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Indiana Medicaid Therapeutics Committee **Therapeutic Class Review Summary**

Therapeutic Class:

Selective 5-HT₁ Agonists

Overview:

The traditional pharmacological treatments for acute migraine attacks include simple analgesics (acetaminophen, aspirin), NSAIDs, combination analgesics (Midrin, Fioricet), ergot alkaloids, and opioids. Serotonin receptor agonists or “triptans” are considered an advancement in migraine treatment. The triptans exert pharmacological activity in three ways:

- Vasoconstriction of intracranial vessels through 5-HT_{1B} receptors,
- Inhibition of neuropeptide from trigeminal perivascular nerve through 5-HT_{1D} receptors, and
- Interruption of the pain signal through 5-HT_{1D} receptors.

All triptans are contraindicated in patients with ischemic heart disease and uncontrolled hypertension, due to partial vasoconstrictive effect on coronary artery. In addition, triptans are not indicated for hemiplegic and basilar migraines and should not be used within 24 hours of ergotamines.

The first marketed triptan was sumatriptan. Since then, six more triptans have become available. In addition to oral tablets, sumatriptan is available as a subcutaneous injection, intranasal spray, and in a combination tablet with naproxen (Treximet®). The subcutaneous route of administration provides the fastest onset of action. Rizatriptan and zolmitriptan are both available as an orally disintegrating tablet, which provides the advantage of easy administration. However, the pharmacokinetic profiles, such as time to peak plasma level (T_{max}) and half-life, do not improve from regular tablet. The half-lives of triptans are between 2-4 hours, except for naratriptan (6 hours) and frovatriptan (26 hours). Information to associate the length of half-life with migraine recurrence is limited. Most clinical trials compare newer agents with sumatriptan oral tablets. Some studies have shown marginal benefit with newer agents; others failed to show any differences. Sumatriptan tablets, injection, and nasal spray are now available generically; and rizatriptan tablets and orally disintegrating tablets have received tentative approval. Triptans are indicated for use in acute treatment of migraine with or without aura in adults. Axert (almotriptan) is the only triptan indicated for use in adolescent patients 12 to 17 years of age, and the injectable formulation of sumatriptan is indicated for use in cluster headache episodes. The coadministration of a 5-HT₁ agonist with a selective serotonin uptake inhibitor or a serotonin and norepinephrine reuptake inhibitor could lead to serotonin syndrome and this combination should be used with extreme caution.



Generic Name	Brand Name	Manufacturer
Almotriptan	Axert [®]	Ortho McNeil Pharmaceutical, Inc
Eletriptan	Relpax [®]	Pfizer
Frovatriptan	Frova [®]	Elan
Naratriptan	Amerge [®]	GlaxoSmithKline
Rizatriptan	Maxalt [®] Maxalt-MLT [®]	Merck & Co
Sumatriptan	Imitrex [®] Sumavel [™] Dosepro [™]	GlaxoSmithKline Zogenix, Inc.
Sumatriptan/Naproxen	Treximet [™]	GlaxoSmithKline
Zolmitriptan	Zomig [®] Zomig-ZMT [®]	AstraZeneca, Medpointe

Summary:

Most triptans oral agents are similar in efficacy and safety. The onset of relief, rate of recurrent headache, and route of administration differentiate these agents and should be considered with formulary inclusion.