Policy Statement

Minimally invasive ablation procedures, radiofrequency ablation, and cryoablation, are considered investigational for the treatment of peripheral neuromas.

Policy Guidelines

Coding
One of the following CPT codes would be used to report these procedures:
- 64632: Destruction by neurolytic agent; plantar common digital nerve
- 64640: Destruction by neurolytic agent; other peripheral nerve or branch

Description

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

Related Policies

- N/A

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

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

Background
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. They may coexist with phantom pain or can predispose to it.

Morton Neuroma
Morton intermetatarsal 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. Morton neuroma is usually associated with a throbbing, burning, or shooting pain localized to the plantar aspect of the foot. It is typically located between the third and fourth metatarsal heads, although it may appear in other proximal locations. Morton neuroma 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.

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.

Ablation Techniques
Several minimally invasive procedures to treat refractory Morton neuroma are aimed at in situ destruction of the pathology: radiofrequency ablation (RFA) and cryoablation (also known
as cryoneurolysis, cryolysis, cryoanalgesia). 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 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.

**Literature Review**

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens, and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

**Clinical Context and Therapy Purpose**

The purpose of peripheral nerve ablation (i.e., radiofrequency ablation [RFA] or cryoablation) in patients who have peripheral neuromas is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Do minimally invasive ablation procedures improve health outcomes in patients with peripheral neuromas?

The following PICOTS were used to select literature to inform this review.

**Patients**
The relevant population of interest is patients with peripheral neuromas, with emphasis on Morton neuroma.

**Interventions**
The therapies being considered are RFA and cryoablation for painful neuromas.

**Comparators**
The following practice is currently being used to make decisions about the treatment of peripheral neuromas: open surgical resection of the nerve pathology.
Outcomes
The general outcomes of interest are pain, typically measured with a visual analog score (VAS), ability to walk, and adverse events related to ablation procedures. The timing ranges from hours for the immediate effect of treatment, to months to assess recurrence of treatment.

Radiofrequency Ablation for Morton Neuroma
Three case series were identified reporting outcomes with RFA for treating Morton neuroma.

Genon et al (2010) reported on a retrospective review of a single center's experience with RFA to treat Morton neuroma according to a clinical algorithm that proceeds from nonoperative interventions to RFA and to open neurectomy if initial approaches failed.27 Thirty-seven patients who had failed conservative management (not described) and had symptoms for at least 12 months in duration were treated with RFA using a NeuroTherm NT1000 (NeuroTherm) radiofrequency generator. At an average follow-up of 11 months (range, 3-21 months), among the 37 patients (38 neuromas) treated, 7 (19%) reported complete relief of symptoms, 21 (58%) reported partial relief, and 10 (27%) reported no relief. Among those with no relief, 8 (22%) of patients had an open surgical revision, with 6 of 8 reporting complete relief, 3 reporting partial relief, and 1 was unchanged. No complications due to RFA were reported.

Moore et al (2012) reported on a second retrospective series of RFA management of Morton neuroma.28 This series included 29 patients (22 women; age range, 23-73 years) who had not responded to conservative management (primarily steroid and alcohol injections) over 1 to 2 months. Patients were treated with RFA (Smith & Nephew) under monitored anesthesia using an electrode inserted dorsally with fluoroscopic guidance. Among the 29 patients, 24 (83%) expressed complete relief of symptoms 1 month after RFA; none reported more pain. The remaining 5 (17%) had minimal to no relief. Of them, one had an open revision, and the others had no additional treatment or were lost to follow-up. One patient reported recurrence 9 months following RFA, and another had superficial cellulitis that responded to antibiotic therapy. All patients returned to normal shoe gear and activities within 2 days of RFA.

Chuter et al (2013) reported on a third retrospective series of RFA to treat Morton neuroma.29 This series included 25 patients (21 women) with a mean age of 55 years (range, 33-73 years) who had mean symptom duration of 3.8 years (range, 6 months to 15 years). All failed conservative management. Before RFA, patients had an average pain score of 6.0 (range, 3.0-9.0) on a 10-point VAS. Four weeks after RFA, the average VAS pain score was 1.7 (range, 0-8.0; p<0.001), an average symptom improvement of 76%. The only complication reported involved a patient who experienced irritation of the posterior tibial nerve following the procedure. Three (10%) patients proceeded to open surgical excision within 6 months of RFA due to incomplete pain relief or recurrence.

Section Summary: Radiofrequency Ablation for Morton Neuroma
Three case series have reported outcomes of RFA to treat Morton neuroma. The body of evidence is highly heterogeneous regarding RFA protocols used, prior conservative management, patient characteristics, follow-up durations, outcome measures, and the reporting of outcomes (e.g., using denominators of “feet,” “neuromas,” or “patients,” which required conversion to “patients”). Although favorable outcomes were achieved in substantial proportions in each study, the outcome measures were unclear as to their clinical meaning, except the VAS used in the Chuter report. Furthermore, in all 3 series, a variable proportion of patients required further surgical excision, making the value of prior RFA uncertain.

Cryoablation for Morton Neuroma
Two retrospective case series on the use of cryoablation to treat peripheral nerve pain have been identified.

One case series by Friedman et al (2012) reported on a series of patients who had undergone sonographically guided cryoneurolysis.30 Among a cohort of 20 patients, 5 had Morton...
neuroma (all women; mean age, 55 years). Cryotherapy was administered with a Frigitronics CE 2000 (Cooper Surgical) device using nitrous oxide coolant. A cryoprobe was inserted into the Morton neuroma, and the probe temperature was decreased to -75°C and left in place until a continuous series of ice balls was created (one or two 3-minute cycles of cooling). Patients were scheduled for follow-up at 4 to 6 weeks. However, actual follow-up varied due to patient discretion. Among the 5 Morton neuroma patients, 3 had "marked relief," 1 had "moderate relief," and 1 had no relief, at a mean follow-up of 14 weeks (range, 6 weeks to 14 months). Complications of cryoablation were not reported.

The second case series, by Cazzato et al (2016), retrospectively described 20 patients (24 lesions) with Morton neuroma who underwent magnetic resonance-guided cryoablation.31 All patients were previously treated with ultrasound-guided corticosteroid injections and had not reported relief. While positioned in the magnetic resonance unit, a cryoprobe (Ice-Seed; Galil Medical) was inserted into the center of the lesion. A single freezing cycle of 150 seconds was performed. Mean procedural time was 41 minutes (range, 35-60 minutes). Patients were followed with a telephone survey. The number of months between procedure and last follow-up ranged from 1 to 50 months. Results were reported by lesion, with data available for 18 of the 24 lesions treated. Patients with 14 (78%) of the 18 lesions were "completely satisfied," 17% were "satisfied with minor reservations," and 6% were "satisfied with major reservations." Mean local pain score was 3.0 on a 0-to-10 VAS. Post-VAS scores were not available.

Section Summary: Cryoablation for Morton Neuroma
Two retrospective case series have investigated cryoablation to treat Morton neuroma. The body of evidence is heterogeneous regarding cryoablation protocols used, prior conservative management, and length of follow-up. Although large proportions of patients reported satisfaction with the procedure in both studies, daily functioning did not clearly improve after the procedure. The weaknesses in the body of evidence preclude conclusions on the efficacy of cryoablation for Morton neuroma.

Other Painful Neuromas
The literature review for this update did not identify any controlled studies on the use of ablative techniques to treat painful peripheral neuromas other than Morton neuroma. Two recent review articles reported little evidence for any other sites.1,30

Section Summary: Other Painful Neuromas
The current literature base on the use of ablative techniques for peripheral neuromas other than Morton neuroma provides insufficient data on which to form conclusions about treatment efficacy.

Summary of Evidence
For individuals who have Morton neuroma who receive RFA, the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. Three case series identified reported outcomes for RFA to treat Morton neuroma. The body of evidence is highly heterogeneous regarding RFA protocols, 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 the effects of the technology on health outcomes.

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 end points. The evidence is insufficient to determine the effects of the technology on health outcomes.
For individuals who have peripheral neuroma(s) other than Morton neuroma who receive ablation, the evidence is very limited: no published literature was identified. Relevant outcomes are symptoms, functional outcomes, and treatment-related morbidity. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Supplemental Information**

**Practice Guidelines and Position Statements**
The Association of Extremity Nerve Surgeons (2014) published clinical practice guidelines relevant to this evidence review. The guidelines stated that "We do not recommend ablation in the primary treatment of Intermetatarsal Entrapment (Morton's Neuroma)." The guidelines warned that cryoablation should be used with extreme caution, and, if used, should be performed in an open technique, not percutaneously. The guidelines also warned that radiofrequency ablation might cause thermal necrosis of adjacent tissues.

**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 unpublished trials that might influence this review are listed in Table 1.

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<td>Dec 2020</td>
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**References**


Documentation for Clinical Review

- No records required

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

IE

The following services may be considered investigational.

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<th>Type</th>
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<td>Destruction by neurolytic agent; plantar common digital nerve</td>
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Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

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Definitions of Decision Determinations

Medically Necessary: A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. 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 covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.