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Section:	Prescription Drugs	Effective Date:	January 1, 2026
Subsection:	Analgesics and Anesthetics	Original Policy Date:	March 17, 2017
Subject:	Dihydroergotamine	Page:	1 of 7

Last Review Date: December 12, 2025

Dihydroergotamine

Description

Atzumi Nasal Powder* (dihydroergotamine)

Brekiya Injection** (dihydroergotamine)

Migranal Nasal Spray* (dihydroergotamine)

Trudhesa Nasal Spray* (dihydroergotamine)

Covered product: generic Migranal (dihydroergotamine)

*Non-covered medications must go through prior authorization and the formulary exception process.

**Product awaiting tiering and may not be available yet

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 (1-4).

Regulatory Status

FDA-approved indication:

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- Dihydroergotamine Nasal Sprays are indicated for the acute treatment of migraine headaches with or without aura (1-3).
- Brekiya is indicated for the acute treatment of migraine with or without aura and the acute treatment of cluster headaches in adults (4).

Limitations of Use:

- Dihydroergotamine Nasal Spray is not indicated for the preventative treatment of migraine or for the management of hemiplegic or basilar migraine (1-2).
- Atzumi nasal powder and Brekiya are not indicated for the preventative treatment of migraine or for the management of hemiplegic migraine or migraine with brainstem aura (3-4).

Dihydroergotamine has 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 (1-4).

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

The recommended dose of Atzumi is 5.2 mg and is administered as a powdered medicine into one nostril. The dose may be repeated, if needed, a minimum of 1 hour after the first dose. The maximum dose in a 24-hour period is two doses of Atzumi 5.2 mg. The safety of taking more than 4 doses in a 7-day period or 12 doses within a 30-day period has not been established (3).

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The recommended dose of Brekiya is 1 mg and is administered subcutaneously as an autoinjector. The dose may be repeated, as needed, at 1-hour intervals. Patients should not use more than 3 doses in a 24-hour period or 6 doses in a week (4).

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 (1-7).

The safety and effectiveness in pediatric patients less than 18 years of age have not been established (1-4).

Related policies

5-HT1 Agonists, Butalbital analgesics, Elyxyb, Maxalt, Migraine CGRP Antagonists IV, Migraine CGRP Antagonists Nasal, Migraine CGRP Antagonists Oral, Migraine CGRP Antagonists SC, Migraine Powders

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Dihydroergotamine may be considered **medically necessary** if the conditions indicated below are met.

Dihydroergotamine may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following

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1. Migraine, with aura (classic or classical)
2. Migraine, without aura (common)
3. **Brekiya only:** Cluster headaches

AND NONE of the following:

- a. Hemiplegic migraine
- b. Basilar migraine

AND the following:

- a. Inadequate treatment response, intolerance, or contraindication to **TWO** of the 5-HT₁ receptor agonist (triptans) alternatives

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following

1. Migraine, with aura (classic or classical)
2. Migraine, without aura (common)
3. **Brekiya only:** Cluster headaches

AND NONE of the following:

- a. Hemiplegic migraine
- b. Basilar migraine

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Drug	Package Size	Quantity Limit
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Dihydroergotamine 4 mg/mL (generic Migranal)	8 nasal devices per kit	24 nasal devices (3 kits) per 90 days
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OR

Drug with Approved Formulary Exception Only	Package Size	Quantity Limit
Atzumi 5.2 mg	8 nasal devices per carton	40 nasal devices (5 cartons) per 90 days OR
Brekiya 1 mg/mL	4 autoinjectors per carton	72 autoinjectors (18 cartons) per 90 days OR
Migranal 4 mg/mL	8 nasal devices per kit	24 nasal devices (3 kits) per 90 days OR
Trudhesa 4 mg/mL	4 nasal devices per kit	36 nasal devices (9 kits) per 84 days

Duration 6 months

Prior – Approval Renewal Limits

Same as above

Rationale

Summary

DHE (dihydroergotamine) is used for the treatment of migraine headache with or without aura. Brekiya is also indicated for the acute treatment of cluster headaches. 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 (1-7).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Dihydroergotamine Nasal Spray, while maintaining optimal therapeutic outcomes.

References

1. Migranal Nasal Spray [package insert]. Bridgewater, NJ: Bausch Health US, LLC; September 2022.
2. Trudhesa Nasal Spray [package insert]. Seattle, WA: Impel NeuroPharma Inc; September 2021.
3. Atzumi Nasal Powder [package insert]. Durham, NC: Satsuma Pharmaceuticals, Inc.; April

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2025.

4. Brekiya [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; July 2025.
5. Beithon J, Gallenberg M, Johnson K, et al. Institute for Clinical Systems Improvement. Diagnosis and Treatment of Headache. https://www.icsi.org/_asset/qwrznnq/Headache.pdf. Updated January 2013.
6. 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.
7. Silberstein S. Practice parameter: evidence-based guidelines for migraine headache. Report of the Quality Standards Subcommittee of the American Academy of Neurology. 2000.

Policy History

Date	Action
March 2017	New addition to PA
June 2017	Annual review
March 2018	Annual editorial review and reference update
November 2018	Annual editorial review and reference update
March 2019	Annual review
December 2019	Annual review and reference update
March 2020	Annual review
June 2020	Annual review
June 2021	Annual review
September 2021	Annual review
September 2021	Added Trudhesa Nasal Spray and renamed policy Dihydroergotamine Nasal Sprays. Changed the Migranal PA Qty Limit from 32/90 to 24/90.
December 2021	Annual review
March 2022	Annual review. Per SME, removed requirement "concurrent use with one migraine prophylactic therapy: antidepressant, antiepileptic, clonidine, ACE inhibitor, ARB inhibitor"
December 2022	Annual review. Moved Trudhesa and brand Migranal to FE + PA only. Changed policy number to 5.70.060
March 2023	Annual review and reference update
September 2023	Annual review
March 2024	Annual review
December 2024	Annual review
March 2025	Annual review
June 2025	Annual review. Addition of Atzumi nasal powder to PA

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October 2025 Addition of Brekiya to PA. Expanded dosage forms in policy. Changed Trudhesa quantity limit to 36 nasal devices per 84 days

December 2025 Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 12, 2025 and is effective on January 1, 2026.