2.01.97 Alcohol Injections for Treatment of Peripheral Neuromas

Policy Statement

Alcohol injections are considered investigational for treatment of Morton neuroma.

Policy Guidelines

Coding

The following CPT code would be used to report these procedures:

- 64632: Destruction by neurolytic agent, plantar common digital nerve

Description

Morton neuroma is a common and painful compression neuropathy of the dorsal foot that may be referred to by other names, including intermetatarsal neuroma, interdigital neuroma, interdigital neuritis, and Morton metatarsalgia. Historically, Morton neuroma has been treated with conservative measures, surgery, or minimally invasive procedures. Alcohol injection is a minimally invasive alternative to open surgery to treat Morton neuroma. Alcohol causes chemical neurolysis through dehydration, necrosis, and precipitation of the treated area, ultimately destroying the lesion after multiple injections.

Related Policies

- Ablation Procedures for Peripheral Neuromas

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

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.

Rationale

Background

Neuroma

A neuroma is a growth or tumor consisting of nerve tissue that develops as part of a normal reparative process following nerve injury. The injury may be due to chronic irritation, pressure, stretch, poor repair of nerve lesions or previous neuromas, laceration, crush injury, or blunt trauma.1 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 a 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, postthoracotomy, postmastectomy, and posthemiorrhaphy pain syndromes. They 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, or Morton metatarsalgia.\(^1\)\(^-\)\(^3\) It is histologically characterized by perineurial 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. The incidence and prevalence of Morton neuroma are not clear, but it appears 10-fold more often in women than in men, with an average age at presentation of around 50 years.\(^4\)

The pain associated with Morton neuroma is usually throbbing, burning, or shooting, 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.\(^1\)\(^,\)\(^2\) 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 of Morton Neuroma**

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.\(^1\) 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).\(^5\)

**Treatment of Morton Neuroma**

Management of patients with a diagnosis of 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.\(^3\) These approaches are aimed at reducing pressure and irritation of the affected nerve. They may provide relief, but they do not alter the underlying pathology. There is little evidence supporting the effectiveness or comparative effectiveness of these practices.\(^2\)\(^,\)\(^6\)\(^,\)\(^7\) In 1 case series (1995), investigators evaluated a 3-stage protocol of private practice patients (N=115) who 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 did not bring relief within 3 months.\(^8\) Overall, 97 (85%) of 115 patients believed that pain had been reduced with the treatment program. However, twenty-four (21%) patients eventually required surgical excision of the nerve and 23 (96%) of those had satisfactory results.

**Surgical Techniques**

Surgical intervention is considered the definitive therapy. The most common procedure is open excision of the interdigital nerve pathology through a dorsal or plantar approach. A second procedure is nerve decompression with neurolysis or translocation of the affected part of the interdigital nerve. Although this second approach uses smaller incisions and seems to have more
rapid recovery than open excision, it is considered a more demanding surgical procedure, requiring specialist training and equipment and is less common in practice.² No randomized controlled trials have been identified comparing the effectiveness of different surgical approaches for Morton neuroma.

A 2004 Cochrane review concluded there was insufficient evidence to assess the effectiveness of surgical and nonsurgical interventions for Morton neuroma.⁷ A 2013 review summarized the results of surgical excision case series that included 250 patients.² In general, the series were poorly reported and highly heterogeneous, used disparate outcome measures, had short follow-up periods (average, 2-10 years), and could not be directly compared.

In the only prospective comparative study (1997) of surgical methods (N=52), the dorsal approach showed more favorable results than the plantar approach in earlier weight bearing (mean, 16 days vs 23 days, respectively) and return to work (mean, 22 days vs 37 days, respectively) at an average follow-up of 3 years.⁹ Painful scars were more common with the plantar approach (n=5) compared with the dorsal approach (n=2), with only 1 patient in each group experiencing symptom recurrence. Other case series of primary neurectomy have shown reductions in pain in 50% to 100% of patients, with self-reported satisfaction rates ranging from 52% to 86% at a mean follow-up of 24 to 126 months.² Common complications have included paresthesia (range, 51%-82%), scar tenderness or hypersensitivity (range, 6%-32%), and wound infection (range, 1.4%-9.7%).

Long-term outcomes of surgical resection have been reported in 2 additional series (2010, 2013) that involved a total of 159 cases refractory to conservative management. One series (N=78) reported mean follow-up of 4.6 years (range, 0.8-8.1 years).¹⁰ With a dorsal approach, 82% of patients with long-standing symptoms (mean duration, 33 months) reported excellent or good results, 10% had a fair result with restriction of activities or pain, while 8% had no improvement postsurgery. Complications included wound infections (n=8), persistent hypersensitive scars (n=5), and local keloid formations (n=4). Eight (10%) cases required revision due to neuroma recurrence at a mean of 2 years after the index surgery. Another series (N=81) reported a mean follow-up of 15.3 years (range, 10-20 years).¹¹ With a mostly dorsal approach (97% of cases), outcomes were reported as excellent in 45%, good in 32%, and fair in 15%, 8% reported poor results postsurgery and were referred for revision. Paresthesia in the supplying area of the resected nerve was reported in 72% of cases, while normal sensation was reported in 26%. Other surgical complications were not reported in this series.

Ablation Techniques
Alternative approaches to treat refractory Morton neuroma include minimally invasive procedures aimed at in situ destruction, including intralesional alcohol injections.² 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.

Literature Review
Assessment of the efficacy of therapeutic interventions involves a determination whether an intervention improves health outcomes. The optimal study design for this purpose is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. For Morton neuroma, relevant outcomes are pain, functional outcomes, and patient satisfaction. Because the outcomes are primarily subjective, evidence from RCTs with placebo controls is particularly important to assess the procedure’s efficacy.
Intralesional Alcohol Injections for Morton Neuroma

No RCTs or nonrandomized interventional trials were identified. Several case series have been published on the use of alcohol injections to treat Morton neuroma. Summaries of these series appear in Table 1.

Treatment in all the case series consisted of injections of alcohol combined with an anesthetic (e.g., lidocaine or bupivacaine). Injections were repeated at 2-week intervals, if symptoms persisted. On average, across studies, each patient received approximately 4 injections. Ultrasound guidance was used in all of the series described in Table 1. Outcomes were patient-reported and consisted of various measures of pain and satisfaction.

The largest series identified was reported by Pasquali et al (2015), who described a retrospective 2-center case series of 508 patients who received ultrasound-guided alcohol injection from 2001 to 2012 for Morton neuroma. Eligible patients presented with 2nd or 3rd web space symptoms and had failed 3 months of conservative treatment with insoles and nonsteroidal anti-inflammatory drugs. Patients were injected with a 50% alcohol plus mepivacaine solution, with a mean of 3 injections (range, 1-4 injections) per neuroma. Pain at the Morton neuroma site was assessed on a visual analog scale (VAS) ranging from 0 to 10, by local adverse reactions at 1 week postprocedure (0=no reaction; 1=minimal swelling, pain, redness; 2=significant swelling, pain redness), and patient-reported satisfaction. Pain scores improved from a mean preinjection VAS score of 8.7 to a mean postinjection score of 3.6 at 1 year (change in VAS score, p<0.001). At 1 year postinjection, 74.5% of patients were completely satisfied with the procedure. Fifty (9.3%) feet eventually required operative excision.

Table 1. Case Series of Intralesional Alcohol Injections for Morton Neuroma

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>N</th>
<th>Treatment</th>
<th>Mean FU, mo</th>
<th>Results</th>
<th>Surgical FU, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perini et al (2016)¹³</td>
<td>220</td>
<td>Alcohol, lidocaine</td>
<td>19</td>
<td>• Median NRS pain score improved from 9 to 3</td>
<td>14 (6%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• 88.6% reported improved limitations of everyday activities</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>• Reduction in neuropathic pain (100% to 45%)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>• No change in nociceptive pain (47% to 53%)</td>
<td></td>
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<tr>
<td>Pasquali et al (2015)¹²</td>
<td>508</td>
<td>Alcohol, mepivacaine</td>
<td>12</td>
<td>• Mean VAS pain score improved from 8.7 to 3.6</td>
<td>50 (9%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• 74.5% completely satisfied</td>
<td></td>
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<tr>
<td>Musson et al (2012)¹⁴</td>
<td>75</td>
<td>Alcohol, bupivacaine</td>
<td>14</td>
<td>• Mean VAS pain score improved from 8.5 to 4.2</td>
<td>17 (20%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• 32% complete symptom relief; 33% partial relief; 35% no relief</td>
<td></td>
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<tr>
<td>Hughes et al (2007)¹⁵</td>
<td>101</td>
<td>Alcohol, bupivacaine</td>
<td>12</td>
<td>• Mean VAS pain score improved from 8 to 0</td>
<td>3 (3%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• 84% “essentially pain free”; 8% “mild/moderate pain”; 8% “no difference”</td>
<td></td>
</tr>
<tr>
<td>Fanucci et al (2004)¹⁶</td>
<td>40</td>
<td>Alcohol, carbocaine</td>
<td>10</td>
<td>• 21 completely satisfied; 9 satisfied with minor complications; 6 satisfied with major complications; 4 dissatisfied</td>
<td>4 (10%)</td>
</tr>
</tbody>
</table>

FU: follow-up; NRS: numeric rating scale; VAS: visual analog scale.

Morgan et al (2014)¹⁷ reported on a systematic review that included the studies above published through February 2012 plus another by Dockery (1999)¹⁸ and compared the need for subsequent surgery after alcohol injections for Morton neuroma with or without ultrasound guidance. Reviewers concluded that use of ultrasound guidance for alcohol injections to treat Morton neuroma could reduce the need for subsequent surgery better than unguided treatments.
Summary of Evidence
For individuals who have Morton neuroma who receive intraleisonal alcohol injection(s), the evidence includes retrospective case series. Relevant outcomes are symptoms, resource utilization, 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 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 to alternative therapies, and there are no controlled studies comparing outcomes for alcohol injections to those for surgery in surgical candidates. The evidence is insufficient to determine the effects of the technology on health outcomes.

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.

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
American College of Foot and Ankle Surgeons
In 2009, the American College of Foot and Ankle Surgeons released a clinical practice guideline (now referred to as a clinical consensus statement) on the diagnosis and treatment of forefoot disorders.3 The statement reported that 3 to 7 injections of dilute 4% alcohol administered at 5- to 10-day intervals have been associated with an 89% success rate, with 82% of patients achieving complete relief of symptoms. The statement’s pathway for treatment of intermetatarsal space neuroma listed decompression, excision, and cryogenic neuroablation under surgical management options.

Association of Extremity Nerve Surgeons
The Association of Extremity Nerve Surgeons issued the 2014 practice guidelines,19 which drew the following conclusions about 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, there is not enough data to support the use of alcohol. As a general rule, we do not advocate the use of alcohol injections.”

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

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

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in May 2017 did not identify any ongoing or unpublished trials that would likely influence this review.
References


Documentation for Clinical Review

- No records required
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Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement.

IE

The following services may be considered investigational.

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
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<tr>
<td>CPT®</td>
<td>64632</td>
<td>Destruction by neurolytic agent, plantar common digital nerve</td>
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<tr>
<td>HCPCS</td>
<td>None</td>
<td></td>
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<tr>
<td>ICD-10 Procedure</td>
<td>None</td>
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<tr>
<td>ICD-10 Diagnosis</td>
<td>All Diagnoses</td>
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</table>

Policy History

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

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
<th>Reason</th>
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<tbody>
<tr>
<td>07/31/2015</td>
<td>BC BSA Medical Policy adoption</td>
<td>Medical Policy Committee</td>
</tr>
<tr>
<td>08/01/2016</td>
<td>Policy revision without position change</td>
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</tr>
</tbody>
</table>

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.