Minimally Invasive Ablation Procedures for Morton and Other Peripheral Neuromas

Policy # 00574
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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 minimally invasive ablation procedures, including intralesional alcohol injection, radiofrequency ablation (RFA), and cryoablation for the treatment of Morton and other peripheral neuromas to be **investigational.***

Background/Overview

Neuroma

A neuroma is a pathology of a peripheral nerve that develops as part of a normal reparative process. Neuromas may develop after nerve injury or result from chronic irritation, pressure, stretch, poor repair of nerve lesions or previous neuromas, laceration, crush injury, or blunt trauma. Neuromas typically appear 6 to 10 weeks after trauma, with most presenting within 1 to 12 months after injury or surgery. They may gradually enlarge over 2 to 3 years and may or may not be painful. Pain from a neuroma may be secondary to traction on the nerve by scar tissue, compression of the sensitive nerve endings by adjacent soft tissues, ischemia of the nervous tissue, or ectopic foci of ion channels that elicit neuropathic pain. Patients may describe the pain as low-intensity dull pain or intense paroxysmal burning pain, often triggered by external stimuli such as touch or temperature. Neuroma formation has been implicated as a contributor of neuropathic pain in residual limb pain, post thoracotomy, postmastectomy, and post herniorrhaphy pain syndromes. Neuromas may coexist with phantom pain or can predispose to it.

Morton Neuroma

Morton neuroma is a common and painful compression neuropathy of the common digital nerve of the foot that may also be referred to as interdigital neuroma, interdigital neuritis, and interdigital or

Morton metatarsalgia. It is histologically characterized by perineural fibrosis, endoneurial edema, axonal degeneration, and local vascular proliferation. Thus, some investigators do not consider Morton neuroma to be a true neuroma; instead, they consider it to be an entrapment neuropathy occurring secondary to compression of the common digital nerve under the overlying transverse metatarsal ligament. Morton neuroma appears 10-fold more often in women than in men, with an average age at presentation of around 50 years.

The pain associated with Morton neuroma is usually throbbing, burning, or shooting, and localized to the plantar aspect of the foot. It is typically located between the 3rd and 4th metatarsal heads, although it may appear in other proximal locations. The pain may radiate to the toes and can be associated with paresthesia. The pain can be severe, and the condition may become debilitating to the extent that patients are apprehensive about walking or touching their foot to the ground. It is aggravated by walking in shoes with a narrow toe box or high heels that cause excessive pronation and excessive forefoot pressure; removal of tight shoes typically relieves the pain.

Diagnosis
Although a host of imaging methods are used to diagnosis Morton neuroma, including plain radiographs, magnetic resonance imaging, and ultrasonography, objective findings are unique to this condition and are primarily used to establish a clinical diagnosis. Thus, a patient's toes often show splaying or divergence. Patients may describe the feeling of a "lump" on the foot bottom or a feeling of walking on a rolled-up or wrinkled sock. Clinical examination with medial and lateral compression may reproduce the painful symptoms with a palpable "click" on interspace compression (Mulder sign).

Treatment
Management of patients diagnosed with Morton neuroma typically starts with conservative approaches, such as the use of metatarsal pads in shoes and orthotic devices that alter supination and pronation of the affected foot. These approaches try to reduce pressure and irritation of the affected nerve. They may provide relief, but do not alter the underlying pathology. There is scant evidence to support the effectiveness or comparative effectiveness of these practices. In a case series, Bennett et al (1995) evaluated a 3-stage protocol of "stepped care" through which private practice patients (N=115) advanced from stage I (education plus footwear modifications, and a metatarsal pad) to stage II (steroid injections with local anesthetic or local anesthetic alone), and into stage III (surgical resection) if stages I and II were not relieved within 3 months. Overall, 97 (85%) of 115 patients

believed that pain had been reduced with the treatment program. However, 24 (21%) patients eventually required surgical excision of the nerve, and 23 (96%) of them had satisfactory results.

Minimally Invasive Ablation Procedures
Several minimally invasive procedures to treat refractory Morton and other peripheral neuromas are aimed at in situ destruction of the pathology, including intralesional alcohol injection, radiofrequency ablation (RFA) and cryoablation (also known as cryoneurolysis, cryolysis, and cryoanalgesia).

Dehydrated ethanol has been shown to inhibit nerve function in vitro, has high affinity for nerve tissue, and causes direct damage to nerve cells via dehydration, cell necrosis, and precipitation of protoplasm, leading to neuritis and a pattern of Wallerian degeneration. Technically, ethanol is a sclerosant that causes chemical neurolysis of the nerve pathology but is considered an ablative procedure for this evidence review. The use of ultrasound guidance during this procedure has been shown to increase surgical accuracy, improve outcomes, and shorten procedure duration. RFA uses heat generated by an electrode that conducts electromagnetic energy into a tissue or lesion to denature proteins and destroy cells. RFA is used to ablate a wide range of tissues or lesions, including osteoid osteoma; cardiovascular system pathologies; cervical pain syndromes; liver, lung, and other cancers; and varicosities. Cryoablation uses coolant to chill a cryoprobe to temperatures below -75°C, which when inserted into a lesion, freezes and kills the tissue. It has been used to treat Morton neuroma, other chronic nerve pain syndromes, and conditions for which RFA has been used.

This review primarily focuses on evidence for the use of intralesional alcohol injection, RFA, and cryoablation on painful neuromas, with emphasis on Morton neuroma and the comparative effectiveness of these less invasive therapies with open surgical resection of the nerve pathology.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Alcohol injection for Morton neuroma is a surgical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration (FDA).

Although RFA probes and generators and cryoablation equipment have been cleared for marketing by the FDA through the 510(k) process, none appear to be specifically indicated for the treatment of Morton neuroma or any other specific peripheral neuroma.

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.

Morton neuroma is a common and painful compression neuropathy of the dorsal foot that is also referred to as intermetatarsal neuroma, interdigital neuroma, interdigital neuritis, and Morton metatarsalgia. Morton neuroma has been treated with conservative measures (pads, orthotics, drugs) or surgery. Minimally invasive procedures, including intralesional alcohol injection, radiofrequency ablation (RFA) and cryoablation, have been investigated as alternatives to open surgery. These methods have also been used to treat other peripheral neuromas.

Summary of Evidence

For individuals who have Morton neuroma who receive intralesional alcohol injection(s), the evidence includes retrospective case series. Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. The body of evidence is limited, consisting of case series reporting on the treatment response of patients with refractory Morton neuroma. The available case series have generally reported that some patients experience pain relief and express satisfaction with the procedure. Some evidence has suggested that surgery after failed cases of alcohol injections is more complex and challenging than in untreated patients due to the presence of fibrosis. There is a lack of controlled trials comparing alcohol injections with alternative therapies, and there are no controlled studies comparing outcomes for alcohol injections with those for surgery in surgical candidates. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have Morton neuroma who receive RFA, the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. Four case

series identified reported outcomes for radiofrequency ablation (RFA) to treat Morton neuroma. The body of evidence is highly heterogeneous regarding RFA protocols, descriptions of prior conservative management, patient characteristics, follow-up durations, outcome measures, and reporting of outcomes. Variable proportions of patients require surgery after RFA, making the benefit of RFA for avoiding more invasive treatment uncertain. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have Morton neuroma who receive cryoablation, the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. Only 2 retrospective case series on the use of cryoablation to treat peripheral nerve pain were identified in a literature review. The case series were heterogeneous regarding cryoablation protocols and length of follow-up. Outcome measures did not provide information on functional endpoints. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have peripheral neuroma(s) other than Morton neuroma who receive ablation no published literature was identified. Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2015 Input

In response to requests, input was received from 2 specialty societies and 5 academic medical centers while this policy was under review in 2015. Input was consistent that the use of alcohol injections to treat Morton neuroma is investigational.

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.

Association of Extremity Nerve Surgeons
The Association of Extremity Nerve Surgeons issued practice guidelines (2020)[42,] which drew the following conclusions:

- We do not recommend ablation in the primary treatment of Intermetatarsal Nerve Entrapment ("Morton's Neuroma").
    - Alcohol injections: The literature regarding alcohol injections is equivocal. There may be some short-term positive effect, but long-term effect is poor for this therapy. Some of the literature recommends using 30% alcohol solution to get effective results. However, new research has shown the use of 30% alcohol does not create any measurable change in the histology of nerve tissue. There is also a moderate risk of necrosis of surrounding tissues. As a general rule, we do not advocate the use of alcohol injections.
    - Radiofrequency ablation: Radiofrequency ablation has use in the lower extremity, but must be done with caution as this procedure has the potential for thermal necrosis of the adjacent tissues. Judicious use of fluoroscopy and other visualization techniques is advised while utilizing radiofrequency ablation...further research in this technique is needed.
    - Cryoablation: Cryoablation (cryotherapy) should be used with extreme caution, as the amount of literature in the lower extremity is limited. If cryotherapy is used, it should ideally be performed with an open technique rather than percutaneously for optimal results.

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 and unpublished 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			
NCT05501262	Comparative Effectiveness of Cryoablation Using the ICE-Seed Cryoablation Needle With Steroid and Lidocaine Versus Steroid and Lidocaine Alone for Treatment of Morton's Neuroma	32	Dec 2023
Unpublished			
NCT02838758	A 3-Arm Randomized Controlled Study Comparing Ultrasound-Guided Cryoablation, Ultrasound-Guided Perineural Lidocaine, and Ultrasound-Guided Perineural Saline to Treat Intrametatarsal Neuroma	66 (actual enrollment: 10)	Jun 2018*

NCT: national clinical trial.
*As of May 2021, no results posted.

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10/05/2017	Medical Policy Committee review
10/18/2017	Medical Policy Implementation Committee approval. New policy.
10/04/2018	Medical Policy Committee review
10/17/2018	Medical Policy Implementation Committee approval. No change to coverage.
10/03/2019	Medical Policy Committee review
10/09/2019	Medical Policy Implementation Committee approval. No change to coverage.
10/01/2020	Medical Policy Committee review
10/07/2020	Medical Policy Implementation Committee approval. No change to coverage.
10/07/2021	Medical Policy Committee review
10/13/2021	Medical Policy Implementation Committee approval. No change to coverage.
10/06/2022	Medical Policy Committee review
10/11/2022	Medical Policy Implementation Committee approval. Title changed. Intralesional alcohol injection added as investigational. Morton neuromas added as investigational.
08/17/2023	Coding update
10/05/2023	Medical Policy Committee review
10/11/2023	Medical Policy Implementation Committee approval. No change to coverage.
10/03/2024	Medical Policy Committee review
10/08/2024	Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 10/2025

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

Code Type	Code
CPT	64632, 64640 Delete code effective 09/01/2023: 0441T
HCPCS	No codes
ICD-10 Diagnosis	G57.60-G57.63

*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.

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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.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.