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/or 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.

Medical Necessity Requirements for NOURIANZ (istradefylline) and ONGENTYS (opicapone)

Criteria for Initial Therapy:

Prescriber Qualifications
- A physician specializing in Parkinson's disease or in consultation with a Neurologist

Indication
- Parkinson's disease with "off" episodes adjunctive to carbidopa/levodopa

ORIGINAL EFFECTIVE DATE: 11/21/2019 | ARCHIVE DATE: | LAST REVIEW DATE: 11/20/2025 | LAST CRITERIA REVISION DATE: 11/20/2025

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Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Parkinson's disease is Hoehn and Yahr Stage 2 or greater
- At least 2 hours of off time per day
- Will continue use of levodopa/carbidopa

Alternative Therapies
- Failure, contraindication per FDA label, intolerance, or not a candidate for **ALL** the following:
  - **One trial of dopamine agonist:** pramipexole or ropinirole
  - **One trial of monoamine oxidase B inhibitor:** selegiline (capsule or tablet) or rasagiline mesylate tablet
  - **One trial of catechol O methyltransferase inhibitor (COMT):** entacapone or tolcapone

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No severe hepatic impairment (Child Pugh Class C)
- No end stage renal disease (CrCl less than 15 mL/min or requiring dialysis)
- **Nourianz:** No concurrent use of strong CYP 3A4 inducers (carbamazepine, rifampin, phenytoin, St. John's wort, etc.)
- **Ongentys:** No FDA label contraindications including:
  - History of pheochromocytoma, paraganglioma, or other catecholamine secreting tumors
  - Concurrent use with non selective MAO inhibitors such as phenelzine, isocarboxazid, tranylcypromine

Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes
  - Lab results
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

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Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications

- Continues to be seen by a physician specializing in Parkinson's disease or in consultation with a Neurologist

Clinical Response

- Positive clinical response defined as **THREE** of the following:
  - No evidence of disease progression
  - Functionality retained for most activities of daily living
  - Reduction in off time maintained
  - Increase in on time of at least 1 hour maintained

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- No significant adverse effects such as:
  - Emergent or worsening dyskinesia
  - Emergent or worsening hallucinations or psychotic behaviors
  - Impulse control or compulsive behaviors
- No severe hepatic impairment (Child Pugh Class C)
- No end stage renal disease (CrCl less than 15 mL/min or requiring dialysis)
- **Nourianz:** No concurrent use of strong CYP 3A4 inducers (carbamazepine, rifampin, phenytoin, St. John's wort, etc.)
- **Ongentys:** No FDA label contraindications including:
  - History of pheochromocytoma, paraganglioma, or other catecholamine secreting tumors
  - Concurrent use with non selective MAO inhibitors such as phenelzine, isocarboxazid, tranylcypromine

Documentation Requirements

- Chart notes
- Lab values confirming safe use
- Supporting clinical documentation with evidence of improvement

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Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

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.
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

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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 07-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 27, 2025.

Ongentys (opicapone) product information, revised by Amneal Pharmaceuticals LLC. 02-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 27, 2025.

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 2025. Topic last updated September 16, 2025. Accessed September 19, 2025.

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 2025. Topic last updated May 22, 2025. Accessed September 19, 2025.

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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 2025. Topic last updated July 21, 2025. Accessed September 19, 2025.

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