BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

NOURIANZ™ (istradefylline)
ONGENTYS® (opicapone)
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Nourianz (istradefylline), Ongentys (opicapone) and/ or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of Parkinson's disease (PD) in an individual experiencing "off" episodes and **ALL** of the following:
    a. Parkinson's disease is Hoehn and Yahr Stage 2 or greater
    b. There is at least 2 hours of off time per day

4. Individual will continue to use levodopa/carbidopa

5. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for a trial of **ONE** agent from **EACH** of the following:
    a. **One trial** of dopamine agonist: pramipexole **or** ropinirole
    b. **One trial** of monoamine oxidase inhibitor (MAO) B inhibitor: selegiline (capsule or tablet) **or** rasagiline mesylate tablet
    c. **One trial** of catechol O-methylase inhibitor (COMT): entacapone **or** tolcapone

6. **Additional criteria for Ongentys only:** There are **NO** FDA-label contraindications such as:
    a. Concomitant use of non-selective monoamine oxidase (MAO) inhibitors (e.g., phenelzine, isocarboxazid, tranylcypromine)
    b. History of pheochromocytoma, paraganglioma, or other catecholamine secreting neoplasms

7. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

8. Individual does not have severe hepatic impairment (Child-Pugh Class C)

9. Individual does not have severe renal impairment (CrCl < 15 mL/min) or end-stage renal disease requiring hemodialysis

10. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation as follows:
    a. **For Nourianz:** Strong CYP 3A4 inducers such as carbamazepine, rifampin, phenytoin, St. John's wort, etc.
    b. **For Ongentys:** Concurrent use with non-selective MAO inhibitors such as phenelzine, isocarboxazid, tranylcypromine

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Nourianz (istradefylline), Ongentys (opicapone) and/ or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist

2. Individual's condition has responded while on therapy with response defined as **THREE** of the following:
    a. No evidence of disease progression
    b. Functionality retained most activities of daily living
    c. Achieved and maintains a reduction in off time
    d. Achieved and maintains an increase in on time of at least 1 hour

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Emergent or worsening dyskinesia
        ii. Emergent or worsening hallucinations or psychotic behaviors
        iii. Impulse control or compulsive behaviors

6. Individual does not have severe hepatic impairment (Child-Pugh Class C)

7. Individual does not have severe renal impairment (CrCl < 15 mL/min)

8. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation as follows:
    a. **For Nourianz:** Strong CYP 3A4 inducers such as carbamazepine, rifampin, phenytoin, St. John's wort, etc.
    b. **For Ongentys:** Concurrent use with non-selective MAO inhibitors such as phenelzine, isocarboxazid, tranylcypromine

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Nourianz (istradefylline) is an adenosine receptor antagonist indicated as adjunctive treatment to levodopa/carbidopa in adult patients with Parkinson's disease (PD) experiencing "off" episodes. The mechanism of action of istradefylline is unknown. In *in vitro* studies and in *in vivo* animal studies, istradefylline was demonstrated to be an adenosine A_{2A} receptor antagonist.

Ongentys (opicapone) is a peripheral, selective and reversible catechol-O-methyltransferase (COMT) inhibitor indicated as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing "off" episodes.

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Patients with Parkinson disease (PD) who take levodopa chronically are increasingly likely to develop motor fluctuations and dyskinesia as the disease progresses and nigrostriatal dopaminergic neurons continue to degenerate and lose presynaptic dopamine storage capacity.

Dyskinesia consists of several types of abnormal involuntary movements, most often choreiform, brought on by levodopa or other dopaminergic agents. Dyskinesia is caused by overstimulation of dopamine receptors by the use of levodopa, but also by agents that either stimulate or enhance the effect of dopamine at the receptor (e.g., dopamine agonists, monoamine oxidase type B [MAO B] inhibitors, and catechol-O-methyl transferase [COMT] inhibitors).

Motor fluctuations are alterations between periods of a positive response to medication (commonly referred to as "on" periods), and periods of reemergence of parkinsonian symptoms (commonly referred to as "off" periods). The transition from on to off can be sudden and unpredictable. Unpredictable off periods can also occur that have no relationship to timing of levodopa and the wearing off phenomena. Use of home diaries and direct observation can help determine any relationship of levodopa dosing to the off period. Many unpredictable off moments turn out to be end of levodopa dosing wearing off.

“Wearing off" is characterized by the recurrence of parkinsonian symptoms as the effect of levodopa diminishes near the end of the dose interval, usually three to four hours after a dose. Wearing off is often the first and most commonly encountered fluctuation. A majority of patients’ experience wearing off after five years of levodopa treatment; however, in a minority this phenomenon may occur earlier. Other motor fluctuations include freezing of gait that can lead to falls and ultimately loss of independence, acute akinesia, and failed or lack of an on response to levodopa.

Wearing off may be managed initially by increasing the dose of levodopa and/or interval adjustments and use of longer acting levodopa preparations. If levodopa adjustments for wearing off are not adequate or tolerated, the addition of an adjunctive therapy (e.g., dopamine agonist (pramipexole or ropinirole), COMT inhibitor, MAO B inhibitor, or istradefylline) to the levodopa regimen can help to reduce "off" time.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Hoehn and Yahr Scale and the Modified Hoehn and Yahr Scale:

Stage	Hoehn and Yahr Scale	Modified Hoehn and Yahr Scale
0	No signs of disease	No signs of disease
1	Unilateral involvement only, usually minimal or no functional disability	Unilateral involvement only
1.5	--	Unilateral and axial involvement
2	Bilateral or midline involvement without impairment of balance	Bilateral involvement without impairment of balance
2.5	--	Mild bilateral disease with recovery on pull test

3	Bilateral disease: mild to moderate disability with impaired postural reflexes; physically independent	Mild to moderate bilateral disease; some postural instability; physically independent
4	Severely disabling disease; still able to walk or stand unassisted	Severely disability; still able to walk or stand unassisted
5	Confined to bed or wheelchair unless aided	Wheelchair bound or bedridden unless aided
Hoehn M, Yahr M: Parkinsonism: onset, progression and mortality. Neurology 1967; 17 (5):427-442		

Resources:

Nourianz (istradefylline) product information, revised by Kyowa Kirin Inc 03-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 26, 2024.

Ongentys (opicapone) product information, revised by Amneal Pharmaceuticals LLC. 12-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 26, 2024.

Liang TW. Medical management of motor fluctuations and dyskinesia in Parkinson disease. In: UpToDate, Hurtig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2024. Topic last updated September 23, 2024. Accessed September 24, 2024.

Chou KL. Clinical manifestations of Parkinson disease. In: UpToDate, Hurtig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2024. Topic last updated March 14, 2024. Accessed September 24, 2024.

Spindler MA. Initial pharmacologic treatment of Parkinson disease. In: UpToDate, Hurtig HI, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2024. Topic last updated July 15, 2024. Accessed September 24, 2024.