MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

Health Plan of San Joaquin

POLICY:	Migraine Therapy	**P&T DATE:**	9/12/2023
CLASS:	Neurological Disorders	**REVIEW HISTORY** (MONTH/YEAR)	9/22, 12/20 12/19, 12/18, 9/17, 12/16, 9/15, 2/15, 2/10, 5/07
LOB:	MCL		

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

Effective 1/1/2022, the Pharmacy Benefit is regulated by Medi-Cal Rx. Please visit https://medi-calrx.dhcs.ca.gov/home/ for portal access, formulary details, pharmacy network information, and updates to the pharmacy benefit.

All medical claims require that an NDC is also submitted with the claim. If a physician administered medication has a specific assigned CPT code, that code must be billed with the correlating NDC. If there is not a specific CPT code available for a physician administered medication, the use of unclassified CPT codes is appropriate when billed with the correlating NDC.

OVERVIEW

Migraine is a common disorder than can be debilitating for individuals suffering frequent attacks. While there is no cure for migraines, abortive agents are useful in relieving acute migraine attacks and the American Headache Society (AHS) and the American Academy of Neurology (AAN) have developed recommendations for pharmacotherapy options for migraine preventive therapies. This review will examine the management guidelines of migraines and the currently available anti-migraine agents and their coverage criteria.

Table 1: Available Anti-Migraine Agents *(Current as of 4/2023)*

ABORTIVE AGENTS				
CPT Code	**Generic Name (Brand Name)**	**Available Strengths**	**Pharmacy Benefit**	**Medical Benefit (Restrictions)**
SEROTONIN AGONISTS				
--	**Rizatriptan** (Maxalt)	Tablet: 5 mg, 10 mg, ODT tablet: 5 mg, 10 mg	Yes	No
J3030	**Sumatriptan** (Imitrex, Zembrace Symtouch, Onzetra Xsail, Sumavel DosePro)	25 mg, 50 mg, 100 mg, tablet Nasal spray: 5 mg/act , 20 mg/act, 4 mg/0.5 ml Injection: 6 mg/0.5 ml Injection, Nasal powder: 11 mg	Yes	Yes, for injections only
--	**Naratriptan** (Amerge)	Tablet: 1 mg, 2.5 mg	Yes	No
--	**Zolmitriptan** (Zomig)	Tablet: 2.5 mg, 5 mg, 5 mg ODT	Yes	No
--	**Almotriptan** (Axert)	*Tablet*: 6.25 mg	Yes	No
--	**Eletriptan** (Relpax)	Tablet: 20 mg, 40 mg	Yes	No.

--	**Frovatriptan** (Frova)	Tablet: 2.5mg	Yes	No
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonist				
--	**Rimegepant** (Nurtec ODT)	Tablet, orally-disintegrating: 75 mg	Yes	No
--	**Ubrogepant** (Ubrelvy)	Tablet: 50 mg, 100 mg	Yes	No
H3L-ANALGESIC,NON-SALICYLATE,BARBITURATE,XANTHINE COMBINATION				
--	**Butalbital/Acetaminophen/ Caffeine** (Fioricet)	Capsules	Yes	No
--	**Butalbital/Acetaminophen/ Caffeine** (Esgic, Alagesic LQ, Vanatol LQ)	50 mg/325 mg/ 40mg Capsules, tablets, liquid	Yes	No
H3M-NARCOTIC,NON-SALICY.ANALGESIC,BARBITURATE,XANTHINE				
--	**Butalbital/Acetaminophen/ Caffeine/Codeine**	50 mg/300 mg/ 40 mg/30 mg Capsule	Yes	No
--	**Butalbital/Acetaminophen/ Caffeine/Codeine**	50 mg/325 mg/ 40 mg/30 mg Capsule	Yes	No
H3O-ANALGESIC, SALICYLATE, BARBITURATE,& XANTHINE CMB				
--	**Butalbital/Aspirin/Caffeine** (Fiorinal)	50 mg/325 mg/40 mg Capsule	Yes	No
H3R-NARCOTIC AND SALICYLATE ANALGESIC, BARBITURATE & XANTHINE COMBINATION				
--	**Butalbital/Aspirin/Caffeine/ Codeine** (Fiorinal with Codeine)	50 mg/325 mg/40 mg/ 30mg capsule	Yes	No
ERGOT ALKALOIDS/ OTHER				
--	**Ergotamine Tartrate/Caffeine** (Cafergot)	1 mg/100 mg Tablets, 2 mg/100 mg Suppository	Yes	No
--	**Ergotamine Tartrate** (Ergomar)	Tablet: 2 mg SL	Yes	No
--	**Isometheptene/ Dichloralphen/ Acetaminophen**	Capsule: 65 mg/100 mg/ 325 mg	Yes	No
--	**Dihydroergotamine** (Trudhesa)	Aerosol solution: 0.725 mg/ACT Solution: 1 mg/mL, 4 mg/mL	Yes	No
PROPHYLACTIC AGENTS				

CPT code	GENERIC NAME (BRAND NAME)	Dosage forms	Pharmacy Benefit	Medical Benefit (restrictions)
MIGRAINE-PREVENTIVE AGENTS				
--	**Amitriptyline**	Tablet: 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg (usual range: 25-150 mg per day)	Yes	No
--	**Atenolol**	Tablet: 25 mg, 50 mg, 100 mg (usual range 100 mg per day)	Yes	No
--	**Divalproex/Valproic Acid**	Oral capsules, solutions, tablets: 125 mg, 250 mg, 500 mg (usual range 400-1,000 mg per day)	Yes	No
--	**Metoprolol Tartrate**	Tablet, capsules, solution: 25 mg, 50 mg, 75 mg, 100 mg, 200 mg (usual range 47.5-200 mg per day)	Yes	No
--	**Propranolol**	Capsule, tablets: 10 mg, 20 mg, 40 mg, 60 mg, 80 mg, 120 mg, 160 mg (usual range 120-240 mg per day)	Yes	No
--	**Timolol**	Tablets: 5 mg, 10 mg, 20 mg (usual range 10-30 mg per day)	Yes	No
--	**Topiramate**	Oral capsule, tablets, solution: 25 mg, 50 mg, 100 mg, 200 mg (usual range 25-200 mg per day)	Yes	No
--	**Venlafaxine**	Tablets: 37.5 mg, 75 mg, 150 mg, 225 mg (usual range 150 mg per day)	Yes	No
J0585	**OnabotulinumtoxinA Injection** (Botox)	100 units, 200 units vials	Yes	Yes (PA, QL)
--	**Erenumab-aooe Auto-Injector** (Aimovig)	Auto-injector: 70 mg/1 ml, 140 mg/ml	Yes	No
J3031	**Fremanezumab** (Ajovy)	Solution Auto-injector, Prefilled Syringe: 225 mg/1.5 ml	Yes	No
--	**Galcanezumab** (Emgality)	Auto-injector, Prefilled Syringe: 100 mg/mL 120 mg/ml	Yes	No
J3032	**Eptinezumab-jjmr** (Vyepti)	100 mg/mL vial	Yes	Yes (PA, QL)
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonist				
--	**Atogepant** (Quilpta)	Tablet: 10 mg, 30 mg, 60 mg	Yes	No
--	**Rimegepant** (Nurtec ODT)	Tablet, orally-disintegrating: 75 mg	Yes	No
PREVENTIVE AGENTS W/ NSAIDS				
--	**Ibuprofen**	Tablets, capsules, solution: 100 mg, 200 mg, 600 mg, 800 mg (usual range: 200 mg twice daily)	Yes	No
--	**Naproxen**	Tablets, suspension: 125 mg, 250 mg, 375 mg, 500 mg (usual range 500-1,000 mg per day)	Yes	No

PA = Prior Authorization Required; QL = Quantity Limit

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not

covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

Serotonin Agonists

Sumatriptan Injection

- ❒ **Coverage Criteria:** None
- ❒ **Limits:** None

Migraine Prophylactic Agents

OnabotulinumtoxinA (Botox) Injection

- ❒ **Coverage Criteria:** ALL of the following must be met:
  [A] For patients age 18 years or older
  [B] Must be prescribed by a Neurologist
  [C] **ALL** of the following criteria must be met:
  (1) ≥ 15 or more days per month for ≥ 3 month
  (2) ≥ 4 hours a day or longer duration, as indicated by 5 or more attacks with **ALL** of the following:
  (a) Headache symptoms, as indicated by 2 or more of the following: *Aggravation by or causing avoidance of routine physical activity, or *Moderate or severe pain intensity, or *Pulsating quality, or *Unilateral location
  (b) Migraine-associated symptoms, as indicated by 1 or more of the following: *Nausea or vomiting, or *Photophobia and phonophobia
  (c) Other potential causes of headaches have been excluded
  (3) Use **2 (two)** different preventive medications at therapeutic dose (eg, beta-blocker, Calcium channel blocker, tricyclic antidepressant, anticonvulsant) unless therapy has been ineffective or not tolerated for trial of at least **8 (eight) weeks** each
  (4) No neuromuscular disease (eg, myasthenia gravis)
- ❒ **Limits:** 1 injection per 3 months
- ❒ **Required Information for Approval:** Clinical documentations, chart notes, and pharmacy fill history indicating all of the criteria listed above are met.
- ❒ **Other Notes:** None

Eptinezumab (Vyepti) Solution

- ⌖ **Coverage Criteria:** PA required. Reserved for patients who have failed 6 months of therapy with **Botox**, **Atogepant** (Qulipta), prophylactic-dosed **Rimegepant** (Nurtec), **Erenumab** (Aimovig), **Fremanezumab** (Ajovy), or **Galcanezumab** (Emgality) and are 18 years of age or older. Must be prescribed by a Neurologist.
- ⌖ **Limits:** One infusion per 3 months.
- ⌖ **Required Information for Approval:** Clinical documentation, chart notes, and pharmacy fill history indicating all of the criteria listed above are met.
- ⌖ **Other Notes:** None

⌖ CLINICAL JUSTIFICATION

Frequent migraine attacks are not only disabling and lead to a poor quality of life, but frequent use of abortive therapies can lead to chronic migraines. For this reason, patients experiencing more than 2 headaches per month[1] or patients with headaches lasting more than 2 days duration are candidates for migraine prophylaxis.[2,3] The 2012 AHS/AAN Guidelines recommend the following medications as migraine prophylaxis therapies: divalproex/valproic acid, metoprolol, propranolol, and topiramate.[4] 2013 AHS/AAN Guideline updates include timolol as one of the agents for migraine prevention.[16] NSAID use for migraine prevention has shown modest to significant benefit—particularly for naproxen and ibuprofen.[5] The time it takes to observe the therapeutic benefits of migraine prophylaxis varies between individuals, so international guidelines suggest a minimum of a two to three month trial.[6]

In regards to abortive therapies, serotonin agonists are similar in migraine relief but some are faster-acting than others. Sumatriptan formulations are the fastest-acting. Almotriptan, Eletriptan, Rizatriptan, and Zolmitriptan are intermediate-acting while Frovatriptan and Naratriptan have the slowest onset. Frovatriptan costs 3 times more than Naratriptan tablets per fill. With similar onset times and a limited cost-benefit ratio, Frovatriptan will remain non-formulary. Sumatriptan injections are marketed to have the fastest onset (10 minutes vs <30 minutes for sumatriptan tablets). However, its cost-benefit ratio is not cost-effective since sumatriptan injections cost approximately 10 times more than Sumatriptan tablets. For this reason, sumatriptan injections are non-formulary. Zembrace (Sumatriptan SQ injections) comes in a 3mg/0.5 mL pre-filled auto-injector that can have a maximum daily dose of 12 mg, equating to a cost of almost 90 times more than Sumatriptan tablets.[7]

Sumatriptan nasal spray is currently on formulary for patients who have a documented inability to use tablets/capsules (including ODT). This allows for an alternate formulation besides oral agents for acute migraine therapy. Onzetra Xsail is a new formulation of Sumatriptan that also acts via the nasal passageway but is administered via first piercing one of the 11 mg nosepieces to release Sumatriptan from the capsule, followed by attaching both nosepieces from the device body into each nostril so it makes a tight seal, then rotating the whole device so the mouthpiece could be placed into the mouth, and finally having the patient forcefully blow through the mouthpiece to deliver the Sumatriptan powder into the nasal cavity.[8] The patient would then need to repeat all the above steps a second time to obtain a total recommended dose of 22 mg per administration.

In the 2019 American Headache Society consensus statement, CGRP inhibitors are a suitable option for the prevention of migraines. CGRP inhibitors should only be tried after an inability to tolerate or inadequate response with other agents (including onabotulinumtoxinA). Because of long-term safety evidence and efficacy, onabotulinumtoxinA should still be tried before using any CGRP inhibitor.[34]

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⌖ REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Topiramate review 5-07.doc	5/2007	Allen Shek, PharmD
Updated Policy	Triptan_utilization_review_2-16-10.docx	2/2010	Allen Shek, PharmD
Updated Policy	Opioid Coverage Policy 2015-02-17.docx	2/2015	Jonathan Szkotak, PharmD
Updated Policy	HPSJ Coverage Policy – Neurologic – Migraines 2015-02.docx	2/2015	Jonathan Szkotak, PharmD
Updated Policy	HPSJ Coverage Policy – Neurologic – Migraines 2015-09.docx	9/2015	Johnathan Yeh, PharmD
Updated Policy	HPSJ Coverage Policy – Neurologic – Migraines 2016-12.docx	12/2016	Johnathan Yeh, PharmD
Updated Policy	HPSJ Coverage Policy – Neurologic – Migraines 2017-09.docx	9/2017	Johnathan Yeh, PharmD
Updated Policy	HPSJ Coverage Policy – Neurologic – Migraines 2018-12.docx	12/2018	Matthew Garrett, PharmD
Updated Policy	HPSJ Coverage Policy – Neurologic – Migraines 2019-12.docx	12/2019	Matthew Garrett, PharmD
Updated Policy	HPSJ Coverage Policy – Neurologic – Migraines 2020-12.docx	12/2020	Matthew Garrett, PharmD
Updated Policy	Migraines	12/2021	Matthew Garrett, PharmD
Update to Policy	Migraines	11/2022	Matthew Garrett, PharmD
Update to Policy	Migraines	9/2023	Matthew Garrett, PharmD

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy