

DRUG CLASS: Ergotamine derivatives
BRAND NAME: Migranal nasal spray
(Generic) (dihydroergotamine tartrate) nasal spray

FDA INDICATIONS:

Dihydroergotamine (DHE) nasal spray is indicated for the acute treatment of migraine headaches with or without aura and not intended for the prophylactic therapy of migraine or for the management of hemiplegic or basilar migraine.

ICD-9 Code:

Migraine – with aura (“classic”): 346.0
Migraine – idiopathic/without aura (“common”): 346.1

QUANTITY LIMITATIONS

(QL) CRITERIA:

Migranal nasal spray

Short Term:

16 mg per 30 days
1 kit (2 mg/amp, 8 amps/kit)

Extended Supply:

48 mg per 90 days
3 kits (2 mg/amp, 8 amps/kit)

If a patient requires amounts in excess of these limits, please follow criteria developed for Migranal.

RATIONALE:

According to the package insert, the maximum dose of Migranal is 4 mg per week, or 16 mg per month. The QL limit is one kit per month.

CRITERIA FOR EXCEEDING QL:

1. Convey to physician the amount of the drug that the patient has already received (refer to QL) and ask if the patient needs more than that amount. **AND**
2. Patient must have diagnosis of moderate to severe migraine headache. (Tension-type and chronic daily headaches are NOT appropriate diagnoses). **AND**
3. Must have tried and failed at least 2 other abortive migraine therapy. Examples of medications used for abortive therapy include:
 - Ibuprofen (Motrin®)
 - Diclofenac (Voltaren®)
 - Flurbiprofen (Ansaid®)
 - Imitrex (sumatriptan)
 - Amerge (naratriptan)
 - Maxalt (rizatriptan)
 - Zomig (zolmitriptan)
 - Ergotamine-containing products (Cafergot, Wigraine, Ergomar, etc.)
 - Isometheptene mucate/Dichloralphenazone/Acetaminophen (Midrin, etc.) **AND**
4. If patient experiences > 4 migraine headaches per month, prophylactic therapy should have been given an adequate trial (see table below). **AND**
5. **Deny** if to be used in combination with triptans (e.g., Imitrex) due to possibility of increased blood pressure effect. **AND**
6. **Deny** if used in conjunction with a beta-blocker due to possibility of increase in vasoconstrictive activity. (Note: Beta-blockers, by blocking vasodilatory effects of epinephrine, may potentiate the vasoconstrictive action of ergotamine.)

BLACK BOX WARNINGS:

Serious and/or life-threatening peripheral ischemia has been associated with the coadministration of dihydroergotamine with potent CYP 3 A4 inhibitors including protease inhibitors and macrolide antibiotics. Because CYP 3 A4 inhibition elevates the serum levels of dihydroergotamine, the risk of vasospasm leading to cerebral ischemia and /or ischemia of the extremities is increased. Hence, concomitant use of these medications is contraindicated.

RATIONALE:

- Aspirin, acetaminophen, NSAIDs and combination products containing these key ingredients are generally considered first line abortive therapy for migraine.
- Prophylactic migraine therapy may reduce the frequency and severity of migraine attacks.
- Combinations of Migranal and certain other medications (e.g., beta-blockers, triptans, macrolides, protease inhibitors) lead to drug interactions with possibly serious effects.
- Utilization management criteria are intended to prevent inappropriate use of Migranal.

NURSING ASSESSMENT:

1. Gather a complete medical history; note any contributing factors (i.e., smoker, alcohol consumption, use of OTC medications, stress, etc.). Include migraine history and any precipitating factors.
2. This product **should not** be used with any patient with a documented history of ischemia or vasospastic coronary vascular disease (CAD).
3. Note any present use of macrolide antibiotics (e.g., erythromycin, clarithromycin, azithromycin, dirithromycin). Macrolides may increase the plasma levels of ergot alkaloids, which could result in vasospastic reactions.
4. Note any prior hypersensitivity to ergot alkaloids (e.g., Cafergot, Wigraine, Ergomar, D.H.E. 45, etc.).

PROVIDER EDUCATION:

1. Each ampul contains one complete dose of Migranal nasal spray, which is 1 spray (0.5mg) in each nostril followed in 15 minutes by an additional spray in each nostril, for a total of 4 sprays (2mg).
2. Once the Migranal ampule has been opened, it must be discarded after 8 hours.
3. Studies have shown no additional benefit of acute doses greater than 2 mg (4 sprays) for a single migraine attack. The safety of doses greater than 3 mg (6 sprays) in a 24-hour period and 4 mg (8 sprays) in a 7-day period have not been established.
4. Valeant Drug Information: 800-548-5100
5. Migranal Patient Information: 888-697-3543

MISUSE AND CHRONIC DAILY HEADACHE:

“Chronic Daily Headache (CDH) is a syndrome that consist of a group of disorders that can be subclassified into primary and secondary types. Drug-induced daily headache frequently arises during headache therapy. It can result from the daily use of ergotamines and excessive amounts of common analgesics. CDH usually manifests itself as a constant dull pressure in the frontal and occipital areas. Most patients will complain of headache upon awakening in the morning. The symptomatic medications used for the immediate relief of headache may actually perpetuate the headache if used frequently and in excessive quantities. Therapy for drug-induced headache is withdrawal of the responsible medication.”

CLINICAL OUTCOMES:

Reversal of acute migraine attack and relief of associated symptoms.

DOSAGE AND ADMINISTRATION:

For the acute treatment of migraine, one spray (0.5 mg) of Migranal nasal spray should be administered in each nostril (1 mg). Fifteen minutes later, an additional one spray (0.5 mg) should be administered in each nostril for a total dosage of 4 sprays (2 mg) of DHE.

Once an applicator has been prepared, it should be discarded after 8 hours. Therefore, if a patient requires the maximum daily dose of 3 mg and it has been more than 8 hours since their first dose, they will need to start a new applicator.

ADVERSE EVENTS:

1. Side effects are mostly due to the route of administration and include: rhinorrhea, sneezing, dryness, burning or swelling of the nasal mucosa, nasal obstruction, congestion, and taste disturbances.
2. Monitor closely for signs and symptoms of ergotism (abdominal cramping, weak pulse, vomiting, etc.) as a result of prolonged administration or overdosage of ergotamines.

RISK FACTORS/CONTRAINDICATIONS/PRECAUTIONS:

1. DHE nasal spray may cause coronary artery vasospasm. Therefore, patients who experience signs and symptoms suggestive of angina following DHE administration should be evaluated for the presence of coronary artery disease or a predisposition to variant angina before receiving additional doses. Similarly, patients who experience other signs or symptoms suggestive of decreased arterial flow, such as ischemic bowel syndrome or Raynaud's phenomenon, following the use of any 5-HT agonist are candidates for further evaluation.
2. Migranal **should not** be administered within 24 hours of using 5-HT agonists, ergot-containing medications, or methysergide.
3. Migranal is contraindicated in patients with severe hepatic or renal impairment and patients with hypersensitivity to ergot alkaloids. It is also contraindicated with the concurrent use of potent CYP 3A4 inhibitors.
4. Migranal is pregnancy **category X**, and should not be used in lactating mothers or in children.

DRUG INTERACTIONS:

Migranal **should not** be used with peripheral vasoconstrictors, 5-HT agonists (e.g., sumatriptan, zolmitriptan), propranolol, nicotine, macrolide antibiotics and protease inhibitors. Migranal should be used with caution in patients concomitantly receiving SSRIs (e.g., fluoxetine [Prozac[®]], paroxetine [Paxil[®]], etc.).

Migraine therapy options and considerations:

1. Diagnosis of migraine must exist (tension-type and chronic daily headache are not appropriate diagnosis).
2. Migranal is used for headaches refractory to other abortive migraine treatments:
 - Ergot alkaloids (Cafergot, Wigraine, Ergomar, D.H.E.-45)
 - Analgesics (aspirin, acetaminophen)
 - NSAIDs (ibuprofen, naproxen)
 - Combination products (Midrin)
3. Patient is currently receiving prophylactic therapy (due to refractory nature of the patient's migraine) or previous use with either insufficient results or intolerance. Patients should consider prophylactic therapy if migraine frequency is > 4 migraines per month.

Migraine therapy options:

Examples of Prophylactic therapy for migraine headache (this list may not be complete). An adequate trial of 2-3 months of treatment should be given before drug considered ineffective:

DRUG CLASS	NAME
• Antidepressants	Amitriptyline Fluoxetine
• Calcium Channel Blockers	Nifedipine Verapamil Diltiazem
• Anticonvulsants	Divalproex sodium/sodium valproate Carbamazepine Gabapentin Topiramate
• NSAIDs	Naproxen Aspirin Ketoprofen
• Other	Feverfew Magnesium Vitamin B2 (Riboflavin)

Initial Date: January 1999

Review Date: 1/12/2007

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