

INBRIJA™ Fact Sheet



About INBRIJA

- INBRIJA is the **first and only** orally inhaled levodopa used for intermittent treatment of OFF episodes in people with Parkinson's disease treated with carbidopa/levodopa
- **One dose, two 42 mg capsules (84 mg)**, of INBRIJA can be **orally inhaled** as needed for symptoms of OFF periods

Selected Important Safety Information

No more than 1 dose (2 capsules) should be taken for any OFF period. No more than 5 doses (10 capsules) of INBRIJA should be taken in a day.

INBRIJA is for oral inhalation only. INBRIJA capsules are not to be swallowed or opened.

About OFF Periods in Parkinson's

Approximately

ONE MILLION

people in the United States have Parkinson's and approximately

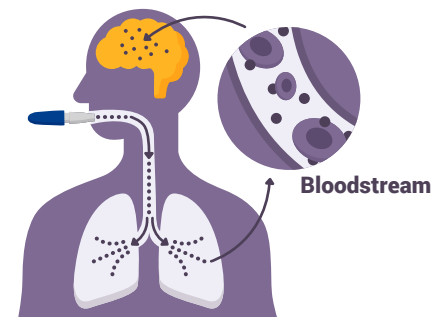
40%

of people with Parkinson's have OFF periods

- Many people with Parkinson's **fluctuate** between:
 - ON periods, during which symptoms are **controlled**
 - OFF periods, during which Parkinson's symptoms **return**
- OFF periods result from **low levels of dopamine** between doses of carbidopa/levodopa, the gold standard baseline Parkinson's treatment
- OFF periods can be **unpredictable** and appear more often over time
- Motor symptoms during OFF periods can affect a person's **ability to move**

How INBRIJA is Delivered

- The INBRIJA inhaler is **breath-actuated**, which means it's powered by inhalation
 - The inhaler releases INBRIJA into the lungs without needing to be pressed or manipulated in coordination with inhalation
 - Please refer to Instructions For Use at www.INBRIJA.com/prescribing-information.pdf
 - When used properly, the INBRIJA inhaler makes a unique "whirl" (spin) sound so the user knows the inhaler is working and the medicine is being delivered
- Due to the effects of food and gastrointestinal challenges of the disease, absorption of oral medication can be variable and contribute to the development of OFF periods
- INBRIJA enters from the mouth into the lungs, through the bloodstream into the brain and does not depend on absorption in the digestive tract



99.8% of people (628 of 629 in two clinical trials) demonstrated the ability to self-administer INBRIJA during an OFF period after instruction

Selected Important Safety Information

INBRIJA is not to be used if patients take or have taken a nonselective monoamine oxidase inhibitor such as phenelzine or tranylcypromine within the last two weeks.

How Was INBRIJA Developed?

More than

20 YEARS

of research and development has been spent on the ARCUS[®] technology platform that is used in the manufacturing of INBRIJA

ARCUS is an innovative technology platform that **transforms the size and shape of particles containing levodopa** to enable its delivery through inhalation.

The idea for this technology originated in the lab of Robert Langer, Sc.D. at the Massachusetts Institute of Technology (MIT).

INBRIJA Efficacy in SPANSM-PD

The U.S. Food and Drug Administration (FDA) approval of INBRIJA was based on a development program with approximately 900 people with Parkinson's experiencing OFF periods.

The Phase 3 pivotal efficacy trial – SPAN-PD – was a 12-week, randomized, placebo controlled, double blind study evaluating the effectiveness of INBRIJA in people with mild to moderate Parkinson's experiencing OFF periods for at least two hours per day.

INBRIJA treated patients were 45-82 years of age (mean 63.5 years of age) and were predominantly male (72%) and white (94%). All patients were also treated with oral carbidopa/levodopa (at dose no higher than 1600 mg/day of levodopa). The mean UPDRS Part III scores at screening in the ON state were 14.9 for patients randomized to INBRIJA 84 mg and 16.1 for patients randomized to placebo.

In SPAN-PD, at 12 weeks:

People treated with INBRIJA significantly improved their motor function

30 MINUTES

after use vs. placebo

Improvement was measured by the Unified Parkinson's Disease Rating Scale (UPDRS) Part III motor score (average change of -9.8 points with INBRIJA 84 mg vs. -5.9 points with placebo; p=0.009, statistically significant)

Onset of action was seen as early as

10 MINUTES

58%

of people treated with INBRIJA 84 mg returned to ON and sustained that ON through 60 minutes vs. **36%** of people who received placebo (p=0.003, statistically significant)

Selected Important Safety Information

Before using INBRIJA, patients should tell their healthcare provider about all their medical conditions, including:

- asthma, chronic obstructive pulmonary disease (COPD), or any chronic lung disease
- daytime sleepiness from a sleep disorder or if they get drowsy/sleepy without warning or take a medicine that increases sleepiness such as sleep medicines, antidepressants, or antipsychotics
- feel dizzy, nausea, sweaty, or faint when standing from sitting/lying down
- history of abnormal movement (dyskinesia)
- mental health problem such as hallucinations or psychosis
- uncontrollable urges (for example, gambling, increased sexual urges, intense urges to spend money, or binge eating)
- glaucoma
- pregnancy or plans to become pregnant. It is not known if INBRIJA will harm an unborn baby.
- breastfeeding or plans to breastfeed. Levodopa (the medicine in INBRIJA) can pass into breastmilk and it is unknown if it can harm the baby.

INBRIJA Safety in SPAN-PD

In the 12-week SPAN-PD trial, the most common side effects in at least 5% of people treated with INBRIJA and higher than placebo were:



Cough
(15% INBRIJA
vs. 2% placebo)



**Upper respiratory
tract infection**
(6% INBRIJA vs. 3% placebo)



Nausea
(5% INBRIJA vs.
3% placebo)



**Change in the color
of saliva or spit**
(5% INBRIJA vs. 0% placebo)

In the INBRIJA 84 mg group, 5% discontinued due to side effects. The most common of these side effects was cough leading to 2% discontinuation. In the placebo group, 3% discontinued due to side effects and no discontinuation was attributed to cough.

INBRIJA Long-term Lung Function Data

A Phase 3 long-term, active-controlled, randomized, open-label study assessed lung function over one year. Patients with chronic obstructive pulmonary disease (COPD), asthma, or other chronic respiratory disease within the last five years were excluded from the study.

There was

NO DIFFERENCE IN LUNG FUNCTION

between the INBRIJA group and the observational group over one year based on forced expiratory volume in one second (FEV₁)

Selected Important Safety Information

Patients should tell their healthcare provider if they take:

- MAO-B inhibitors
- dopamine D2 receptor antagonists (including phenothiazines, butyrophenones, risperidone, metoclopramide), or isoniazid
- iron salts or multivitamins that contain iron salts

Patients are not to drive, operate machinery, or do other activities until they know how INBRIJA affects them. Sleepiness and falling asleep suddenly can happen as late as a year after treatment is started.

Additional Important Safety Information

INBRIJA can cause serious side effects including the following. Patients should tell their healthcare provider if they experience them:

- **falling asleep during normal daily activities** (such as driving, doing physical tasks, using hazardous machinery, talking, or eating) and can be without warning. If patients become drowsy while using INBRIJA, they should not drive or do activities where they need to be alert. Chances of falling asleep during normal activities increases if patients take medicines that cause sleepiness.
- **withdrawal-emergent hyperpyrexia and confusion** (symptoms including fever, confusion, stiff muscles, and changes in breathing and heartbeat) in patients who suddenly lower or change their dose or stop using INBRIJA or carbidopa/levodopa medicines.
- **low blood pressure** with or without dizziness, fainting, nausea, and sweating. Patients should get up slowly after sitting or lying down.
- **hallucinations and other psychosis** – INBRIJA may cause or worsen psychotic symptoms including hallucinations (seeing/hearing things that are not real); confusion, disorientation, or disorganized thinking; trouble sleeping; dreaming a lot; being overly suspicious or feeling people want to harm them; believing things that are not real, acting aggressive, and feeling agitated/restless.
- **unusual uncontrollable urges** such as gambling, binge eating, shopping, and sexual urges has occurred in some people using medicines like INBRIJA.
- **uncontrolled, sudden body movements (dyskinesia)** may be caused or worsened by INBRIJA. INBRIJA may need to be stopped or other Parkinson's medicines may need to be changed.
- **bronchospasm** – people with asthma, COPD, or other lung diseases may wheeze or have difficulty breathing after inhaling INBRIJA. If patients have these symptoms, they should stop taking INBRIJA and call their healthcare provider or go to the nearest hospital emergency room right away.
- **increased eye pressure** in patients with glaucoma. Healthcare providers should monitor this.
- **changes in certain lab values** including liver tests

The most common side effects of INBRIJA include cough, upper respiratory tract infection, nausea, and change in the color of saliva or spit.

Please see Instructions For Use, Patient Information Leaflet, and Full Prescribing Information at www.INBRIJA.com/prescribing-information.pdf.