Remote Electrical Neuromodulation for Migraines

Policy # 00797
Original Effective Date: 08/08/2022
Current Effective Date: 08/14/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers remote electrical neuromodulation for acute migraine to be **investigational.***

Background/Overview

Migraine is a neurologic disease characterized by recurrent moderate to severe headaches with associated symptoms that can include aura, photophobia, nausea, and/or vomiting. Overall migraine prevalence in the United States is about 15% but varies according to population group. Prevalence is higher in women (21%), among American Indian/Alaska Natives (22%), and among 18- to 44-year-olds (19%). Social determinants including low education level (18%), use of Medicaid (27%), high poverty level (23%), and being unemployed (22%) are also associated with higher rates of migraine.

Migraine is categorized as episodic or chronic depending on the frequency of attacks. Generally, episodic migraine is characterized by 14 or fewer headache days per month and chronic migraine is characterized by 15 or more headache days per month. Specific International Classification of Headache Disorders diagnostic criteria are as follows:

- Episodic migraine:
    1. Untreated or unsuccessfully treated headache lasting 4 to 72 hours
    2. Headache has at least 2 of the following characteristics:
        a. Unilateral location
        b. Pulsating quality
        c. Moderate or severe pain intensity
        d. Aggravation by or causing avoidance of routine physical activity
    3. At least 1 of the following during headache:

a. Nausea and/or vomiting
b. Photophobia or phonophobia.

- Chronic migraine:
  1. Migraine-like or tension-type headache on 15 or more days per month for more than 3 months
  2. At least 5 headache attacks without aura meet episodic migraine criteria 1 to 3, and/or at least 5 headache attacks with aura meet episodic migraine criteria 2 to 3
  3. On more than 8 days per month for more than 3 months, fulfilling any of the following criteria:
     a. For migraine without aura, episodic migraine criteria 2 and 3
     b. For migraine with aura, episodic migraine criteria 1 and 2
     c. Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative.

Migraine attacks, whether due to episodic or chronic migraine, require acute management. The goal of acute treatment is to provide pain and symptom relief as quickly as possible while minimizing adverse effects, with the intent of timely return to normal function. Pharmacologic interventions for treatment of acute migraine vary according to migraine severity. First-line therapy for an acute episode of mild or moderate migraine includes oral non-steroidal anti-inflammatory drugs (NSAIDs) or acetaminophen. Moderate to severe migraine can be treated through the use of triptans or an NSAID-triptan combination. Antiemetics can be added for migraine accompanied by nausea or vomiting, though certain antiemetic medications used as monotherapy can also provide migraine relief. Other pharmacologic interventions used to treat acute migraine include calcitonin-gene related peptide antagonists, which can be used in patients with an insufficient response or contraindications to triptans, lasmiditan, and dihydroergotamine. Migraine can be managed at home, although acute migraine is a frequently cited reason for primary care and emergency department visits. Regular use of pharmacologic interventions can result in medication overuse, which in turn could lead to rebound headache and increased risk of progression from episodic to chronic migraine.

Remote electrical neuromodulation (REN) may offer an alternative to pharmacologic interventions for patients with acute migraine or it may decrease the use of abortive medications and the risk of medication overuse to treat acute migraines. The only currently available REN device (Nerivio™‡) cleared for use by the Food and Drug Administration (FDA) is worn on the upper arm and stimulates the peripheral nerves to induce conditioned pain modulation (CPM). The conditioned pain in the

arm induced by the Nerivio REN device is believed to reduce the perceived migraine pain intensity. Control of the REN device is accomplished through Bluetooth communication between the device and the patient's smartphone or tablet. At onset of migraine or aura and no later than within 1 hour of onset, the user initiates use of the device through their mobile application. Patient-controlled stimulation intensity ranges from 0 to 100%, corresponding to 0 to 40 milliamperes (mA) of electrical current. Patients are instructed to set the device to the strongest stimulation intensity that is just below their perceived pain level. The device provides stimulation for up to 45 minutes before turning off automatically. The Nerivio manufacturer indicates that the device can be used instead of or in addition to medication.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

In May 2019, Nerivio Migra™‡ (Theranica Bio-Electronics Ltd.) was granted a de novo classification by the FDA (class II, special controls, product code: QGT). This new classification applied to this device and substantially equivalent devices of this generic type. Nerivio Migra was initially cleared for treatment of acute migraine in adults who do not have chronic migraine.

In October, 2020, Nerivio was cleared for marketing by the FDA through the 510(k) process (K201824). FDA determined that this device was substantially equivalent to Nerivio Migra for use in adults. The device name changed to just "Nerivio" and the exclusion of chronic migraine patients was removed. The Nerivio device can provide more treatments than the predicate Nerivio Migra (12 treatments vs. 8 treatments) and has a longer shelf life (24 months vs. 9 months). In January, 2021, the Nerivio device was cleared for use in patients aged 12 to 17 years.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Migraine attacks due to episodic or chronic migraine require acute management. Current first-line therapy for treatment of acute migraine involves use of various pharmacologic interventions.

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Regular use of pharmacologic interventions can result in medication overuse and increased risk of progression from episodic to chronic migraine. Nonpharmacologic remote electrical neuromodulation (REN) may offer an alternative to pharmacologic interventions for patients with migraine.

Summary of Evidence

For individuals with acute migraine due to episodic or chronic migraine who receive REN, the evidence includes 2 randomized controlled trials (RCTs) and nonrandomized, uncontrolled studies. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Use of an active REN device resulted in more patients with improved pain and symptoms at 2-hour follow-up compared with a sham device based on 2 small (N=212) RCTs with numerous relevance limitations. Based on the existing evidence, it is unclear how Nerivio™‡ would fit into the current acute migraine management pathway. The specific intended use and associated empirically-documented recommended regimen(s) must be specified in order to adequately evaluate the net health benefit. Additionally, functional outcomes and quality of life must be evaluated in well-designed and conducted studies in defined populations using documented Nerivio regimens. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Headache Society

In 2021, the American Headache Society (AHS) issued guidance on the integration of new migraine treatments, including REN, into clinical practice. The AHS addressed the use of neuromodulatory devices as a group that included electrical trigeminal nerve stimulation, noninvasive vagus nerve stimulation, single-pulse transcranial magnetic stimulation and REN; no guidance specific to REN use was issued.

The AHS determined that initiation of a neuromodulatory device is appropriate when all of the following criteria are met:

- Prescribed/recommended by a licensed clinician
- Patient is at least 18 years of age (*the guidance noted that 3 devices, including REN, are approved for use in patients age 12 to 17 years*)
- Diagnosis of ICHD-3 migraine with aura, migraine without aura, or chronic migraine
- Either of the following:
    - Contraindications to or inability to tolerate triptans
    - Inadequate response to 2 or more oral triptans, as determined by EITHER of the following:
        - Validated acute treatment patient-reported outcome questionnaire (Migraine Treatment Optimization Questionnaire, Patient Perception of Migraine Questionnaire-Revised, Functional Impairment Scale, Patient Global Impression of Change)
        - Clinician attestation.

American Academy of Neurology/American Headache Society
A 2019 joint guideline issued by the American Academy of Neurology and the American Headache Society on the treatment of acute migraine in children and adolescents did not address the use of REN or other nonpharmacologic treatments.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently ongoing trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04828707[a]	A Prospective, Randomized, Double-blind, Sham-controlled Multi-center Clinical Study Assessing the Safety and Efficacy of Nerivio for the Preventive Treatment of Migraine	300	Sep 2022
NCT05102591	A Pilot Clinical Trial of a New Neuromodulation Device for Acute Attacks of Migraine in Children and Adolescents Visiting the Emergency Department	40	Feb 2025

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

References

1. VanderPluym JH, Halker Singh RB, Urtecho M, et al. Acute Treatments for Episodic Migraine in Adults: A Systematic Review and Meta-analysis. JAMA. Jun 15 2021; 325(23): 2357-2369. PMID 34128998
2. Burch R, Rizzoli P, Loder E. The prevalence and impact of migraine and severe headache in the United States: Updated age, sex, and socioeconomic-specific estimates from government health surveys. Headache. Jan 2021; 61(1): 60-68. PMID 33349955
3. Singh RBH, VanderPluym JH, Morrow AS, et al. Acute Treatments for Episodic Migraine. Rockville (MD): Agency for Healthcare Research and Quality (US); December 2020.
4. Ailani J, Burch RC, Robbins MS. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. Headache. Jul 2021; 61(7): 1021-1039. PMID 34160823
5. Burch RC, Loder S, Loder E, et al. The prevalence and burden of migraine and severe headache in the United States: updated statistics from government health surveillance studies. Headache. Jan 2015; 55(1): 21-34. PMID 25600719

6. Nierenburg H, Stark-Inbar A. Nerivio (R) remote electrical neuromodulation for acute treatment of chronic migraine. Pain Manag. Apr 2022; 12(3): 267-281. PMID 34538078
7. U.S. Food and Drug Administration. De Novo Classification Request for Nerivio Migra.
8. U.S. Food and Drug Administration. 501(k) Summary: Theranica Bio-Electronics LTDs Nerivio.
9. U.S. Food and Drug Administration. 510(k) Summary: Nerivio Approval in Adolescents.
10. Tassorelli C, Diener HC, Silberstein SD, et al. Guidelines of the International Headache Society for clinical trials with neuromodulation devices for the treatment of migraine. Cephalalgia. Oct 2021; 41(11-12): 1135-1151. PMID 33990161
11. Diener HC, Tassorelli C, Dodick DW, et al. Guidelines of the International Headache Society for controlled trials of acute treatment of migraine attacks in adults: Fourth edition. Cephalalgia. May 2019; 39(6): 687-710. PMID 30806518
12. Yarnitsky D, Volokh L, Ironi A, et al. Nonpainful remote electrical stimulation alleviates episodic migraine pain. Neurology. Mar 28 2017; 88(13): 1250-1255. PMID 28251920
13. Yarnitsky D, Dodick DW, Grosberg BM, et al. Remote Electrical Neuromodulation (REN) Relieves Acute Migraine: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial. Headache. Sep 2019; 59(8): 1240-1252. PMID 31074005
14. Marmura MJ, Lin T, Harris D, et al. Incorporating Remote Electrical Neuromodulation (REN) Into Usual Care Reduces Acute Migraine Medication Use: An Open-Label Extension Study. Front Neurol. 2020; 11: 226. PMID 32318014
15. Rapoport AM, Bonner JH, Lin T, et al. Remote electrical neuromodulation (REN) in the acute treatment of migraine: a comparison with usual care and acute migraine medications. J Headache Pain. Jul 22 2019; 20(1): 83. PMID 31331265
16. Ailani J, Rabany L, Tamir S, et al. Real-World Analysis of Remote Electrical Neuromodulation (REN) for the Acute Treatment of Migraine. Front Pain Res (Lausanne). 2021; 2: 753736. PMID 35295483
17. Hershey AD, Irwin S, Rabany L, et al. Comparison of Remote Electrical Neuromodulation and Standard-Care Medications for Acute Treatment of Migraine in Adolescents: A Post Hoc Analysis. Pain Med. Apr 08 2022; 23(4): 815-820. PMID 34185084
18. Hershey AD, Lin T, Gruper Y, et al. Remote electrical neuromodulation for acute treatment of migraine in adolescents. Headache. Feb 2021; 61(2): 310-317. PMID 33349920
19. Nierenburg H, Vieira JR, Lev N, et al. Remote Electrical Neuromodulation for the Acute Treatment of Migraine in Patients with Chronic Migraine: An Open-Label Pilot Study. Pain Ther. Dec 2020; 9(2): 531-543. PMID 32648205

20. Tepper SJ, Lin T, Montal T, et al. Real-world Experience with Remote Electrical Neuromodulation in the Acute Treatment of Migraine. Pain Med. Dec 25 2020; 21(12): 3522-3529. PMID 32935848
21. Grosberg B, Rabany L, Lin T, et al. Safety and efficacy of remote electrical neuromodulation for the acute treatment of chronic migraine: an open-label study. Pain Rep. Nov-Dec 2021; 6(4): e966. PMID 34667919
22. Nierenburg H, Rabany L, Lin T, et al. Remote Electrical Neuromodulation (REN) for the Acute Treatment of Menstrual Migraine: a Retrospective Survey Study of Effectiveness and Tolerability. Pain Ther. Dec 2021; 10(2): 1245-1253. PMID 34138449
23. Oskoui M, Pringsheim T, Holler-Managan Y, et al. Practice guideline update summary: Acute treatment of migraine in children and adolescents: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Headache Society. Headache. Sep 2019; 59(8): 1158-1173. PMID 31529481

Policy History

Original Effective Date: 08/08/2022
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07/07/2022	Medical Policy Committee review
07/13/2022	Medical Policy Implementation Committee approval. New policy.
07/06/2023	Medical Policy Committee review
07/12/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/12/2023	Coding update

Next Scheduled Review Date: 07/2024

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2022 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	Add code effective 01/01/2024: A4540 Delete code effective 01/01/2024: K1023
ICD-10 Diagnosis	All related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety,

effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.