BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 5/16/19**
SECTION: DRUGS	**LAST REVIEW DATE: 5/16/19**
	LAST CRITERIA REVISION DATE:
	ARCHIVE DATE:

INBRIJA™ (levodopa) oral inhalation capsule

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

INBRIJA™ (levodopa) oral inhalation capsule (cont.)

Criteria:

- **Criteria for initial therapy:** Inbrija (levodopa) oral inhalation powder is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in Neurology or is in consultation with a Neurologist
  2. Individual is 18 years of age or older
  3. A confirmed diagnosis of Parkinson's disease in an individual who is having intermittent OFF episodes while on continuous Carbidopa/Levodopa therapy
  4. A baseline Movement Disorder Society United Parkinson's Disease Rating Scale (MDS-USDRS) part III motor score must be submitted with request
  5. Will be used in combination with continuous carbidopa/levodopa treatment
  6. Individual has failed, or is intolerant to, or has a contraindication such that the individual is unable to use **ALL** the following preferred step therapy agents:
     - **Two** of the following dopamine acting agents: benztopine (Parlodel or generic), pramipexole (Mirapex or generic), or ropinirole (Requip or generic)
     - Amantadine immediate release
  7. There are **NO** contraindications
     - Contraindications include:
       - Currently taking a 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))
  8. Will not be used in a patient with a major psychotic disorder
  9. 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) oral inhalation powder is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in Neurology or is in consultation with a Neurologist
  2. Individual's condition responded or has worsened while on therapy [this can be modified or changed depending on drug or condition]
     - Response is defined as **THREE** of the following:
       - No evidence of disease progression

INBRIJA™ (levodopa) oral inhalation capsule (cont.)

- Functionality retained in most activities of daily living
- Reduction in number of hours of "off" time per day
- Increase in number of hours of "on" time per day
- 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

4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
   - Contraindications as listed in the criteria for initial therapy section
   - Significant adverse effect such as:
     - Hallucinations, confusion, insomnia, and excessive dreaming
     - Exacerbation of psychosis such as personality changes, agitation, aggressive behavior, paranoia, suicidality, and depression
     - 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
     - New or exacerbation of dyskinesia
     - Daytime sleepiness or sleep attacks (falling asleep during activities of daily living)

5. There are no significant interacting drugs

Renewal duration: 12 months

- Inbrija (levodopa) oral inhalation powder for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

1. Lack of final approval from the Food and Drug Administration, and
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
3. Insufficient evidence to support improvement of the net health outcome, and
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*

- Treatment with dosing or frequency outside the FDA-approved dosing and frequency

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™ (levodopa) oral inhalation capsule (cont.)

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:

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

INBRIJA™ (levodopa) oral inhalation capsule (cont.)

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	

Resources:

Inbrija (levodopa) product information accessed 05-14-19 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a906f8e1-6e1c-480a-8276-c01bc65dd3be

UpToDate: Diagnosis and differential diagnosis of Parkinson disease. Current through Apr 2019.

UpToDate: Clinical manifestations of Parkinson disease. Current through Apr 2019.

UpToDate: Initial pharmacologic treatment of Parkinson disease. Current through Apr 2019.

UpToDate: Motor fluctuations and dyskinesia in Parkinson disease. Current through Apr 2019

Goetz CG, Tilley BC, Shaftman ST, et al.: Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale Presentation and Clinimetric Testing Results. Movement Disorders 2008; 23 (15): 2129-2170

Shulman LM, Gruber-Baldini AL, Anderson KE, et al: The clinically important difference on the unified Parkinson's disease rating scale. Arch Neurol. 2010 Jan; 67(1):64-70. doi: 10.1001/archneurol.2009.295.

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.