:

A. Parkinson's disease WITHOUT documentation of motor fluctuations, "wearing off"
B. Restless Leg Syndrome
C. Promotion of Breathing Plasticity in Amyotrophic Lateral Sclerosis (ALS)

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Prescriber attests that member will be using istradefylline (Nourianz) in combination with carbidopa/levodopa; **AND**
IV. Documentation that member has a reduction in wearing off period from baseline

Supporting Evidence

I. Due to the complexity around the diagnosis of Parkinson's disease (PD) and the treatment options, therapy should be prescribed by, or in consultation with, a neurologist.
II. There is a lack of safety and efficacy data in the use of istradefylline (Nourianz) in those under the age of 18.
III. Motor symptoms in PD affect as many as 77% of patients; these include physical, visible signs of PD: resting tremor, muscular rigidity, postural instability. These advance into falls, axial postural deformities, dysphagia, and in advanced disease, these pharyngeal dysfunctions have an increase aspiration risk and lead to higher numbers of upper respiratory tract infections and pneumonia. Pharmacotherapies for managing the symptoms of PD show the greatest efficacy early in the course of the disease. As symptoms become refractory to standard therapies, levodopa, patients begin experiencing fluctuations in symptoms (OFF periods) within two years of beginning therapy.
IV. Levodopa, administered in oral carbidopa/levodopa formulations, is the mainstay and most effective medication for management of PD motor symptom management. Currently, motor fluctuations are managed by increasing the patient's levodopa dose, reducing intake of dietary protein with levodopa administration, using longer acting carbidopa/levodopa formulations, and adding other agents that can be clinically useful in extending "on" time (e.g., dopamine agonists, COMT inhibitors, and MAO-B inhibitors).
V. The efficacy of istradefylline (Nourianz) as adjunctive treatment to levodopa/carbidopa in patients with PD experiencing "off" episodes was shown in four 12-week placebo-controlled trials that included a total of 1,143 patients. In these pivotal clinical trials, patients were experiencing at least two hours of daily OFF time and were receiving the following concomitant

therapies: dopamine agonists (85%), COMT inhibitors (38%), MAO-B inhibitors (40%), anticholinergics (13%), and/or amantadine (33%). The primary efficacy endpoint was the change from baseline in the daily awake percentage of "off" time, or the change from baseline in daily "off" time. In all four studies, patients treated with istradefylline (Nourianz) experienced a statistically significant decrease compared to patients receiving a placebo.

VI. The 2018 International Parkinson and Movement Disorder Society Evidence-Based Medicine Review reported istradefylline (Nourianz) to be "likely efficacious" and "possibly useful" for clinical practice due to conflicting evidence but generally positive outcomes. Guidelines do not recommend one adjunctive therapy approach over another. The 2019 update did not give other guidance on motor therapies.

Investigational or Not Medically Necessary Uses

I. Parkinson's disease WITHOUT documentation of motor fluctuations, "wearing off"
   A. Istradefylline (Nourianz) has not been studied in patients with Parkinson's disease who aren't experiencing motor fluctuations; therefore, it would be considered investigational when requested in this setting.
II. Restless Leg Syndrome
III. Promotion of Breathing Plasticity in Amyotrophic Lateral Sclerosis (ALS)

References

1. Nourianz [Prescribing Information]. Kyowa Kirin Inc.: Bedminster, NJ. August 2019.
2. Fox, SH, et al. International Parkinson and Movement Disorder Society Evidence-Based Medicine Review: Update on Treatments for the Motor Symptoms of Parkinson's Disease. Movement Disorders 2018; 00:1-16. Available at: www.movementdisorders.org/MDS-Files1/Resources/PDFs/TreatmentsforMotorSymptomsofPD-2018.pdf
3. American Parkinson Disease Association (April 2017). Motor Fluctuations in Parkinson's Disease – What You Need to Know. Available at: www.aoic.net/APDA/APDA1609arc/APDA%20Motor%20Fluctuations%20Fact%20Sheet.pdf
4. UpToDate, Inc. Medical management of motor fluctuations and dyskinesia in Parkinson's disease. UpToDate [database online]. Waltham, MA. Last updated May 17, 2019 Available at: http://www.uptodate.com/home/index.html.
5. Food and Drug Administration [online press release]. FDA approves new add-on drug to treat off episodes in adults with Parkinson's disease. Available at: www.fda.gov/news-events/press-announcements/fda-approves-new-add-drug-treat-episodes-adults-parkinsons-disease. Updated August 27, 2019.
6. LeWitt PA, Guttman M, Tetrud JW, et al. Adenosine A2A receptor antagonist istradefylline (KW-6002) reduces "off" time in Parkinson's disease: a double-blind, randomized, multicenter clinical trial (6002-US-005). Ann Neurol 2008;63:295-302.
7. Hauser RA, Shulman LM, Trugman JM, et al. Study of istradefylline in patients with Parkinson's disease on levodopa with motor fluctuations. Mov Disord 2008;23:2177-2185.
8. Stacy M, Silver D, Mendis T, et al. A 12-week, placebo-controlled study (6002-US-006) of istradefylline in Parkinson disease. Neurology 2008;70:2233-2240.

9. Pourcher E, Fernandez HH, Stacy M, Mori A, Ballerini R, Chaikin P. Istradefylline for Parkinson's disease patients experiencing motor fluctuations: results of the KW-6002-US-018 study. Parkinsonism Relat Disord 2012;18:178-184.

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
pimavanserin (Nuplazid)	Parkinson's Disease
levodopa_Inbrija	
apomorphine_Apokyn_Kynmobi	

Policy Implementation/Update:

Action and Summary of Changes	Date
Annual updates; changes to initial requirements were made with removal of duration of OFF time requirement, addition of age, and reformatting of criteria requirements.	11/2023
Policy Created	9/2019