Trudhesa™
(dihydroergotamine mesylate) nasal spray
0.725 mg per spray

NATIONWIDE AVAILABILITY ONLY THROUGH PHIL AND CAREPOINT PHARMACY

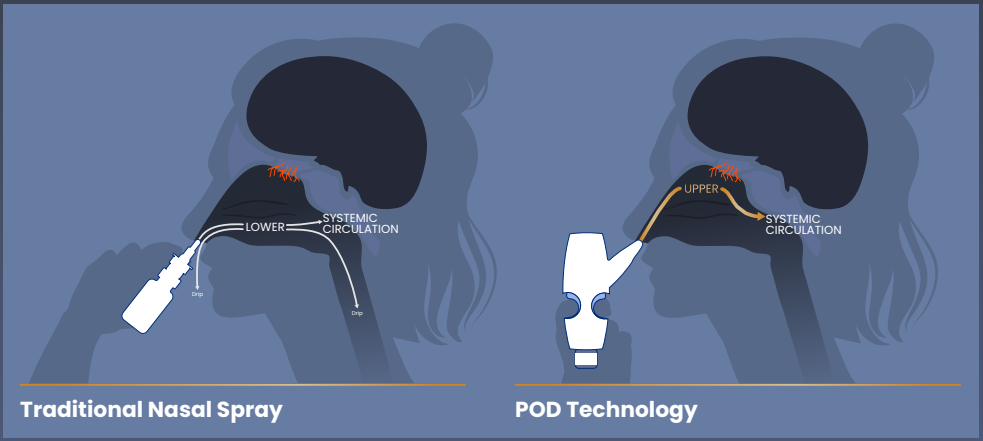
DISCOVER UPPER NASAL SPACE

WHERE FEW MIGRAINE MEDS HAVE GONE BEFORE[1,2]

pod® TECHNOLOGY

Trudhesa™ is the only migraine treatment that uses advanced Precision Olfactory Delivery (POD®) technology to gently and consistently deliver dihydroergotamine mesylate (DHE) to the vascular-rich upper nasal space.[1-3]

There's nasal, and then there's upper nasal[1]



Traditional Nasal Spray | **POD Technology**

The upper nasal space is highly permeable and vascular-rich, providing[2-4]:

- ✓ Consistent and predictable medication delivery (vs the significant drug loss common with lower nasal space delivery)
- ✓ Increased bioavailability–Trudhesa achieved an absolute DHE bioavailability four times that of traditional DHE nasal spray
- ✓ Rapid and sustained IV-like DHE plasma concentrations with no initial C_{max} spike
- ✓ Rapid absorption into the bloodstream

Trudhesa has the potential to give patients rapid, sustained, consistent pain relief, with no dosing window.[3-6]

Important Safety Information

Indication

Trudhesa is an ergotamine derivative indicated for the acute treatment of migraine with or without aura in adults.

WARNING: PERIPHERAL ISCHEMIA FOLLOWING COADMINISTRATION WITH POTENT CYP3A4 INHIBITORS

Serious and/or life-threatening peripheral ischemia has been associated with the coadministration of dihydroergotamine with strong CYP3A4 inhibitors. Because CYP3A4 inhibition elevates the serum levels of dihydroergotamine, the risk for vasospasm leading to cerebral ischemia and/or ischemia of the extremities is increased. Hence, concomitant use of Trudhesa with strong CYP3A4 inhibitors is contraindicated.

Limitations of Use

Trudhesa is not indicated for the preventive treatment of migraine or for the management of hemiplegic or basilar migraine.

Please see the enclosed Trudhesa Prescribing Information, including **Boxed Warning** and Medication Guide.

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POD® technology—far from just a nasal spray[1]

POD is manually actuated and propellant-powered, so coordinated inhaling is not needed[1]

- ✓ Gently and consistently delivers DHE into the upper nasal space[1,3]
- ✓ Prevents DHE from spilling down the front of the lip or down the throat to enable consistent drug delivery and possibly reduce adverse taste[3]
- ✓ Avoids GI tract degradation and first-pass metabolism of oral treatments[7]
- ✓ Circumvents the impact of autonomic dysfunction associated with migraine[1,8]

Using POD to rapidly and consistently deliver DHE, Trudhesa achieves increased bioavailability compared to a traditional DHE nasal spray and circumvents common GI issues.[1-3,8]

Scan the QR code or visit trudhesaHCP.com/upper-nasal to watch a video on Trudhesa and the upper nasal space

Contraindications

Trudhesa is not recommended in patients with:

- Concomitant use of strong CYP3A4 inhibitors such as protease inhibitors (eg, ritonavir, nelfinavir, or indinavir) and macrolide antibiotics (eg, erythromycin or clarithromycin)
- Ischemic heart disease or coronary artery vasospasm
- Uncontrolled hypertension, known peripheral arterial diseases, sepsis, following vascular surgery, or severe hepatic or renal impairment
- Hypersensitivity to ergot alkaloids
- Concomitant use of other 5-HT_1 agonists (eg, sumatriptan) or ergotamine-containing or ergot-type medications within 24 hours
- Concomitant use of peripheral and central vasoconstrictors

Warnings and Precautions

Trudhesa may cause:

- **Cardiac events:** Cardiac events in patients with risk factors of coronary artery diseases: Consider administration of the first dose of Trudhesa under medical supervision (including the use of an electrocardiogram)
- **Cerebrovascular events:** Cerebrovascular events (eg, cerebral hemorrhage, subarachnoid hemorrhage, and stroke) have been reported, particularly with dihydroergotamine mesylate injection
- **Vasospasm/elevated blood pressure:** Dihydroergotamine may cause vasospasm or elevation in blood pressure
- **Fibrotic complications:** Rare cases have been reported following prolonged daily use of dihydroergotamine mesylate. Administration of Trudhesa should not exceed the dosing guidelines or be used for chronic daily administration
- **Medication overuse headache:** Detoxification may be necessary
- **Preterm labor:** Advise pregnant women of the risk
- **Local irritation:** Local irritation has been reported following administration of Trudhesa

Most Common Adverse Reactions

Most common adverse reactions (incidence >1%) were rhinitis, nausea, altered sense of taste, application site reactions, dizziness, vomiting, somnolence, pharyngitis, and diarrhea.

Use in Special Populations

Pregnancy: Available data from published literature indicate an increased risk of preterm delivery with Trudhesa use during pregnancy.

Lactation: Patients should not breastfeed during treatment with Trudhesa and for 3 days after the last dose.

Please see the Trudhesa Full Prescribing Information, including **Boxed Warning** and Medication Guide.

The risk information provided here is not comprehensive. The FDA-approved product labeling can be found at www.trudhesaHCP.com or 1-800-555-DRUG. You can also call 1-833-TRUDHESA (1-833-878-3437) for additional information.

References: 1. Trudhesa. Prescribing information. Impel NeuroPharma; 2021. **2.** Shrewsbury SB, Jeleva M, Satterly KH, Lickliter J, Hoekman J. STOP 101: a phase 1, randomized, open-label, comparative bioavailability study of INP104, dihydroergotamine mesylate (DHE) administered intranasally by a I123 Precision Olfactory Delivery (POD®) Device, in healthy adult subjects. *Headache.* 2019;59(3):394-409. **3.** Smith TR, Winner P, Aurora SK, Jeleva M, Hocevar-Trnka J, Shrewsbury SB. STOP 301: a phase 3, open-label study of safety, tolerability, and exploratory efficacy of INP104, Precision Olfactory Delivery (POD®) of dihydroergotamine mesylate, over 24/52 weeks in acute treatment of migraine attacks in adult patients [published online ahead of print, 2021 Aug 7]. *Headache.* 2021;10.1111/head.14184. doi:10.1111/head.14184. **4.** Data on File. Impel NeuroPharma. 2020. **5.** Tepper SJ, Ailani J, Shrewsbury SB, Aurora SK. Recurrence rates for INP104 for the acute treatment of migraine: results from the phase 3 STOP 301 study. Poster presented at: American Headache Society Virtual Annual Scientific Meeting, June 3-6, 2021. **6.** Aurora SK, Ray S, Satterly K, Shrewsbury SB, Hoekman J. Does dihydroergotamine treat the "whole migraine"? Poster presented at: American Headache Society Virtual Annual Scientific Meeting, June 2020. **7.** Hoekman J, Ray S, Aurora SK, Shrewsbury SB. The upper nasal space—a novel delivery route ideal for central nervous system drugs. *US Neurology.* 2020;16(1):25-31. **8.** Aurora SK, Papapetropoulos, Kori S. Gastric stasis in migraineurs: etiology, characteristics, and clinical and therapeutic implication. *Cephalalgia.* 2013;33(6):408-415.

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