Clinical Policy Title: Cryoneurolysis

Clinical Policy Number: CCP.1299

Effective Date: May 1, 2017
Initial Review Date: April 19, 2017
Most Recent Review Date: March 5, 2019
Next Review Date: March 2020

Related policies:

CCP.1010 Radiofrequency ablation treatment for spine pain
CCP.1098 Spinal cord stimulators for chronic pain
CCP.1063 Spinal surgeries
CCP.1003 Spine pain — epidural steroid injections
CCP.1030 Spine pain — facet joint injections
CCP.1043 Chiropractic care
CCP.1101 Hierarchy of chronic pain management
CCP.1127 Aquatic therapy

Policy contains:
- Chronic pain, nonmalignant.
- iovera® (manufactured by Myoscience, Inc.).
- Nerve ablation.
- Osteoarthritis.

ABOUT THIS POLICY: First Choice VIP Care Plus has developed clinical policies to assist with making coverage determinations. First Choice VIP Care Plus’ clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by First Choice VIP Care Plus when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements shall control. First Choice VIP Care Plus’ clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. First Choice VIP Care Plus will update its clinical policies as necessary. First Choice VIP Care Plus’ clinical policies are not guarantees of payment.

Coverage policy

First Choice VIP Care Plus considers the use of cryoneurolysis to be investigational and, therefore, not medically necessary.

For Medicare members:
First Choice VIP Care Plus considers the use of cryoneurolysis to be clinically proven and, therefore, medically necessary for treatment of occipital neuralgia, when only temporary relief of symptoms is obtained from an occipital nerve block. Neurolysis of the greater occipital nerve may be considered via multiple techniques including radiofrequency and cryoanalgesia (L36850 Peripheral Nerve Blocks).

Limitations:

All other uses of cryoneurolysis are not medically necessary.

Alternative covered services:

- Pharmacologic therapy (e.g., analgesics, topical or oral non-steroidal anti-inflammatory drugs, cyclo-oxygenase 2 inhibitors, antidepressants, anticonvulsants, muscle relaxants). These should be considered before opioids.
- Physical and occupational therapy.
- Aquatic therapy.
- Implanted electrotherapy devices.
- Injectable nerve blocks.
- Surgery.

Background

The American Society of Interventional Pain Physicians) defines chronic pain as: “...a complex and multifactorial phenomenon with pain that persists six months after an injury and/or beyond the usual course of an acute disease or a reasonable time for a comparable injury to heal, that is associated with chronic pathologic processes that cause continuous or intermittent pain for months or years, that may continue in the presence or absence of demonstrable pathology and may not be amenable to routine pain control methods with healing never occurring” (Manchikanti, 2009a).

Chronic nonmalignant pain occurs in approximately 15 percent of the adult population, and the majority of chronic pain disorders arise from the spine. The most commonly reported pain condition is low back pain, followed by severe headache or migraine pain, neck pain, and facial ache or pain (Manchikanti, 2009a). Persons covered by Medicaid only and dual-eligibles covered by Medicaid and Medicare are more likely to have these pain disorders than those with private insurance, no insurance, or Medicare only (Pleis, 2010). Chronic pain and its associated psychological and physical comorbidities exact a significant burden on individuals, health systems, and societies at large.

Pharmacologic and noninvasive medical therapies are usually the first-line treatments for chronic pain, but concerns about the growing misuse of, and addiction to, prescription painkillers, particularly opioids, highlight the need for alternative long-term solutions to chronic pain management. Invasive pain management techniques may offer temporary or long-term relief from chronic pain. These techniques
include: surgical resection; injections (blocks) of steroids or anesthetic into joints, ligaments, muscles, or around nerves; implanted electrotherapy devices; and ablation. Ablative techniques may use chemical, high-temperature radiofrequency, laser, or extreme cold neurolysis to block nerve impulses and achieve anesthesia (Trescot, 2003).

Cryoneurolysis:

Cryoneurolysis, also referred to as cryoanalgesia, cryoneuromodulation, or cryoneuroablation, is a percutaneous procedure used to temporarily block nerve conduction along peripheral nerve pathways. The technique uses landmarks, fluoroscopy, ultrasound, or a built-in peripheral nerve stimulator to guide placement of a probe. When in place, the probe applies a fluid (typically nitrous oxide or carbon dioxide gas) or liquid nitrogen to create extreme cold (minus 70–180 degrees F) at the tip, which freezes and kills the nerve but leaves the myelin sheath intact. Cryoneurolysis creates a period of analgesia and allows the nerve to regenerate without neuroma formation (Trescot, 2016).

Cryoneurolysis is proposed for the destruction of large, myelinated nerves such as the occipital, intercostal, pudendal, or superior gluteal nerves (Trescot, 2003). Cryoneurolysis is performed after an accurate diagnostic block. The degree of cold obtained and the length of time of exposure will affect the extent and duration of the analgesic effect. Bleeding diathesis and infection (local or systemic) are the main contraindications to the procedure.

Searches

First Choice VIP Care Plus searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services.

We conducted searches on January 22, 2019. Search terms were: "Nerve Block"(MeSH), "Chronic Pain"(MeSH), and free text terms “cryoneurolysis,” “cryoneuroablation,” “cryoneuromodulation,” “cryoanalgesia,” “cryodenervation,” and iovera.

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews.**
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.
Findings

We found two systematic reviews (Manchikanti, 2009b; Hansen, 2007) and two evidence-based guidelines of intervention for chronic spinal pain (Manchikanti, 2009b, American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine; 2010), six small case series, and no economic analyses for this policy. The evidence base consisted of uncontrolled case series of patients with refractory pain who experienced various origins of pain, durations of pain, and pain treatment prior to cryoneurolysis.

Manchikanti (2009b) identified one study that evaluated percutaneous cryoneurolysis of medial branches for treatment of chronic lumbar pain, representing the best available evidence published at that time (Birkenmaier, 2007). This prospective case series recruited 50 patients with positive diagnostic medial branch blocks. A positive block was defined as definite improvement in the patients’ specific low back pain of ≥50 percent for at least three hours. Percutaneous medial branch cryodenervation was performed, and patients were followed for one year. In all, 46 patients completed the study. Thirteen patients (28 percent) showed no or little improvement. For the remainder, there was a statistically significant improvement in mean low back pain of ≥50 percent (P < 0.0001) at all time points when compared to pretreatment pain levels. Where present before cryoneurolysis, limitations in activities of daily living improved parallel to reduced pain. The only complication reported was a vagus-induced syncope, which was treated with atropine.

Since then, several small, retrospective case series have been published for a number of pain indications (Bellini, 2015; Friedman, 2012; Kim, 2015; Moore, 2010; Wolter, 2011; Yoon, 2016). Results from these case series suggest significant short-term improvement in pain scores that lasts up to a few months. One study of cryoneurolysis for zygapophyseal joint pain showed longer duration of pain relief (mean 1.7 years, range 6 to 52 months) and statistically significant improvements in pain-related disability and depression scores. Adverse effects were rare but reported inconsistently.

There is a lack of consensus among professional organizations regarding the clinical role of cryoneurolysis in chronic pain management. The American Society of Interventional Pain Physicians Interventional Pain Management guidelines agree with the above findings (Manchikanti, 2009b). The American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine (2010) recommended cryoablation in selected patients (e.g., postthoracotomy pain syndrome, low back pain [medial branch], and peripheral nerve pain) based on findings from limited observational studies reporting pain relief from one to 12 months, but representatives from these two organizations disagreed about its clinical value. Both guidelines found stronger evidence and issued stronger recommendations for conventional radiofrequency ablation for chronic pain of neck or lower back origin.

Although results of case series suggest cryoneurolysis is a safe procedure and provides some short-term pain relief, the evidence is insufficient to support cryoneurolysis for treatment of any chronic
nonmalignant pain indication. Controlled studies with more explicit inclusion criteria and systematic assessment of adverse effects, pain-related disability, and resource utilization are needed to further define the relative benefits of cryoneurolysis to more established alternatives.

Updates:

In January, 2018, we added four publications in the professional society guideline/other category and three peer-reviewed publications to the reference list. The focused cold treatment delivered by a mechanism marketed as “iovera°,” manufactured by Myoscience, Inc. (Fremont, California), was approved for marketing by the Food and Drug Administration in March, 2017. The iovera° device delivers focused liquid nitrous oxide to nervous tissue through a handheld device that features three hollow closed-end metal needle-like tips which are chilled by filling with nitrous oxide. The tips freeze and temporarily kill the nerve, stopping its ability to transmit pain signals, after which the nerve begins to regenerate at the rate of 1-2 mm per day. As regeneration progresses, the nerves again become able to conduct signals, reducing the effect of the treatment by about three months after treatment.

We identified a single peer-reviewed publication describing manufacturer-funded clinical research on iovera° for chronic pain, on a sample of 239 participants with osteoarthritis of the knee (Radnovich, 2017). While the results were encouraging, the treatment effect had diminished to being similar to the control group by four months post-baseline. The results are based on a one-time treatment and the authors state that patients may receive repeated treatments as needed, yet, no data exist on repeated treatments with the iovera° device or on comparison of outcomes across a range of treatment modalities for osteoarthritis including iovera°.

A second potential use of iovera° is as a treatment prior to total knee arthroplasty. Preliminary data are encouraging. A retrospective chart review compared 50 individuals who underwent cryoneurolysis five days before total knee arthroplasty with the 50 persons who had the same surgery immediately before cryoneurolysis was introduced as an element of the protocol for standard pain management (Dasa, 2016). The length of stay as measured by percent staying two days or more was lower in the treatment group (six percent compared with 67 percent in the control group), as was opioid use in the 12 weeks post-surgery (45 percent fewer opioids in the treatment group). A clinical trial examining a a sample of 120 (60 treatment, 60 control) was expected to be complete in June, 2018 (Clinicaltrials.gov, 2019). However, the findings are not yet posted.

The American Academy of Orthopaedic Surgeons updated their clinical practice guidelines for the treatment of osteoarthritis of the knee in 2013, and added revisions in August, 2016 and April, 2017. Neither the recommendations nor the revisions include any mention of cryoneurolysis or focused cold treatment. A review of pain treatments for osteoarthritis noted that cryoneurolytic procedures targeting peripheral nerves may offer benefits, but research is needed on their efficacy profiles and long-term effects (Miller, 2018).
In January, 2019, we did not identify any relevant new publications. The policy ID changed from 09.02.08 to CCP.1299.

References

Professional society guidelines/other:


Peer-reviewed references:


**Centers for Medicare & Medicaid Services National Coverage Determinations:**

No National Coverage Determinations identified as of the writing of this policy.

**Local Coverage Determinations:**

L33933 Peripheral nerve blocks.
L36850 Peripheral nerve blocks.

**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

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