Inbrija®
(levodopa inhalation powder)
42 mg capsules

Orally inhaled levodopa

A BRIDGE BETWEEN DOSES®

of CD/LD when PD symptoms start to return

INBRIJA® is indicated for intermittent treatment of OFF episodes in patients with Parkinson's disease (PD) treated with carbidopa/levodopa (CD/LD).

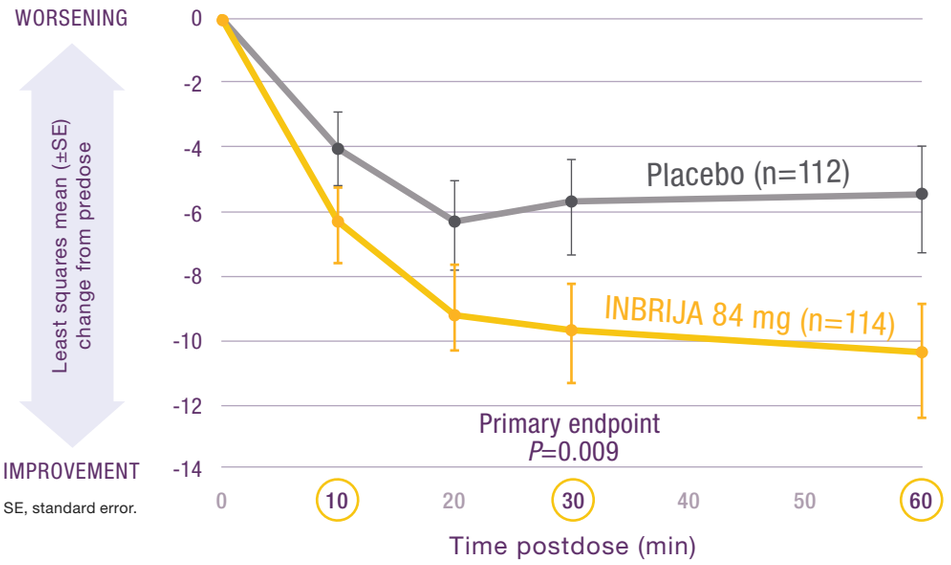
Selected Important Safety Information

- INBRIJA is contraindicated in patients taking or who have recently taken (within 2 weeks) nonselective monoamine oxidase (MAO) inhibitors (e.g., phenelzine and tranylcypromine) due to risk of hypertension. Discontinue use of nonselective MAO inhibitors at least 2 weeks prior to initiating INBRIJA.

Please see additional Important Safety Information on pages 12-13.

INBRIJA HELPS PATIENTS REGAIN MOTOR FUNCTION

UPDRS Part III score change from 0-60 minutes postdose at week 12



SE, standard error.

Please see pages 14-15 for SPAN[SM]-PD study design and baseline characteristics.

Selected Important Safety Information

- Patients treated with levodopa, the active ingredient in INBRIJA, have reported falling asleep during activities of daily living, including operation of motor vehicles, which sometimes resulted in accidents. Many patients reported somnolence but some reported no warning signs (sleep attack). This may occur more than a year after initiating treatment. Reassess patients for drowsiness/sleepiness including occurrence during specific activities. Advise patients of potential for drowsiness and ask about factors that may increase this risk (e.g., sedating medications, sleep disorders).
  - Consider discontinuing INBRIJA in patients who report significant daytime sleepiness or falling asleep during activities that require active participation. If continuing INBRIJA, advise patients not to drive and to avoid activities that may result in harm. There is insufficient information that dose reduction will eliminate episodes of falling asleep during activities of daily living.

USED AS NEEDED, INBRIJA SHOWED:

10 MINUTES

Onset of action:
as early as 10 minutes postdose

30 MINUTES

Primary endpoint:
significant improvement in motor function at 30 minutes postdose (*P*=0.009)

60 MINUTES

Continuation of effect:
60 minutes postdose

HELP YOUR PATIENTS RETURN TO ON WHEN THEY NEED IT

A significantly greater proportion of patients taking INBRIJA 84 mg (58%) vs placebo (36%) returned to an ON state and sustained that ON through 60 minutes postdose (*P*=0.003).

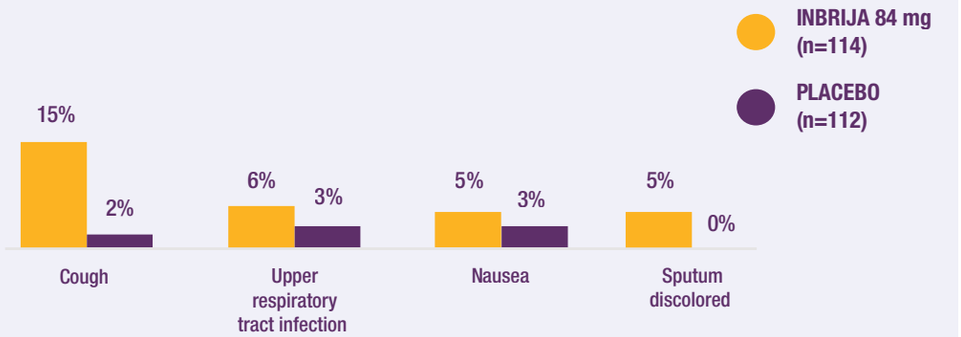
Average use in SPAN-PD was ~2 doses/day

Please see additional Important Safety Information on pages 12-13.

CONSISTENT SAFETY PROFILE ACROSS STUDIES

SPAN-PD SAFETY RESULTS:

Adverse Reactions Occurring in ≥5% of INBRIJA-treated Patients and at a Higher Rate Than Placebo



- Cough was the most common adverse reaction at the time of administration
- Two patients taking INBRIJA 84 mg discontinued therapy because of cough
- Discontinuations due to adverse reactions: 6 patients (5%) on INBRIJA 84 mg and 3 patients (3%) on placebo

Selected Important Safety Information

- INBRIJA may cause or exacerbate dyskinesias. If troublesome dyskinesias occur, consider stopping INBRIJA or adjusting other PD medications.
- Geriatric patients (n=56) experienced more of the following adverse reactions than patients <65 (n=58): cough (25% vs 5%), upper respiratory tract infection (11% vs 2%), nausea (7% vs 3%), vomiting (4% vs 2%), pain in extremities (4% vs 0%), and discolored nasal discharge (4% vs 0%).

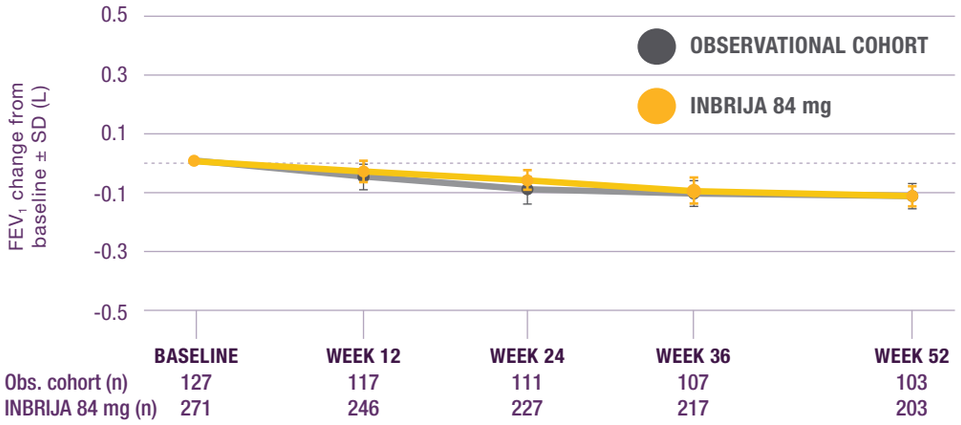
ONE-YEAR PULMONARY SAFETY RESULTS[1]:

A **randomized, controlled, open-label study** assessed the effect of INBRIJA 84 mg (n=271) on **pulmonary function** vs a control group (n=127) observed on their regular PD medications **over 1 year.**

Patients with COPD, asthma, or other chronic respiratory disease were excluded.

Pulmonary function was assessed by spirometry every 3 months in both groups.

Forced expiratory volume in 1 second (FEV_1)



	BASELINE	WEEK 12	WEEK 24	WEEK 36	WEEK 52
Obs. cohort (n)	127	117	111	107	103
INBRIJA 84 mg (n)	271	246	227	217	203

SD, standard deviation.

After 1 year, the average reduction in forced expiratory volume in 1 second (FEV_1) from baseline was the same in both groups (-0.1 L).

- The most common adverse reactions (≥5% of INBRIJA-treated patients and at a higher rate than observational cohort) were cough (13.3% vs 0.8%), fall (8.1% vs 5.5%), nasopharyngitis (6.6% vs 5.5%), and dyskinesia (6.3% vs 3.9%)
- Of the 36 patients who reported cough, 28 (78%) were within the first 30 days of treatment
- The most common adverse reaction leading to discontinuation was cough in 3 patients in the INBRIJA cohort
- There were no discontinuations due to adverse reactions in the observational cohort

Please see additional Important Safety Information on pages 12-13.

SAFETY AND TOLERABILITY OF INBRIJA FOR EARLY MORNING OFF

EARLY MORNING OFF SAFETY RESULTS[2]:

- A randomized, placebo-controlled, double-blind, 2-way crossover study with 1:1 randomization to 2 crossover dosing periods to evaluate the safety and tolerability of INBRIJA for early morning OFF
- Patients withheld oral CD/LD overnight and in the morning until arriving at study site. Last oral CD/LD dose was taken more than 8 hours prior to study treatment
- Patients in an OFF state used INBRIJA 84 mg or placebo immediately after the first oral CD/LD dose on the study day
- Key inclusion and exclusion criteria were the same as for SPAN-PD

Mean Baseline Characteristics (N=36)	
Age (range, 39-81 yr)	62.9 yr
Gender (male)*	58.3%
Ethnicity (white)*	94.4%
Time since diagnosis	7.9 yr
Daily oral levodopa dose	727.5 mg
Oral levodopa morning dose	183.8 mg

*Not mean value.

Adverse Reactions Occurring in ≥5% of INBRIJA-treated Patients and at a Higher Rate Than Placebo

Adverse Reaction	INBRIJA 84 mg n=36 n (%)	PLACEBO n=36 n (%)
Cough	4 (11.1)	1 (2.8)
Moderate dyskinesia	2 (5.6)	1 (2.8)

- There were no discontinuations due to adverse reactions

A single dose of INBRIJA administered immediately after oral CD/LD for early morning OFF resulted in no additional safety concerns

Selected Important Safety Information

- The most common adverse reactions (≥ 5% and > placebo) were cough (15% vs 2%), upper respiratory tract infection (6% vs 3%), nausea (5% vs 3%), and sputum discolored (5% vs 0%).
- INBRIJA may cause or exacerbate dyskinesias. If troublesome dyskinesias occur, consider stopping INBRIJA or adjusting other PD medications.
- Geriatric patients (n=56) experienced more of the following adverse reactions than patients <65 (n=58): cough (25% vs 5%), upper respiratory tract infection (11% vs 2%), nausea (7% vs 3%), vomiting (4% vs 2%), pain in extremities (4% vs 0%), and discolored nasal discharge (4% vs 0%).

Please see additional Important Safety Information on pages 12-13.

Inbrija®
(levodopa inhalation powder)
42 mg capsules

ORALLY INHALED LEVODOPA

INBRIJA—FOR USE AS NEEDED WHEN PD SYMPTOMS START TO RETURN

99.8% OF PATIENTS (628/629) IN 2 CLINICAL TRIALS DEMONSTRATED THE ABILITY TO SELF-ADMINISTER INBRIJA WHILE IN AN OFF PERIOD AFTER INSTRUCTION[3]

Dosing and Administration

- One dose (84 mg) = two 42-mg capsules
  - For oral inhalation only; INBRIJA capsules must not be swallowed as the intended effect will not be obtained
- No more than 1 dose per OFF period
- May be taken as needed up to a maximum of 5 doses per day when symptoms return
  - Average number of doses in clinical trials: ~2 per day
- No titration
- No pre-medication
- Effective only in combination with CD/LD-based regimen
- Capsules should be stored in their blister package and only removed immediately before use
- INBRIJA capsules are only for use with the INBRIJA inhaler

HELPFUL HINTS TO GET YOUR PATIENTS STARTED WITH INBRIJA

Before getting your patients started, remind them that using INBRIJA may take some practice at first.

Keep the following helpful hints in mind:

1. **Stand or sit up straight** and look straight ahead while breathing in
2. **Breathe in slowly and gently**, just enough to hear or feel the capsule whirl
3. **They may take more than one breath** per capsule
4. **It is quite common to cough** when breathing in, but try not to

Some patients have found that sipping liquid before and after breathing in INBRIJA helps with cough. For some people, coughing may feel like the sensation of choking.

Please see Instructions For Use.

VISIT INBRIJA-HCP.COM FOR MORE HELPFUL HINTS

Selected Important Safety Information

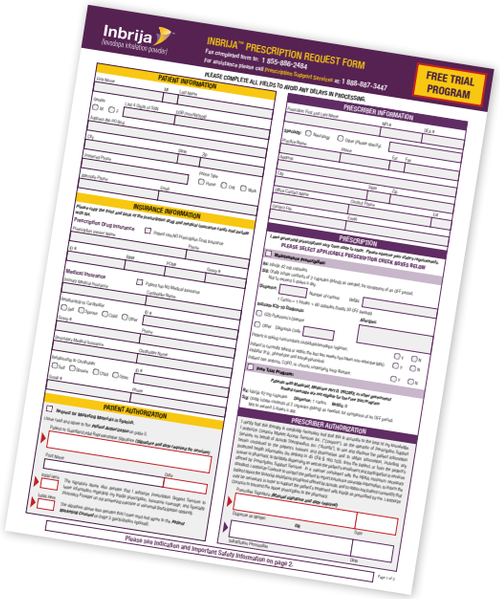
- Neuroleptic malignant syndrome-like symptoms (e.g., elevated temperature, muscular rigidity, altered consciousness, autonomic instability) have been reported with rapid dose reduction, withdrawal of, or changes in dopaminergic therapy.
- Hallucinations (with or without confusion, insomnia, and excessive dreaming) may occur and may respond to reducing levodopa therapy. Abnormal thinking and behavior may present with paranoid ideation, delusions, hallucinations, confusion, psychotic-like behavior, disorientation, aggressive behavior, agitation, and delirium.
- INBRIJA is not recommended in patients with asthma, COPD, or other chronic underlying lung disease because of the risk of bronchospasm.

Please see additional Important Safety Information on pages 12-13.

HOW TO PRESCRIBE INBRIJA

Get your patients started on INBRIJA today by completing a Prescription Request Form (PRF)

- Fill in the information and sign and date the form
- Patient signs and dates the form if they would like to access manufacturer-sponsored programs
- Submit the form by faxing to **Prescription Support Services** at **1-855-886-2484**
- INBRIJA will be delivered directly to your patient's door


Inbrija
(levodopa inhalation powder)
INBRIJA™ PRESCRIPTION REQUEST FORM
FREE TRIAL PROGRAM
PATIENT INFORMATION
PRESCRIBER INFORMATION
INSURANCE INFORMATION
PRESCRIPTION
PATIENT AUTHORIZATION
PRESCRIBER AUTHORIZATION

GO TO HTTP://RESOURCES.INBRIJA-HCP.COM FOR PATIENT RESOURCES AND PRESCRIBING SUPPORT

INBRIJA RESOURCES AND PATIENT SUPPORT

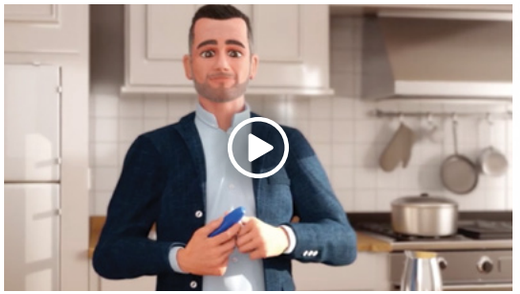
Prescription Support Services

Prescription Support Services is available to support your patients with the process of verifying and obtaining insurance reimbursement for INBRIJA. In addition to performing a benefits investigation, Prescription Support Services will also determine eligibility for the following programs:

- **INBRIJA Co-pay Assistance**
- **FREE Trial Program**
- **Patient Assistance Program (PAP)**

Training Resources

- Demonstration video
- Demonstration kit
- Helpful Hints brochure
- Instructions For Use



Nurse Educators

Patients starting INBRIJA will be contacted by Prescription Support Services and offered the opportunity to speak with a Nurse Educator who will reinforce how to use INBRIJA.

Please see additional Important Safety Information on pages 12-13.

Inbrija®
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42 mg capsules

IMPORTANT SAFETY INFORMATION

- INBRIJA is contraindicated in patients taking or who have recently taken (within 2 weeks) nonselective monoamine oxidase (MAO) inhibitors (e.g., phenelzine and tranylcypromine) due to risk of hypertension. Discontinue use of nonselective MAO inhibitors at least 2 weeks prior to initiating INBRIJA.
- Patients treated with levodopa, the active ingredient in INBRIJA, have reported falling asleep during activities of daily living, including operation of motor vehicles, which sometimes resulted in accidents. Many patients reported somnolence but some reported no warning signs (sleep attack). This may occur more than a year after initiating treatment. Reassess patients for drowsiness/sleepiness including occurrence during specific activities. Advise patients of potential for drowsiness and ask about factors that may increase this risk (e.g., sedating medications, sleep disorders).
  - Consider discontinuing INBRIJA in patients who report significant daytime sleepiness or falling asleep during activities that require active participation. If continuing INBRIJA, advise patients not to drive and to avoid activities that may result in harm. There is insufficient information that dose reduction will eliminate episodes of falling asleep during activities of daily living.
- Neuroleptic malignant syndrome-like symptoms (e.g., elevated temperature, muscular rigidity, altered consciousness, autonomic instability) have been reported with rapid dose reduction, withdrawal of, or changes in dopaminergic therapy.
- Hallucinations (with or without confusion, insomnia, and excessive dreaming) may occur and may respond to reducing levodopa therapy. Abnormal thinking and behavior may present with paranoid ideation, delusions, hallucinations, confusion, psychotic-like behavior, disorientation, aggressive behavior, agitation, and delirium.
- INBRIJA should ordinarily not be used in patients with major psychotic disorder due to risk of exacerbating psychosis. Dopamine antagonists used to treat psychosis may exacerbate symptoms of PD and may decrease INBRIJA efficacy.
- Patients on medications that increase central dopaminergic tone such as INBRIJA can experience intense urges to gamble or spend money, increased sexual urges, binge eating, and/or other intense urges, and inability to control them. In some cases, these urges stopped with dose reduction or medication discontinuation. Since some patients may not recognize these behaviors as abnormal, ask patients or their caregivers about development of new or increased urges and consider stopping INBRIJA if this occurs.
- INBRIJA may cause or exacerbate dyskinesias. If troublesome dyskinesias occur, consider stopping INBRIJA or adjusting other PD medications.
- INBRIJA is not recommended in patients with asthma, COPD, or other chronic underlying lung disease because of the risk of bronchospasm.
- Monitor patients with glaucoma for increased intraocular pressure.
- Abnormalities in laboratory tests may include elevations of liver function tests (e.g., alkaline phosphatase, AST, ALT, lactic dehydrogenase, bilirubin), blood urea nitrogen, hemolytic anemia, and positive direct antibody test. Increased levels of catecholamines and their metabolites in plasma and urine may result in false-positive results suggesting pheochromocytoma.
- The most common adverse reactions (≥ 5% and > placebo) were cough (15% vs 2%), upper respiratory tract infection (6% vs 3%), nausea (5% vs 3%), and sputum discolored (5% vs 0%).
- Use of selective MAO-B inhibitors with INBRIJA may be associated with orthostatic hypotension. Monitor patients taking these drugs concurrently.
- Dopamine D2 receptor antagonists (e.g., phenothiazines, butyrophenones, risperidone, metoclopramide) and isoniazid may reduce levodopa efficacy; monitor for worsening symptoms.
- Iron salts or multivitamins with iron salts may reduce levodopa bioavailability.
- INBRIJA should be used during pregnancy/nursing only if potential benefit justifies potential risk. There are no adequate data on INBRIJA in pregnant women or breastfed infants. Animal data shows carbidopa/levodopa is developmentally toxic (including teratogenicity). Levodopa may affect milk production, interfering with lactation. Levodopa has been detected in human milk.
- Safety and effectiveness in pediatric patients have not been established.
- Geriatric patients (n=56) experienced more of the following adverse reactions than patients <65 (n=58): cough (25% vs 5%), upper respiratory tract infection (11% vs 2%), nausea (7% vs 3%), vomiting (4% vs 2%), pain in extremities (4% vs 0%), and discolored nasal discharge (4% vs 0%).

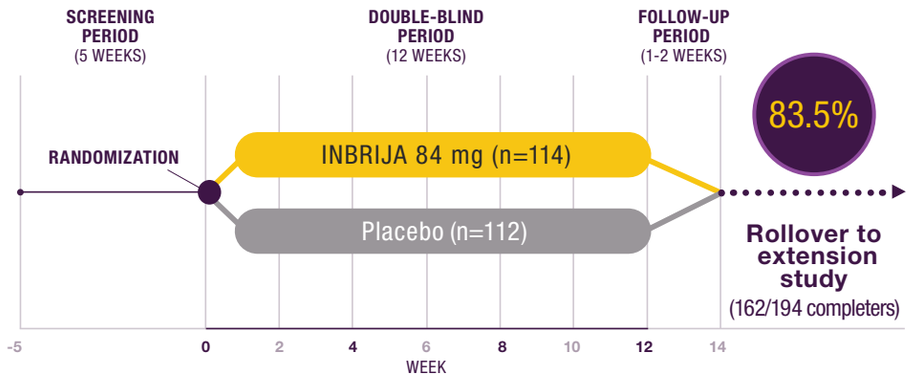
Please see Full Prescribing Information by visiting https://www.inbrija.com/prescribing-information.pdf.

Inbrija®
(levodopa inhalation powder)
42 mg capsules

SPAN-PD: PIVOTAL STUDY IN PATIENTS WITH PD EXPERIENCING A RETURN OF SYMPTOMS[3,4]

SPAN-PD was a 12-week, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of INBRIJA for the treatment of OFF periods in patients with PD treated with CD/LD.

Study Design (N=226)



Use at home:

Used at the start of an OFF period

Continued use of usual PD medications including CD/LD

Self-administered as needed no more than 5 times during the waking day

In-clinic dosing at weeks 0, 4, 8, and 12:

Patients took morning CD/LD as usual and arrived in the ON state

Patients remained in clinic until they transitioned into an OFF period

Patients self-administered study drug at the start of the OFF period

Primary endpoint: UPDRS* Part III motor score at 30 minutes: change from predose OFF to 30 minutes postdose with INBRIJA 84 mg vs placebo

*Unified Parkinson's Disease Rating Scale (UPDRS), Part III is a composite measure of 14 items designed to assess the severity of primary motor symptoms (e.g., tremor, rigidity, bradykinesia, postural instability) in patients with PD. Disability level is evaluated from 27 questions with a maximum score of 108, 108 (total disability) and 0 (no disability).[5]

Patients at baseline had:

- CD/LD regimen not exceeding 1600 mg/day of levodopa
- ≥2 hours of OFF time per day
- Hoehn and Yahr stage <2.5 (64.6% of patients)
- Mean UPDRS Part III motor scores in ON state at screening: 14.9 for INBRIJA 84 mg and 16.1 for placebo

Key exclusion criteria:

- Patients with asthma, COPD, or other chronic respiratory disease
- Use of apomorphine

Mean Baseline Patient Characteristics (N=226)	
Age (range, 38-82 yr)	63.0 yr
Gender (male)*	75%
Ethnicity (white)*	95%
Time since diagnosis	8.0 yr
Number of OFF periods per day†	3.4
Duration of oral levodopa treatment	6.5 yr
Daily oral levodopa dose	830 mg
Number of daily oral levodopa doses	5.1

*Not mean value.
†Includes early morning OFF.

PD Medications Used in Addition to CD/LD

- Dopamine agonists (57.5%)
- Selective MAO-B inhibitors (38.9%)
- Adamantane derivatives (19.9%)
- COMT inhibitors (14.2%)

COMT, catechol-O-methyltransferase; MAO-B, monoamine oxidase B.

Selected Important Safety Information

- INBRIJA should ordinarily not be used in patients with major psychotic disorder due to risk of exacerbating psychosis. Dopamine antagonists used to treat psychosis may exacerbate symptoms of PD and may decrease INBRIJA efficacy.
- Use of selective MAO-B inhibitors with INBRIJA may be associated with orthostatic hypotension. Monitor patients taking these drugs concurrently.

Please see additional Important Safety Information on pages 12-13.

For patients taking CD/LD

INBRIJA—FOR USE AS NEEDED WHEN PD SYMPTOMS START TO RETURN

Inbrija®
(levodopa inhalation powder)
42 mg capsules

Inhaled levodopa

Helps patients
regain motor function

10 MINUTES

Starts to work in
as soon as 10 minutes
postdose

No titration

99.8%

of **629** patients in 2 clinical trials demonstrated the **ability to self-administer INBRIJA** while in an OFF period after instruction[3]

Selected Important Safety Information

- INBRIJA is not recommended in patients with asthma, COPD, or other chronic underlying lung disease because of the risk of bronchospasm
- The most common adverse reactions (≥ 5% and > placebo) were cough, upper respiratory tract infection, nausea, and discolored sputum

Please see additional Important Safety Information on pages 12-13 and Full Prescribing Information by visiting https://www.inbrija.com/prescribing-information.pdf.

References: 1. Grosset DG, et al. *Parkinsonism Relat Disord*. 2020;71:4-10. **2.** Hauser RA, et al. *Parkinsonism Relat Disord*. 2019;64:175-180. **3.** Data on file. Acorda Therapeutics. **4.** LeWitt PA, et al. *Lancet Neurol*. 2019;18:145-154. **5.** Fahn S, et al. In: Fahn S, et al, eds. Recent Developments in Parkinson's Disease, vol 2. 1987:153-163, 293-304.

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