

UTILIZATION MANAGEMENT CRITERIA

DRUG CLASS:	5HT ₁ agonists	
BRAND NAME:	Imitrex	4 mg injection kit or refill
(Generic)	(sumatriptan)	6 mg injection kit or refill
		Injection vial (1 dose)
		5 mg nasal spray
		20 mg nasal spray
		25 mg oral tablet
		50 mg oral tablet
		100 mg oral tablet

FDA INDICATIONS:

Oral sumatriptan, nasal sumatriptan, and sumatriptan injection are indicated for the acute treatment of migraine with or without aura in adults. Sumatriptan injection is also indicated for the acute treatment of cluster headache episodes. The 5-HT₁ agonists are not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic or basilar migraine.

ICD-9 Codes:

Migraine – with aura (“classic”):	346.0
Migraine – idiopathic / without aura (“common”):	346.1
Cluster headache (sumatriptan in only):	346.2

<u>QL Criteria</u>	<u>Short Term:</u>	<u>Extended Supply:</u>
	900 mg (tablet equivalent)* per 30 days	2700 mg (tablet equivalent)* per 90 days
Imitrex tablets 100mg	9 tablets	27 tablets
Imitrex tablets 50mg	18 tablets	54 tablets
Imitrex tablets 25mg	36 tablets	108 tablets
Imitrex injection kits/ refills, 4 mg (8 mg/ml)	4 kits (8 injections)	12 kits (24 injections)
Imitrex injection kits/ refills, 6 mg	4 kits (8 injections)	12 kits (24 injections)
Imitrex nasal 20mg	9 devices	27 devices
Imitrex nasal 5mg	36 devices	108 devices

- Tablet equivalents do not imply exact therapeutic equivalents. One injection ≈ 20 mg nasal spray ≈ 100 mg oral dosage. 5 mg nasal spray ≈ 25 mg tablet.
- *If patient requires amounts in excess of these numbers, please follow the Quantity Limitations (QL) criteria for Imitrex.*

RATIONALE:

- **Imitrex tablets:** The maximum single recommended adult dose is 100 mg. The maximum recommended adult dose that may be given in 24 hours is 200 mg, given in two doses separated by at least two hours.
- **Imitrex injections:** The maximum single recommended adult dose is 6 mg (one injection) injected subcutaneously. The maximum recommended dose that may be given in 24 hours is two 6 mg injections separated by at least one hour.

- **Imitrex nasal spray:** The maximum single recommended adult dose is 20 mg. The maximum recommended dose that may be given in 24 hours is two 20-mg doses. (The 5 mg spray unit should be used for 5 and 10 mg dosages only.)

The safety of treating an average of more than 4 migraine headaches in a 30-day period with Imitrex has not been established. Most people using these medications for migraine treatment do not need quantities in amounts exceeding that necessary to treat a maximum of 4 migraine attacks in a 30-day period. For this reason, the benefit plan provides coverage only for amounts up to those listed. Members may obtain a combination of dosage forms, although quantity limits apply and total mg amount per 30 days may not exceed 900 mg of tablet equivalent.

CRITERIA FOR EXCEEDING QUANTITY LIMITATIONS:

1. Convey to physician the amount of the drug that the patient has already received (refer to QL criteria) and ask if the patient needs more than that amount. **AND**
2. Patient must have diagnosis of moderate to severe migraine headache. Cluster headache is also an appropriate diagnosis for Imitrex injection only. (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®)
 - 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 be considered (see Table below). **AND**
5. The possibility of medication-induced, rebound, or chronic daily headache should be considered. **AND**
6. **Deny** if to be used in combination with another triptan (e.g., Zomig, Amerge, Maxalt, Axert, Frova, Relpax) or an ergotamine (e.g., Migranal, Cafergot) due to possibility of increased blood pressure effect.

BLACK BOX WARNINGS:

None

RATIONALE:

- Aspirin, acetaminophen, non-steroidal anti-inflammatory drugs (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.
- Quantity limitations criteria are intended to prevent inappropriate use of the triptans.

NURSING ASSESSMENT:

1. Gather a complete medical history; note any contributing factors (i.e., smoker, diet, alcohol consumption, use of OTC medications, stress, etc.). Include migraine history and any precipitating factors.
2. Determine any history of cardiac problems or evidence of ischemic cardiovascular disease, as drug is contraindicated.
3. Ensure that a neurological examination has been performed to identify appropriate migraine category.
4. Obtain baseline ECG, liver (AST, ALT), and renal function tests.

PROVIDER EDUCATION:

- Review appropriate method for administration (oral, subcutaneous, intranasal).
- Glaxo SmithKline Drug Information: 800-334-0089

Injection:

1. With subcutaneous (sc) form, have first dose administered in a monitored environment.
2. Monitor vital signs, anticipate transient increase in blood pressure.
3. Injection is for subcutaneous use only (IV use may cause coronary vasospasms).
4. Observe client self-administration for subcutaneous use.
5. Advise that the injection should be given just below the skin as soon as the symptoms of migraine appear or any time during the attack. If the symptoms of migraine return or fail to diminish a second injection may be administered 1 hour later, not to exceed 2 injections within a 24-hour period. (*Controlled clinical trials have failed to show any benefit with the administration of a second 6 mg dose in patients who failed to respond to the first injection*).
6. Review safe handling and proper disposal of syringes.
7. Advise that pain and tenderness may be present at the site of injection for up to an hour post-injection.
8. Advise that if a patient experiences chest, jaw, throat, or neck pain a physician should conduct further medical evaluation.
9. Symptoms of flushing, tingling, as well as dizziness or drowsiness may occur and should be shared with the provider before continuing with sumatriptan injections.
10. Do not use sumatriptan injection if pregnancy is suspected.

Tablet: Nausea, vomiting, malaise, and fatigue are the most common adverse effects.

Nasal Spray: Bitter taste at the back of the mouth is the primary patient complaint.

MISUSE AND CHRONIC DAILY HEADACHE:

“Chronic Daily Headache (CDH) is a syndrome that consist of a group of disorders that can be sub-classified 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 manifest itself as a constant dull pressure in the frontal and occipital areas. Most of the 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 of drug-induced headache is withdrawal of the responsible medication.”

CLINICAL OUTCOME:

1. Reversal of acute migraine attack and relief of associated symptoms.
2. Relief of acute episode of cluster headache. (*injection only*)

DOSAGE AND ADMINISTRATION:

The recommended dose is 4 or 6 mg as a subcutaneous injection, 5, 10 or 20mg as an intranasal solution or 25, 50, or 100mg as an oral dose taken with fluids as soon as possible after the onset of symptoms, but can be given anytime during the migraine attack without a change in efficacy. The oral dose used in the majority of the published clinical studies has been 100mg; however the manufacturer states there is no evidence that an initial dose of 100mg provides substantially greater relief than 50mg. If the patient responds, but satisfactory relief is not obtained within 2 hours, a second dose of up to 100mg can be given. Treatment can be repeated up to a maximum of two subcutaneous injections, two intranasal doses (up to 40mg/day) and two oral doses (up to 200mg/day) per 24-hour period with a minimum of 1 hour between subcutaneous doses and 2 hours between nasal doses and oral doses. If no relief is experienced after the initial dose, a second dose should not be administered. The first dose of the medication (oral, nasal or subcutaneous injection) should be given in a physician’s office or medical clinic if there is a risk of coronary artery disease. In recognizing that patients with cluster headaches are predominantly male and over 40 years of age, which are risk factors for CAD, it is recommended that patients who are intermittent users of Imitrex injection should undergo periodic cardiovascular evaluation.

RISK FACTORS/CONTRAINDICATIONS:

1. Do not use with ergotamine-containing products or within 2 weeks of an MAO-A inhibitor.
2. Do not use with patients with ischemic heart disease or uncontrolled blood pressure.
3. Do not use as a prophylactic agent.
4. Give only where diagnosis of migraine (or cluster headache for injection) is clearly established.
5. Patient should have a successful trial of sumatriptan in the medical office or emergency room to identify efficacy or possible side effects.
6. Contraindications to the use of 5-HT₁ agonists: pregnancy, peripheral vascular disease (i.e., thromboangitis, leuetic arteritis, Raynaud's Syndrome, thrombophlebitis, arteriosclerosis), hepatic or renal impairment, coronary artery disease, uncontrolled hypertension.

DRUG INTERACTIONS:

- Ergot-containing drugs have been reported to cause prolonged vasospastic reactions. Because there is a theoretical basis that these effects may be additive, use of ergotamine-containing or ergot-type medications (like dihydroergotamine) and 5-HT₁ agonists within 24 hours of each other should be avoided.
- MAO-A inhibitors increase the systemic exposure of the 5-HT₁ agonists and concomitant use is contraindicated.
- Concomitant use of more than one 5-HT₁ agonist within 24 hours of each other is not recommended.
- Selective serotonin reuptake inhibitors (SSRIs) have been reported to cause weakness, hyperreflexia, and incoordination when coadministered with 5-HT₁ agonists.

MIGRAINE THERAPY OPTIONS:

Table. Prophylactic therapy for migraine headache

DRUG CLASS	NAME
• Beta Blockers	Propranolol Atenolol Metoprolol Timolol
• 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)

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References supporting average number of migraine attacks per month:

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14. Zagami AS, et al *Neurology* 1997;48(suppl 3):S25-8 (n = 2,058) and Geraud GEA.
15. *Eur Neurol* 1996;32(suppl 2):24-7 (n=606) ~2.9-3.2 per month
16. Fletcher PE, et al. Headache Treatment: Trial Methodology and New Drugs. Lippincott-Raven Publishers, 1997 (n = 701) ~ 2.9 to 3.2 per month
17. Visser WH, et al. *Neurology* 1996;46:522-6 (n = 84) ~ 3-4 per month
18. Dowson A. *Eur Neurol* 1996;36(suppl 2):28-31 (n=40) ~ 2 per month

General References:

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33. <http://headaches.about.com/bl-glossary-b.htm>