Migranal Nasal Spray

**Description**

Migranal Nasal Spray (dihydroergotamine)

**Background**

Migranal is a nasal spray DHE (dihydroergotamine) 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<sub>1D</sub> receptors. Activation of 5-HT<sub>1D</sub> 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).

**Regulatory Status**

FDA approved indication: Migranal Nasal Spray is indicated for the acute treatment of migraine headaches with or without aura (1).

**Limitations of Use:**

Migranal Nasal Spray is not intended for the prophylactic therapy of migraine or for the management of hemiplegic or basilar migraine (1).

Migranal has boxed warnings for serious and/or life-threatening peripheral ischemia which has been associated with the co-administration of dihydroergotamine with potent CYP 3A4 inhibitors including protease inhibitors and macrolide antibiotics. Because CYP 3A4 inhibition elevates the...
serum levels of dihydroergotamine, the risk for vasospasm leading to cerebral ischemia and/or ischemia of the extremities is increased (1).

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 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).

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 one package which contains treatment for up to eight headaches per month. Additionally, preventative therapies are recommended in patients with frequent migraines in order to reduce attack frequency, severity, and duration; improve responsiveness to treatment of acute attacks; and improve function and reduce disability. Many drug categories have been used for the prevention of migraines and the improvement of response to acute therapies for migraines. These drug classes include (but are not limited to): antidepressants, antiepileptic medications, beta-blockers, calcium channel blockers, and other blood pressure medications (1-4).

Safety and effectiveness in pediatric patients have not been established (1).

Related policies
Amerge, Axert, Butalbital analgesics, Frova, Maxalt, Migraine Calcitonin Gene Related Peptide (CGRP) Antagonists, Migraine Powders, Relpax, Reyvow, Sumatriptan, Sumatriptan Injection, Zomig

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

Migranal Nasal Spray may be considered medically necessary in patients 18 years of age or older with migraine headaches with or without aura if the conditions indicated below are met.
Migranal Nasal Spray may be considered investigational in patients less than 18 years and for all other indications.

**Prior-Approval 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)

AND NONE of the following:

a. Hemiplegic migraine
b. Basilar migraine

AND ALL of the following:

a. Inadequate treatment response, intolerance, or contraindication to **TWO** of the 5-HT$_1$ receptor agonist (triptans) alternatives
b. Concurrent use with **ONE** of following migraine prophylactic therapies:
   i. Antidepressant
   ii. Antiepileptic
   iii. Clonidine
   iv. ACE Inhibitor
   v. ARB Inhibitor

**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)
**Section:** Prescription Drugs  
**Effective Date:** January 1, 2020  
**Subsection:** Analgesics and Anesthetics  
**Original Policy Date:** March 17, 2017  
**Subject:** Migranal Nasal Spray  
**Page:** 4 of 5

AND NONE of the following:
   a. Hemiplegic migraine  
   b. Basilar migraine

AND the following:
   a. Concurrent use with ONE of following migraine prophylactic therapies:
      i. Antidepressant  
      ii. Antiepileptic  
      iii. Clonidine  
      iv. ACE Inhibitor  
      v. ARB Inhibitor

### Policy Guidelines

#### Pre-PA Allowance

None

#### Prior - Approval Limits

<table>
<thead>
<tr>
<th>Quantity</th>
<th>32 nasal units (4 kits) per 90 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>6 months</td>
</tr>
</tbody>
</table>

#### Prior – Approval *Renewal* Limits

Same as above

### Rationale

**Summary**

Migranal is a nasal spray DHE (dihydroergotamine) 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 one package which contains treatment for up to eight headaches per month. Safety and effectiveness in pediatric patients have not been established (1-2).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Migranal Nasal Spray, while maintaining optimal therapeutic outcomes.
Section: Prescription Drugs  Effective Date: January 1, 2020
Subsection: Analgesics and Anesthetics  Original Policy Date: March 17, 2017
Subject: Migranal Nasal Spray  Page: 5 of 5

References

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 2017</td>
<td>New addition to PA</td>
</tr>
<tr>
<td>June 2017</td>
<td>Annual review</td>
</tr>
<tr>
<td>March 2018</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>November 2018</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>March 2019</td>
<td>Annual review</td>
</tr>
<tr>
<td>December 2019</td>
<td>Annual review and reference update</td>
</tr>
</tbody>
</table>

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective on January 1, 2020.