



**BlueCross
BlueShield**

Federal Employee Program.

DIHYDROERGOTAMINE NASAL SPRAYS

Migranal Nasal Spray (dihydroergotamine)
Trudhesa Nasal Spray* (dihydroergotamine)

*This medication is currently pending tier determination and may not be available at this time

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

DHE (dihydroergotamine) is used for the treatment of migraine headache with or without aura. DHE targets receptors in both the central and the peripheral parts of the nervous system. The therapeutic activity of dihydroergotamine in migraine is generally attributed to the agonist effect at 5-HT_{1D} receptors. Activation of 5-HT_{1D} receptors located on intracranial blood vessels leads to vasoconstriction, which correlates with the relief of migraine headache. Most migraines are characterized by certain types of headache pain with or without other symptoms. One-sided, throbbing, pulsating head pain that can be accompanied by nausea, vomiting, and/or sensitivity to light and noise is typical of migraines. Some people may also experience aura, or visual displays, before or during attacks (1-2).

Regulatory Status

FDA-approved indication: Dihydroergotamine Nasal Sprays are indicated for the acute treatment of migraine headaches with or without aura (1-2).

Limitations of Use:

Migranal Nasal Spray and Trudhesa Nasal Spray are not indicated for the preventative treatment of migraine or for the management of hemiplegic or basilar migraine (1-2).

Migranal and Trudhesa have boxed warnings for serious and/or life-threatening peripheral ischemia which has been associated with the co-administration of dihydroergotamine with potent CYP3A4 inhibitors including protease inhibitors and macrolide antibiotics. 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 (1-2).

For the acute treatment of migraine headaches, one spray (0.5mg) of Migranal should be administered in each nostril. Fifteen minutes later, an additional one spray (0.5mg) of Migranal should be administered in each nostril, for a total dosage of four sprays (2mg) of Migranal. Studies

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have shown no additional benefit from acute doses greater than 2mg for a single migraine administration. The safety of doses greater than 3mg in a 24 hour period and 4mg in a seven-day period has not been established. Migranal should not be used for chronic daily administration (1).

The recommended dose of Trudhesa is 1.45 mg administered as two metered sprays into the nose (one spray of 0.725 mg into each nostril). The dose may be repeated, if needed, a minimum of 1 hour after the first dose. Patients should not use more than 2 doses of Trudhesa within a 24-hour period or 3 doses within a 7-day period (2).

Frequent use of acute medications is generally thought to cause medication-overuse headache. To decrease the risk of medication-overuse headache (“rebound headache” or “drug-induced headache”) many experts limit acute therapy to two headache days per week on a regular basis. Based on concerns of overuse, medication-overuse headache, and withdrawal, the use of dihydroergotamine should be limited and carefully monitored. The quantity limit is set to contain treatment for up to eight headaches per month without exceeding the maximum weekly dose allowed per package insert (1-5).

The safety and effectiveness in pediatric patients less than 18 years of age have not been established (1-2).

Summary

DHE (dihydroergotamine) is used for the treatment of migraine headache with or without aura. DHE targets receptors in both the central and the peripheral parts of the nervous system. Based on concerns of overuse, medication-overuse headache, and withdrawal, the use of dihydroergotamine should be limited and carefully monitored. The quantity limit is set to contain treatment for up to eight headaches per month without exceeding the maximum weekly dose allowed per package insert. Safety and effectiveness in pediatric patients have not been established (1-5).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of



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Dihydroergotamine Nasal Sprays, while maintaining optimal therapeutic outcomes.

References

1. Migranal Nasal Spray [package insert]. Bridgewater, NJ: Bausch Health US, LLC; July 2019.
2. Trudhesa Nasal Spray [package insert]. Seattle, WA: Impel NeuroPharma Inc; September 2021.
3. Beithon J, Gallenberg M, Johnson K, et al. Institute for Clinical Systems Improvement. Diagnosis and Treatment of Headache. https://www.icsi.org/_asset/qwrznq/Headache.pdf. Updated January 2013.
4. Snow V, Weiss K, Wall EM, Mottur-Pilson C; American Academy of Family Physicians; American College of Physicians-American Society of Internal Medicine. Pharmacologic management of acute attacks of migraine and prevention of migraine headache. *Ann Intern Med*. 2002; 137: 840-9.
5. Silberstein S. Practice parameter: evidence-based guidelines for migraine headache. Report of the Quality Standards Subcommittee of the American Academy of Neurology. 2000.