

MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY:	Migraine Therapy	P&T DATE:	9/12/2017
CLASS:	Neurological Disorders	REVIEW HISTORY (MONTH/YEAR)	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.

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 9/2017)

Abortive Agents					
Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Formulary Limits	Average Cost per 30 days	Notes
Serotonin Agonists	Rizatriptan (Maxalt) <i>Tablet, ODT</i>	Tablet: 5mg, 10mg ODT: 5mg, 10 mg	QL	\$12.89	Limit 9 tablets per month.
	Sumatriptan (Imitrex) <i>Tablet</i>	25mg, 50mg, 100mg	QL	\$11.77	Limit 9 tablets per month.
	Sumatriptan (Imitrex) <i>Nasal Spray</i>	5mg/act, 20mg/act	PA; QL	\$218.09	Reserved for patients ≥12 years of age and unable to swallow tablets. Limit 6 units per month.
	Naratriptan (Amerge) <i>Tablet</i>	1mg, 2.5mg	PA; QL	\$83.92	Reserved for treatment failure to either Sumatriptan or Rizatriptan in the last year. Limit 9 tablets per month.
	Zolmitriptan (Zomig) <i>Tablet, ODT</i>	2.5mg, 5mg	PA; QL	\$54.11	Reserved for treatment failure to either Sumatriptan or Rizatriptan in the last year. Limit 9 tablets per month.
	Almotriptan (Axert) <i>Tablet</i>	6.25mg, 12.5mg	PA; QL	\$283.43	Reserved for treatment failure to [1] Sumatriptan/Rizatriptan AND [2] Naratriptan/Zolmitriptan. Limit 9 tablets per month.
	Eletriptan (Relpax) <i>Tablet</i>	20mg, 40mg	PA; QL	\$375.08	Reserved for treatment failure to [1] Sumatriptan/Rizatriptan AND [2] Naratriptan/Zolmitriptan. Limit 9 tablets per month.
	Sumatriptan (Imitrex, Zembrace, Zecuity, Onzetra Xsail) <i>Injection, Patch, Nasal Powder</i>	Injections: 4mg/0.5ml, 6mg/0.5ml Patch: 6.5mg/4hrs Nasal: 11 mg	NF	\$275.35	Non-formulary
	Frovatriptan (Frova) <i>Tablet</i>	2.5mg	NF	\$418.73	Non-formulary
Butalbital Combinations	Butalbital/Acetaminophen /Caffeine (Fioricet) <i>Capsule, Tablet</i>	50mg-325mg-40mg	QL	\$14.32	Limit 30 units per month. Capsules are non-formulary

	Butalbital/Acetaminophen /Caffeine/Codeine <i>Capsule</i>	50mg-325mg- 40mg-30mg	QL	\$24.81	Reserved for patients ≥12 years of age. Limit 30 units per month.
	Butalbital/Aspirin/Caffeine (Fiorinal) <i>Capsule</i>	50mg-325mg- 40mg	QL	\$28.04	Limit 30 units per month.
Ergot Alkaloids/ Other	Ergotamine Tartrate/Caffeine <i>Tablet, Suppository</i>	1mg-100mg Tab, 2mg-100mg Supp	QL	\$195.32	Limit 30 units per month.
	Ergotamine Tartrate <i>SL Tablet</i>	2mg	QL	-	Limit 30 units per month.
	Isometheptene/ Dichloralphen/ Acetaminophen <i>Capsule</i>	65mg-100mg- 325mg	QL	\$78.68	Limit 30 units per month.

Prophylactic Agents

Therapeutic Class	Generic Name (Brand Name)	Usual Dose	Formulary Limits	Average Cost per 30 days	Notes
Migraine- Preventive Agents	Amitriptyline	25-150 mg/day	-	\$15.28	
	Atenolol	100 mg/day	-	\$3.45	
	Divalproex/Valproic Acid	400-1,000 mg/day	-	\$67.22	
	Metoprolol Tartrate	47.5-200 mg/day	-	\$3.39	
	Propranolol	120-240 mg/day	-	\$18.24	
	Topiramate	25-200 mg/day	-	\$11.63	
Preventive Agents w/ NSAIDs	Ibuprofen	200mg twice daily	-	\$5.67	
	Naproxen	500-1,000 mg/day	-	\$7.17	

NF = Non-Formulary; 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 HSPJ Medical Review Guidelines (UM06).

Serotonin Agonists

Sumatriptan Tablet (Imitrex), Sumatriptan Nasal Spray (Imitrex)*, Rizatriptan Tablet (Maxalt)

- Coverage Criteria:** None.
- Limits:** Limit 9 units per 30 days.
- Required Information for Approval:** None.
- Other Notes:** *Sumatriptan nasal spray is reserved for patients ≥12 years of age with documented inability to swallow tablets/capsules (including ODT tablets). Limited to 6 units per 30 days.
 - **Onzetra Xsail, Zecuity, Zembrace Symtouch are Non-Formulary**

Naratriptan (Amerge) Tablet

- Coverage Criteria:** Naratriptan is reserved for treatment failure to either Sumatriptan or Rizatriptan in the last 365 days.
- Limits:** Limit 9 units per 30 days.
- Required Information for Approval:** Prescription history of Sumatriptan or Rizatriptan OR documented intolerance to Sumatriptan or Rizatriptan.
- Other Notes:** None.

Zolmitriptan (Zomig) Tablet/ODT, Almotriptan (Axert) Tablet, Eletriptan (Relpax)

- Coverage Criteria:** Reserved for treatment failure to [1] Sumatriptan/Rizatriptan AND [2] Naratriptan within the last 365 days.
- Limits:** Limit 9 units per 30 days.
- Required Information for Approval:** Prescription history of [1] Sumatriptan or Rizatriptan and [2] Naratriptan OR documented intolerance to Sumatriptan/Rizatriptan and Naratriptan.
- Other Notes:** None.
- Non-Formulary:** Sumatriptan Injection, Frovatriptan

Butalbital Combination Agents

Butalbital/APAP/Caffeine (Fioricet), Butalbital/APAP/Caffeine/Codeine, Butalbital/Aspirin/Caffeine (Fiorinal)

- Coverage Criteria:** None.
- Limits:** Limit 30 tablets/capsules per 30 days.
- Required Information for Approval:** None.
- Other Notes:** Butalbital/APAP/Caffeine/Codeine is restricted to patients ≥ 12 years of age.

Ergot Alkaloids/Other

Ergotamine Tartrate/Caffeine, Ergotamine Tartrate, Isometh/Dichlph/Acetaminophen

- Coverage Criteria:** None.
- Limits:** Limit 30 tablets/capsules per 30 days.
- Required Information for Approval:** None.
- Other Notes:** None.

Migraine Prophylactic Agents

Amitriptyline, Divalproex, Metoprolol, Propranolol, Topiramate, Ibuprofen, Naproxen

- Coverage Criteria:** None.
- Limits:** None.
- Required Information for Approval:** None.
- 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 month¹ 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 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 is markedly more costly at 8 times the cost of 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 40 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, hence as there are other non-oral formulations available and there is not a distinguished cost-effectiveness present with Zembrace, it will also remain non-formulary.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. As there is already a Sumatriptan nasal formulation that is on formulary for half the cost per fill and uses a method of administration that is not completely new to patients, Onzetra Xsail will remain non-formulary.

Zecuity is the only current Sumatriptan patch formulation available with a marketing start date of September 2015. It was marketed for use as a battery powered patch that is wrapped around the upper arm or thigh and should not be placed for longer than four hours. Although it is a new formulation, an FDA Safety Alert, updated on 6/13/16, stated that Teva Pharmaceuticals has temporarily suspended sales, marketing, and distribution of Zecuity due to large numbers of patients reporting burns or scars on the skin where the patch was worn. The patients reported severe redness, pain, skin discoloration, blistering, and cracked skin.⁹ The FDA has instructed that health care providers discontinue prescribing Zecuity and for patients to stop using the patches. Due to the safety concern and availability of other formulations of Sumatriptan for use in acute migraine attacks, Zecuity will remain non-formulary.

REFERENCES

1. Telt-Hansen P. Prophylactic pharmacotherapy of migraine: some practical guidelines. *Neurol Clin* 1997;15: 153-165.
2. Becker WJ. Evidence based migraine prophylactic drug therapy. *Can J Neurol Sci* 1999; 26(suppl 3): S27-S32.
3. Diener HC, Kaube H, Limmroth V. A practical guide to the management and prevention of migraine. *Drugs* 1998; 56: 811-824.
4. 2012 AHS/AAN guidelines for prevention of episodic migraine: a summary and comparison with other recent clinical practice guidelines. *Headache*. 2012; 52: 930-945.
5. Holland S, Silberstein SD, Freitag F, Dodick DW, Argoff C. Evidence-based guideline update: NSAIDs and other complementary treatments for episodic migraine prevention in adults. *Neurology*. 2012;78:1346-1353.
6. Silberstein SD, Silberstein MM. New concepts in the pathogenesis of headache-Part II. *Pain Manag*. 1990;3:334-42.
7. Zembrace Symtouch™ [prescribing information]. San Diego, CA: Dr. Reddy's Laboratories Limited; 2016.
8. Onzetra Xsail™. [prescribing information]. Aliso Viejo, CA: Avanir Pharmaceuticals, Inc.; 2016.
9. FDA. Zecuity (sumatriptan) Migraine Patch: Drug Safety Communication – FDA Evaluating Risk of Burns and Scars. Safety Alerts for Human Medical Products. 2016 June. Accessed September 18, 2016.
10. FDA. Codeine and Tramadol Medicines: Drug Safety Communication – Restricting Use in Children, Recommending Against Use in Breastfeeding Women. 2017 April. Accessed September 9, 2017.
11. 2004 AAN Practice Parameter: Pharmacological treatment of migraine headache in children and adolescents. *Neurology*. 2004; 63: 2215-2224.

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

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