Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 04/11/2024

Calcitonin Gene Related Peptide (CGRP) Antagonists

Vyepti® (eptinezumab-jjmr)

HCPCS: J3032

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. Migraine Prevention:
      i. FDA approved age
      ii. Medication is being used for preventive treatment of migraine headaches.
      iii. There is a persistent history of recurring debilitating headaches (4 or more headache days per month with migraine headache lasting for 4 hours per day or longer).
      iv. Adequate trials (at least 2 month trial) of prophylactic therapy from at least TWO different therapy classes listed in Appendix 1 were not effective, contraindicated, or not tolerated.
      v. Not to be used in combination with other CGRP antagonists for migraine prevention
   b. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in the BCBSM/BCN utilization management medical drug list and/or BCBSM/BCN's prior authorization and step therapy documents

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limit: FDA approved dosing
   b. Authorization Period:
      i. 6 months for initial therapy
      ii. 1 year for continuation of therapy
   c. Renewal Criteria: Documentation of at least a 50% or greater reduction in monthly migraine days (MMDs) from baseline

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Migraines affect 38 million people throughout the United States causing a significant decrease in quality of life and a large economic burden. An estimated 36 billion dollars are spent due to health care and loss of productivity costs. There is a large subset of migraine sufferers that are candidates for migraine prevention, but only a small portion of those candidates actually utilize these medications. Numerous drug classes have been studied for the prevention of migraine. The most recent guidelines published by the American Academy of Neurology in 2018 have shown efficacy for migraine prevention among antiepileptic drugs, antidepressants, antihypertensives, triptans (short term use for menstrually related migraines (MRM)), and botulinum toxin. In addition to drug therapy, neuromodulation and biobehavioral therapy have shown efficacy for the preventive and acute treatment of migraine.

- Guidelines suggest that there is no standard first line agent for the prevention of migraines; however, it does classify the agents by level of efficacy. Level A medications are those with established efficacy, Level B are probably effective, Level C are possibly effective, Level U are inadequate or conflicting data to support use, and Other are established as possibly or probably ineffective. There are many medications that are considered level A, as they have shown efficacy in >2 Class I trials. Divalproex sodium, sodium valproate, topiramate, metoprolol, propranolol, timolol, frovatriptan (short-term prophylaxis for treatment of MRM), and onabotulinumtoxinA are all Level A medications.

- Current abortive treatment options for migraines includes analgesics (such as NSAIDs), triptans and ergot alkaloids. Use of the latter is limited due to uncertainty of clear effectiveness and undesirable side effects. Reyvow® (lasmiditan), a first in class drug, was recently approved and is expected to be used in patients who are not candidates for triptans.

- Calcitonin gene related peptide (CGRP) antagonists are the first agents on the market that have a clearly understood mechanism of action in migraine prophylaxis. CGRP is the most potent endogenous vasodilator. Commonly, migraine sufferers present with elevated serum levels of CGRP even on non-migraine days. Inhibiting this pathway by binding to either the CGRP peptide itself or the CGRP receptor has proven to be an effective method in preventing migraine attacks in both episodic and chronic migraine.

- The CGRP receptor antagonist, Aimovig®, was approved by the FDA on May 17th, 2018. A biologics license application (BLA) was accepted by the FDA based off the results of two phase II and two phase III multicenter, randomized, double-blind, placebo-controlled clinical trials (totaling more than 2,500 patients) conducted in the US and Europe. Safety and efficacy of treatment was established in both episodic and chronic migraine. For episodic migraine, the phase III STRIVE trial looked at Aimovig® 70 mg and 140 mg. The study found a 3.2 day and 3.7 day reduction in monthly migraine days compared to placebo, respectively. Similarly the phase III ARISE trial found a 2.9 day reduction in monthly migraine days. Both the STRIVE and ARISE trials found that Aimovig® was similar in safety and tolerability compared to placebo. The phase IIIb LIBERTY trial evaluated the effectiveness of Aimovig® in preventing migraines in adults with episodic migraines who have failed other prophylactic therapies. The study found that patients receiving Aimovig 140mg had a 50% or greater reduction of monthly migraine days from baseline compared to placebo over weeks 9 to 12. The study included an 52-week open-label extension study that showed reduction of -9.29 migraine days per month from baseline at week 52. . A phase II study for chronic migraine, found statistical differences with Aimovig® over placebo in the mean number of monthly migraine days with a reduction of approximately 6.6 days in the Aimovig group and 4.2 days in the placebo group. There were no statistical differences found in the number of adverse events in the treatment group vs. placebo.

- Vyepti was the 5th anti-CGRP medication and first IV version approved for migraine prophylaxis on 2/21/2020 followed closely by Nurtec, the 6th anti-CGRP and 2nd oral option indicated for the acute treatment of migraines on 2/27/2020.

- The American Headache Society publishes guidelines on all types of headache disorders including migraines. The most recent guidelines were published in 2018 and speak to the acute treatment and prophylaxis of migraines, both episodic and chronic. These guidelines incorporate CGRP antagonists for migraine therapy, which were absent from guidelines in previous years, as second line and adjunctive therapies for migraine prophylaxis in adults. The American Headache Society published guidelines for the treatment of cluster headache in 2016, however, these current guidelines do not include CGRP antagonists. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice from June 2021 continues to recommend adequate trials of established acute and/or preventive treatments before initiating use of newer migraine-specific acute and preventive therapies, in part to due to cost considerations, and no published evidence supports or refutes this hierarchical approach.

Appendix 1: Medications for Prophylaxis of Migraines

Class	Accepted Examples
Anticonvulsants	Depakote® (divalproex), Depakene® (sodium valproate), Topamax® (topiramate), Tegretol® (carbamazepine)
ACE inhibitor or Angiotensin Receptor Blocker	Zestril® (lisinopril), Atacand® (candesartan)
Beta Blockers	Inderal® (propranolol), Lopressor® (metoprolol), Tenormin® (atenolol), Corgard® (nadolol), Blocadren® (timolol), Bystolic® (nebivolol), Visken®(pindolol)
Calcium Channel Blockers	Procardia® (nifedipine), Cardizem® (diltiazem), Calan® (verapamil)
Antidepressants	Elavil® (amitriptyline), Effexor® (venlafaxine)
Botulinum Toxin	OnabotulinumtoxinA

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<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>2.0</td><td>Effective Date: 04/11/2024</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.9</td><td>Effective Date: 04/06/2023</td><td>Updated to include Zavzpret</td></tr>
<tr><td>1.8</td><td>Effective Date: 12/01/2022</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.7</td><td>Effective Date: 12/09/2021</td><td>Update to include Qulipta and remove prescriber requirement and rebound headache criteria</td></tr>
<tr><td>1.6</td><td>Effective Date: 08/12/2021</td><td>Update due to Nurtec ODT’s prevent indication</td></tr>
<tr><td>1.5</td><td>Effective Date: 04/08/2021</td><td>Removed criteria “not to be used in combination with botulinum toxin type A”</td></tr>
<tr><td>1.4</td><td>Effective Date: 08/13/2020</td><td>Updated Appendix 5 from acute episodic cluster headache therapies to prophylaxis episodic cluster headach therapies, affecting criteria requirements for Emgality’s cluster headache diagnosis.</td></tr>
<tr><td>1.3</td><td>Effective Date: 7/1/2020</td><td>UM medical management system update for BCBSM
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.2</td><td>Effective Date: 06/01/2020</td><td>UM medical management system update for MAPPO and BCNA
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<tr><td>1.0</td><td>Effective Date: 4/16/2020</td><td>New full drug review</td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Vyepti™ (eptinezumab-jjmr) J3032

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

This form is to be used by participating physicians to obtain coverage for Vyepti. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	**Name**
ID Number	**Specialty**
D.O.B. ☐Male ☐Female	**Address**
Diagnosis	**City /State/Zip**
Drug Name	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity	**NPI**
Directions	**Contact Person**
Date of Service(s)	**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Initial or Continuation request? ☐ Initial ☐ Continuation *Date patient started therapy:* _____
2. Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
   ☐ Hospital outpatient facility (go to #3) *Reason for Hospital Outpatient:* _____
3. Please specify location of administration if hospital outpatient infusion: _____
4. Please provide the NPI number for the place of administration: _____

5. **Initiation AND Continuation of therapy:**
   a. Please check the patient's diagnosis: ☐ Migraine headache ☐Other_____
   b. What type of headache does the patient have? ☐ Tension ☐ Cluster ☐ Medication overuse
      ☐ Migraine headache ☐ Other: _____
   c. Has an evaluation been performed to rule out headaches caused by medication use (rebound headaches)?
      ☐ Yes ☐ No
      i. If no, have preventative steps been taken to reduce the risk of rebound headaches?
         ☐ Yes ☐ No Explain _____
   d. What long term daily preventative treatments has the patient tried and failed for at least 2 months?
      ☐ Anticonvulsants: _____ ☐ ACE inhibitor/ARB: _____ ☐ B-blockers: _____
      ☐ Calcium Channel Blockers: _____ ☐ Antidepressants: _____ ☐ Botulinum Toxin: _____
      ☐ Other: _____
   e. What is the frequency of migraine headache days (before/after starting Vyepti) as documented by the patient's headache diary or calendar?
      PRIOR TO Vyepti: _____ days/month AND _____ hours/month
      AFTER Vyepti: _____ days/month AND_____ hours/month
   f. Will the patient be using Vyepti in combination with other Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists (for example: Aimovig, Ajovy, or Emgality) or with botulinum toxins (for example: Botox, Dysport, or Xeomin)?
      ☐ Yes ☐ No Explain _____

6. **Continuation request**: (please answer above questions as well): **Vyepti start date**: _____
   a. What is the frequency of migraine headache days (before/after starting Vyepti) as documented by the patient's headache diary or calendar?
      PRIOR TO Vyepti: _____ days/month AND _____ hours/month
      AFTER Vyepti: _____ days/month AND_____ hours/month

Please add any other supporting medical information necessary for our review

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date
Step 2: Checklist	☐ Form Completely Filled Out ☐ Attached Chart Notes	☐ Concurrent Medical Problems ☐ Prior Therapies
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**