Clinical Policy: Levodopa Inhalation Powder (Inbrija)

Reference Number: CP.PMN.267
Effective Date: 12.01.21
Last Review Date: 11.22
Line of Business: Commercial, HIM, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Levodopa inhalation powder (Inbrija®) is an aromatic amino acid.

FDA Approved Indication(s)

Inbrija is indicated for the intermittent treatment of OFF episodes in patients with Parkinson's disease (PD) treated with carbidopa/levodopa.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Inbrija is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Parkinson's Disease (must meet all)**:**

1. Diagnosis of PD;
2. Prescribed by or in consultation with neurologist;
3. Age ≥ 18 years;
4. Inbrija will be used as intermittent treatment for OFF episodes;
5. Prescribed concurrently with carbidopa/levodopa at a dose not exceeding 1,600 mg levodopa per day;
6. Member is experiencing motor fluctuations with a minimum of 2 hours of average daily "off" time per waking day (excluding early morning "off" time) while on carbidopa/levodopa therapy (*see Appendix D*);
7. Failure of at least two anti-Parkinson agents from different therapeutic classes, unless clinically significant adverse effects are experienced or all are contraindicated:*
   a. MAO-B inhibitor: rasagiline;
   b. COMT inhibitor: entacapone (Comtan®/Stalevo®), tolcapone;
   c. Dopamine agonist: ropinirole/ropinirole ER, pramipexole/pramipexole ER;

   **Prior authorization may be required for the above agents*
8. Dose does not exceed both of the following (a and b):
   a. 84 mg (two capsules) per inhalation;
   b. Five inhalations (420 mg) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Parkinson's Disease (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. Member continues to receive concurrent treatment with carbidopa/levodopa;
4. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 84 mg (two capsules) per inhalation;
   b. Five inhalations (420 mg) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

COMT: catechol-O-methyl transferase
FDA: Food and Drug Administration
MAO-B: monoamine oxidase type B
PD: Parkinson's disease

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
COMT Inhibitors		
carbadopa/levodopa/ entacapone (Stalevo)	PO: Dose should be individualized based on therapeutic response; doses may be adjusted by changing strength or adjusting interval. Fractionated doses are not recommended and only 1 tablet should be given at each dosing interval.	1,200 mg levodopa/day
entacapone (Comtan)	PO: 200 mg with each dose of levodopa/carbidopa	1,600 mg/day
tolcapone (Tasmar®)	PO: 100 mg 3 times daily, as adjunct to levodopa/carbidopa	300 mg/day
MAO-B Inhibitors		
rasagiline (Azilect)	PO: Monotherapy or adjunctive therapy (not including levodopa): 1 mg once daily. Adjunctive therapy with levodopa: Initial: 0.5 mg once daily; may increase to 1 mg once daily based on response and tolerability.	1 mg/day
Dopamine Agonists		
pramipexole (Mirapex)	PO: Initial dose: 0.125 mg 3 times daily, increase gradually every 5 to 7 days; maintenance (usual): 0.5 to 1.5 mg 3 times daily	4.5 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
pramipexole ER (Mirapex ER)	PO: Initial dose: 0.375 mg once daily; increase gradually not more frequently than every 5 to 7 days to 0.75 mg once daily and then, if necessary, by 0.75 mg per dose	4.5 mg/day
ropinirole (Requip)	PO: Recommended starting dose: 0.25 mg 3 times/day. Based on individual patient response, the dosage should be titrated with weekly increments: Week 1: 0.25 mg 3 times/day; total daily dose: 0.75 mg; week 2: 0.5 mg 3 times/day; total daily dose: 1.5 mg; week 3: 0.75 mg 3 times/day; total daily dose: 2.25 mg; week 4: 1 mg 3 times/day; total daily dose: 3 mg. After week 4, if necessary, daily dosage may be increased by 1.5 mg/day on a weekly basis up to a dose of 9 mg/day, and then by up to 3 mg/day weekly to a total of 24 mg/day.	24 mg/day
ropinirole ER (Requip ER)	PO: Initial dose: 2 mg once daily for 1 to 2 weeks, followed by increases of 2 mg/day at weekly or longer intervals based on therapeutic response and tolerability	24 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): concomitant use of nonselective monoamine oxidase (MAO) inhibitor (e.g., phenelzine, tranylcypromine) or have recently (within 2 weeks) taken a nonselective MAO inhibitor
- Boxed warning(s): none reported

Appendix D: General Information

- Off time/episodes represent a return of Parkinson's disease symptoms (bradykinesia, rest tremor or rigidity) when the L-dopa treatment effect wears off after each dosing interval.
- Parkinson's disease symptoms, resulting from too little levodopa (L-dopa), are in contrast with dyskinesia which typically results from too much L-dopa. The alterations between "on" time (the time when Parkinson's disease symptoms are successfully suppressed by L-dopa) and "off" time is known as "motor fluctuations".
- The addition of carbidopa to L-dopa prevents conversion of L-dopa to dopamine in the systemic circulation and liver.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PD	Inhale the contents of two capsules (84 mg) as needed for OFF symptoms, up to 5 times daily	84 mg/dose, 420 mg/day

VI. Product Availability

Inhalation powder: one capsule contains 42 mg levodopa; carton containing 4 capsules, 12 capsules, 60 capsules or 92 capsules

VII. References

1. Inbrija Prescribing Information. Pearl River, NY: Acorda Therapeutics, Inc; June 2022. Available at: https://www.inbrija.com/. Accessed August 16, 2022.
2. Efficacy and Safety Study of CVT-301 (Levodopa Inhalation Powder) In Parkinson's Disease Patients With OFF Episodes. ClinicalTrials.gov. May 28, 2019. Available at: https://clinicaltrials.gov/ct2/show/NCT02240030. Accessed August 16, 2022.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Accessed August 16, 2022.
4. Miyasaki J, Martin W, Suchowesky O. Practice parameter: Initiation of treatment for Parkinson's disease: (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2002; 58(1):11-17.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.09.21	11.21
4Q 2022 annual review: no significant changes; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	08.16.22	11.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.