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Section:	Prescription Drugs	**Effective Date:**	April 1, 2022
Subsection:	Analgesics and Anesthetics	**Original Policy Date:**	September 8, 2011
Subject:	Sumatriptan Injection	**Page:**	1 of 7

Last Review Date: March 11, 2022

Sumatriptan Injection

Description

Sumatriptan Injection (Imitrex / 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 Comparisons, pharmacology of the Serotonin 5-HT_1 Receptor Agonists (Triptans), the vascular 5-HT_1 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-HT_1 receptor agonists in migraine most likely can be attributed to agonist effects at 5-$HT_{1B/1D}$ 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 (2-3).

Regulatory Status

The FDA-approved indications for Imitrex injectable are: (2)

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: (3)

1. Acute treatment of migraine with or without aura in adults

Limitations of Use: (2,3)

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: (4)
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).

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 (3).

Sumatriptan injection is contraindicated in patients with (2-3):

- History of coronary artery disease or coronary artery vasospasm
- 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-HT_1 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, Dihydroergotamine Nasal Sprays, Frova, Maxalt, Migraine CGRP Antagonists IV, Migraine CGRP Antagonists SC, Migraine CGRP Antagonists Oral, Migraine Powders, Relpax, 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 or cluster headaches 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 – acute treatment

AND ALL of the following:

a. Patient is currently using migraine prophylactic therapy **OR** the patient has had an inadequate treatment response, intolerance, or contraindication to migraine prophylactic therapy (e.g., divalproex sodium, topiramate, valproate sodium, metoprolol, propranolol, etc.)
b. **NO** hemiplegic migraine
c. **NO** basilar migraine
d. **NO** dual therapy with a calcitonin gene related peptide (CGRP) antagonist for acute migraine treatment (e.g., Nurtec ODT, Ubrelvy)
e. **NO** dual therapy with Reyvow (lasmiditan)
f. **NO** other PA on file for any triptan agent

Prior – Approval *Renewal* 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)
2. Migraine, without aura (common)
3. Cluster headache – acute treatment

AND ALL of the following:

a. **NO** hemiplegic migraine
b. **NO** basilar migraine
c. **NO** dual therapy with a calcitonin gene related peptide (CGRP) antagonist for acute migraine treatment (e.g., Nurtec ODT, Ubrelvy)
d. **NO** dual therapy with Reyvow (lasmiditan)
e. **NO** other PA on file for any triptan agent

Policy Guidelines

Pre - PA Allowance

Age 12 years of age or older
No Pre-PA Allowance for 6-11 years of age

Quantity

4 mg/0.5ml injection kits*	18 kits per 90 days **OR**
6 mg/0.5 ml injection kits*	12 kits per 90 days **OR**
6mg/0.5ml injection vials	25 vials per 90 days **OR**
Zembrace 3mg injection	36 syringes per 90 days

Prior - Approval Limits

Quantity

4 mg/0.5ml injection kits*	27 kits per 90 days **OR**
6 mg/0.5 ml injection kits*	18 kits per 90 days **OR**

	6mg/0.5ml injection vials	35 vials per 90 days **OR**
	Zembrace 3mg injection	54 syringes per 90 days
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 and Zembrace SymTouch while maintaining optimal therapeutic outcomes.

References

1. Serotonin 5-HT1 Receptor Agonists (Triptans). Drug Facts and Comparisons. Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health, Inc; December 2017.
2. Imitrex Injection [package insert]. Research Triangle Park, NC: GlaxoSmithKline; December 2021.
3. Zembrace SymTouch [package insert]. Princeton, NJ: Promius Pharma, LLC; June 2019.
4. Evers S. The Efficacy of Triptans in Childhood and Adolescence Migraine. Curr Pain Headache Rep. 2013 July;17(7)342.

Policy History

Date	Action

February 2006	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).
March 2009	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).
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. Annual review and update
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
March 2020	Annual review and reference update
June 2020	Annual review
February 2021	Revised Pre-PA allowance for the 6mg/0.5 mL vials from 24 vials/90 days to 25 vials/90 days due to pack size
March 2021	Annual review

April 2021	Removed Alsuma and Sumavel due to being discontinued. Added no dual therapy with a CGRP antagonist for acute migraine treatment. Revised no dual therapy requirement after 6 months of a prophylactic CGRP antagonist. Added initiation requirement to be on a migraine prophylactic therapy or have an inadequate treatment response, intolerance, or contraindication to migraine prophylactic therapy
June 2021	Annual review and reference update
September 2021	Annual review and reference update
March 2022	Annual editorial review and reference update. Per SME, removed requirement of “no dual therapy after 6 months with a prophylactic CGRP antagonist”

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 11, 2022 and is effective on April 1, 2022.