BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

INBRIJA™ (levodopa) oral inhalation capsule 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:** Inbrija (levodopa) 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 who is having intermittent **OFF** episodes while on continuous carbidopa/levodopa therapy

ORIGINAL EFFECTIVE DATE: 05/16/2019 | ARCHIVE DATE: | LAST REVIEW DATE: 05/16/2024 | LAST CRITERIA REVISION DATE: 05/16/2024

4. Individual has received and completed a **baseline motor score** (must be submitted with request) for Movement Disorder Society United Parkinson's Disease Rating Scale (MDS-USDRS) part III before initiation of treatment and with continued monitoring of the individual as clinically appropriate

5. Agent will be used in combination with continuous carbidopa/levodopa treatment

6. **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)

7. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **TWO** the following:
    a. Pramipexole (Mirapex or generic)
    b. Ropinirole
    c. Amantadine immediate release

8. Individual is not using any of the following contraindicated per FDA label drugs nonselective monoamine oxidase (MAO) inhibitor or who have recently (within 2 weeks) taken a nonselective MAO inhibitor (such as Nardil (phenelzine), Parnate (tranylcypromine), or Marplan (isocarboxazid))

9. Agent will not be used in a patient with a major psychotic disorder

10. Agent will not be used in a patient with asthma, COPD, or other chronic underlying lung disease

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Inbrija (levodopa) 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 in most activities of daily living
    c. Reduction in number of hours of "off" time per day
    d. Increase in number of hours of "on" time per day
    e. At least a 30% reduction in Parkinson's disease symptoms of tremor, rigidity, bradykinesia, and postural instability using MDS-USDRS part III motor score from baseline

3. Individual has been adherent with the medication and continuous carbidopa/levodopa treatment

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. Hallucinations, confusion, insomnia, and excessive dreaming
        ii. Exacerbation of psychosis such as personality changes, agitation, aggressive behavior, paranoia, suicidality, and depression
        iii. Impulse Control/Compulsive behaviors such as increased gambling urges, sexual urges, binge eating, uncontrolled spending or other urges and the inability to control these urges
        iv. New or exacerbation of dyskinesia
        v. Daytime sleepiness or sleep attacks (falling asleep during activities of daily living)

6. Agent will not be used in a patient with a major psychotic disorder

7. Agent will not be used in a patient with asthma, COPD, or other chronic underlying lung disease

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:

Inbrija oral inhalation powder contains levodopa an aromatic amino acid that is the metabolic precursor of dopamine. Levodopa crosses the blood-brain barrier, and it is converted to dopamine in the brain. Inbrija oral inhalation powder is indicated for the intermittent treatment of “OFF” episodes in patients with Parkinson's disease treated with carbidopa/levodopa.

Parkinson’s disease (PD) is a debilitating neurodegenerative disease affecting about 1% of the population that manifests itself as dopamine (DA) levels in the brain decrease. The result of this DA deficiency is seen as motor symptoms of rest tremor, rigidity, and bradykinesia. These symptoms can severely limit activities of daily living.

Motor symptoms of PD are caused by a progressive degeneration of DA containing neurons located in the substantia nigra. Degeneration of the DA neurons leads to DA deficiency and as a result the development of the classic triad of motor symptoms of resting tremor, muscle rigidity and bradykinesia. Non-motor cognitive and psychiatric symptoms are thought to be due to degeneration of other neurotransmitter systems within the brain.

Drug therapy is targeted at reducing symptoms. Oral DA is not used in the treatment of PD because it does not cross the blood brain barrier. On the other hand, oral levodopa does cross the blood brain barrier and its use has been long recognized in clinical practice guidelines and texts as the standard of care for PD. Levodopa is a

precursor of DA, after crossing the blood brain barrier it is converted to DA. Levodopa is thought to be protective against the dopaminergic neuron damage observed in PD.

Oral medications containing levodopa are the most commonly prescribed treatment for PD. These medications usually work quite well when first given. After some time, some individuals start experiencing motor fluctuations where there are alterations between periods of being "on," during which the patient experiences a positive response to medication, and being "off," during which the patient experiences a reemergence of the Parkinson symptoms. “Off” episodes may be characterized by muscle stiffness, slow movements, or difficulty starting movements. “Off” episodes are common in PD and can happen at any time.

Patients with PD often begin to be aware of a "wearing off" or “end-of-dose” effect less than four hours following a dose of levodopa. In some cases, "wearing off" can be managed initially by increasing the dose of levodopa if the patient is taking a relatively low dose and is not having side effects. For patients with more advanced PD, reducing the interval between doses is often an effective strategy and may require the addition of an extra levodopa dose at the end of the day. Some patients may benefit from alternative levodopa formulations.

Other treatments include DA receptor agonists, catechol-O-methyl-transferase (COMT) inhibitors, selective mono-amine oxidase type-B (MAOI-B) inhibitors, and amantadine. These agents are effective and safe in controlling motor symptoms in patients with advanced PD. There is insufficient evidence to conclude that any one of these medications is clinically superior to another and there is insufficient evidence that shows one PD medication as superior to another in terms of improvement in functional outcomes.

Definitions:

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

Activities of daily living (ADL):

Instrumental ADL: Prepare meals, shop for groceries or clothes, use the telephone, manage money, etc.
Self-care ADL: Bathe, dress and undress, feed self, use the toilet, take medications, not bedridden

Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death related to AE
U.S. Department of Health and Human Services, National Institutes of Health, and National Cancer Institute	

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INBRIJA™ (levodopa) oral inhalation capsule
Generic Equivalent (if available)

Resources:

Inbrija (levodopa) inhalation powder product information, revised by Acorda Therapeutics, Inc. 08-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed March 05, 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 February 2024.Topic last updated May 19, 2023. Accessed March 04, 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 February 2024. Topic last updated February 16, 2024. Accessed March 04, 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 February 2024. Topic last updated February 26, 2024. Accessed March 04, 2024.