RATIONALE FOR INCLUSION IN PA PROGRAM

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\textsubscript{1D} receptors. Activation of 5-HT\textsubscript{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).

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).

**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.

**References**
