Sumatriptan Injection (Imitrex / Alsuma / Sumavel / Zembrace)

Background
The selective serotonin receptor agonists, or "triptans", are a class of medications that have the ability to stop a migraine. Triptans work by binding to serotonin receptors in the brain. Specifically, per Drug Facts and Comparisions pharmacology of the Serotonin 5-HT1 Receptor Agonists (Triptans): The vascular 5-HT1 receptor subtype is present on the human basilar artery and in the vasculature of isolated human dura mater. Current theories on the etiology of migraine headaches suggest that symptoms are caused by local cranial vasodilation or the release of vasoactive and proinflammatory peptides from sensory nerve endings in an activated trigeminal system. The therapeutic activity of the serotonin 5-HT1 receptor agonists in migraine most likely can be attributed to agonist effects at 5-HT1B/1D receptors on the extracerebral, intracranial blood vessels that become dilated during a migraine attack and on nerve terminals in the trigeminal system. Activation of these receptors results in cranial vessel constriction, inhibition of neuropeptide release, and reduced transmission in trigeminal pain pathways (1).

This class of medications has potentially serious side effects, especially when taken in high doses. Life-threatening disturbances of cardiac rhythm and myocardial infarction have been reported, as well as stroke. Excessive use of triptans can lead to medication overuse headache (MOH). MOH was previously called rebound headache, drug-induced headache and medication-misuse headache (2-5).
The FDA-approved indications for Imitrex injectable, Alsuma, and Sumavel are: (2-4)
1. Acute treatment of migraine attacks, with or without aura
2. Acute treatment of cluster headache episodes

The only FDA-approved indication for Zembrace is: (5)
1. Acute treatment of migraine with or without aura in adults

**Limitations of Use:** (2-5)
1. Use only after a clear diagnosis of migraine or cluster headache has been established.
2. Not intended for the prophylactic therapy of migraine.

**Off Label Use:** (6)
Triptans have been found to be safe and effective in the pediatric and adolescent population.

Imitrex is available in a solution for injection. An autoinjection device is available for use with 4- and 6-mg prefilled syringe cartridges to facilitate self-administration in patients using the 4- or 6-mg dose (2).

Alsuma is sumatriptan solution supplied in a single dose auto-injector for subcutaneous use (3).

Sumavel DosePro is a sumatriptan solution supplied in a prefilled single-dose needle free subcutaneous delivery system (4).

Zembrace SymTouch is available as a prefilled, single dose, auto injector containing 3 mg sumatriptan. With Zembrace SymTouch, the needle penetrates approximately ¼ inch (6 mm). The injection is intended to be given subcutaneously (5).

**Sumatriptan injection is contraindicated in patients with:** (2-5):
- History of coronary artery disease or coronary artery vasospams
- Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders
- History of stroke, transient ischemic attack, or hemiplegic or basilar migraine
- Peripheral vascular disease
- Ischemic bowel disease
- Uncontrolled hypertension
- Recent (within 24 hours) use of another 5-HT1 agonist (e.g., another triptan) or of an ergotamine-containing medication
- Concurrent or recent (past 2 weeks) use of monoamine oxidase-A inhibitor
- Hypersensitivity to sumatriptan injection (angioedema and anaphylaxis seen)
- Severe hepatic impairment

**Related policies**
Amerge, Axert, Butalbital analgesics, Frova, Maxalt, Migraine Calcitonin Gene Related Peptide (CGRP) Antagonists, Migranal Nasal Spray, Relpax, Reyvow, Sumatriptan, 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.*

Sumatriptan injection may be considered **medically necessary** for the treatment of migraines (classical, common, unspecified) and if the conditions indicated below are met.

Sumatriptan injection may be considered **investigational** in patients less than 6 years of age and for all other indications.

**Prior-Approval Requirements**

**Age**

6 years of age or older

*Ages 6-11 must be prescribed by a neurologist*

**Diagnoses**

Patient must have **ONE** of the following:

1. Migraine, with aura (classic or classical)
2. Migraine, without aura (common)
3. Cluster headache – treatment of acute episode

**AND NONE** of the following:

- Hemiplegic migraine
- Basilar migraine
- Dual therapy after 6 months of calcitonin gene related peptide (CGRP) antagonist therapy
- Dual therapy with Reyvow (lasmiditan)
- Another PA on file for any triptan agent

**Prior – Approval Renewal Requirements**
Same as above

### Policy Guidelines

#### Pre - PA Allowance

**Age**

12 years of age or older

*No Pre-PA Allowance for 6-11 years of age*

**Quantity**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Allowance</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 mg/0.5ml injection kits*</td>
<td>18 kits per 90 days <strong>OR</strong></td>
</tr>
<tr>
<td>6 mg/0.5 ml injection kits*</td>
<td>12 kits per 90 days <strong>OR</strong></td>
</tr>
<tr>
<td>6mg/0.5ml injection vials</td>
<td>24 vials per 90 days <strong>OR</strong></td>
</tr>
<tr>
<td>Alsuma 6mg/0.5ml injection kits*</td>
<td>12 kits per 90 days <strong>OR</strong></td>
</tr>
<tr>
<td>Sumavel DosePro 4mg/0.5ml system</td>
<td>36 syringes per 90 days <strong>OR</strong></td>
</tr>
<tr>
<td>Sumavel DosePro 6mg/0.5ml system</td>
<td>24 syringes per 90 days <strong>OR</strong></td>
</tr>
<tr>
<td>Zembrace 3mg injection</td>
<td>36 syringes per 90 days</td>
</tr>
</tbody>
</table>

**Duration**

6 months

*4mg and 6mg units are kits which each contain 2 injections*

#### Prior - Approval Renewal Limits

Same as above

### Rationale

**Summary**
Migraine is a chronic, recurrent condition that affects millions of people worldwide. Triptans are serotonin (5-HT) receptor agonists that interrupt attacks or episodes of migraine, but do not prevent migraines from happening. This class of medications has potentially serious side effects, especially when taken in high doses. Life-threatening disturbances of cardiac rhythm and myocardial infarction have been reported, as well as stroke. Triptans have been found to be safe and effective in the pediatric and adolescent population (1-6).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Imitrex, Alsuma, Sumavel DosePro and Zembrace SymTouch while maintaining optimal therapeutic outcomes.

References

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>February 2006</td>
<td>FDA approved 4mg dose for the Imitrex STAT dose system. The new strength was approved February 2, 2006 and will be available at the pharmacy sometime in April 2006. Based on the current FEP/OPM migraine agent criteria, the 4mg quantity limits should be same as the 6mg quantity limits (1,2).</td>
</tr>
<tr>
<td>March 2009</td>
<td>Imitrex (sumatriptan succinate) 4mg and 6mg injection Pre-PA Allowance and Prior-Approval Limits quantities were separated into the two available forms, kits and vials. Both quantity allowances will remain the same for total doses allowed, but the descriptions were separated to avoid confusion between the two available forms, vials and syringe kits. The vials are adjudicated as each’s, while the syringes are adjudicated as kits (2 syringes per kit).</td>
</tr>
</tbody>
</table>
July 2009 FDA approved Sumavel DosePro which is a prefilled, single-dose needle-free subcutaneous delivery system delivering 0.5ml of sterile solution containing 6mg sumatriptan.

October 2010 FDA approved Alsuma, which is a prefilled, auto injector containing 6mg of sumatriptan in 0.5ml of sterile solution.

September 2011 Annual editorial review and reference update.

December 2012 Changed quantity limit to 1.5 x FDA-approved dosage.

April 2013 Revised quantity limits to allow mail order to fill correctly

September 2014 Revision of age to allow pediatric and adolescent use. Annual editorial review and reference update

October 2014 Line-addition of a new strength of Sumavel DosePro 0.4mg/0.5ml

March 2016 Annual editorial review and reference update

Addition of Zembrace SymTouch

Policy code changed from 5.02.11 to 5.70.11

March 2017 Annual editorial review and reference update

March 2018 Annual editorial review and reference update

November 2018 Annual editorial review and reference update. Addition of no dual therapy with CGRP antagonist requirement and no dual therapy with another PA for any triptan agent

March 2019 Annual review

September 2019 Revised quantity limits to quantity per 90 days

November 2019 Addition of no dual therapy with Reyvow

December 2019 Annual review

Keywords

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