Healthy Blue

Medical Policy

Subject:	Cryoneurolysis for Treatment of Peripheral Nerve Pain		
Document#:	SURG.00155	**Publish Date:**	02/27/2020
Status:	New	**Last Review Date:**	02/20/2020

Description/Scope

This document addresses cryoneurolysis for treatment of peripheral nerve pain, including the relief of pain and symptoms associated with osteoarthritis of the knee. Cryoneurolysis is a surgical procedure that creates a reversible nerve block through application of extreme cold to the selected site for treatment of various peripheral nerve pain conditions.

Note: Please see the following related documents for additional information:

- CG-SURG-89 Radiofrequency Neurolysis and Pulsed Radiofrequency Therapy for Trigeminal Neuralgia
- CG-SURG-25 Injection Treatment for Morton's Neuroma
- SURG.00096 Surgical and Ablative Treatments for Chronic Headaches
- SURG.00100 Cryoablation for Plantar Fasciitis and Plantar Fibroma
- SURG.00140 Peripheral Nerve Blocks for Treatment of Neuropathic Pain
- SURG.00142 Genicular Nerve Blocks and Ablation for Chronic Knee Pain
- SURG.00144 Occipital Nerve Block Therapy for the Treatment of Headache and Occipital Neuralgia

Position Statement

Investigational and Not Medically Necessary:

Cryoneurolysis for treatment of peripheral nerve pain is considered **investigational and not medically necessary** for all indications, including osteoarthritis of the knee.

Rationale

Cryoneurolysis has been proposed as a treatment for peripheral nerve pain; however, there have been a limited number of studies published in the peer-reviewed literature addressing the use of this surgical procedure.

In 2016, Dasa and colleagues published a retrospective review of 100 individuals who underwent total knee arthroplasty (TKA) to compare perioperative pain management with and without cryoneurolysis. Cryoneurolysis was performed on the treatment group (n=50) 5 days prior to each TKA as part of a perioperative multimodal pain management program. The control group (n=50) did not receive cryoneurolysis. The results showed a significantly lower number of individuals in the treatment group with a length of stay (LOS) of greater than or equal to 2 days when compared to the control group (6% versus 67%, $p<0.0001$); however, no significant difference between groups was noted for 0 days and 1 day LOS. "The mean ± SE cumulative morphine use during the 12 weeks following surgery was significantly lower for the treatment versus control group (2069.12 ± 132.09 mg vs. 3764.42 ± 287.95 mg, $p<0.0001$)" (Dasa, 2016). Other outcomes evaluated included mean scores on the Knee Injury and

Osteoarthritis Outcome Score (KOOS), Western Ontario and McMaster Universities Arthritis Index (WOMAC), Oxford Knee Score, 12-item Short Form Health Survey (SF-12), and Patient-reported Outcomes Measurement Information System (PROMIS). Significant reductions in the KOOS from baseline to the 6- and 12-week post-operative visits were noted in the treatment group when compared to the control group (p=0.0037 at 6 weeks; p=0.0011 at 12 weeks), in the PROMIS pain intensity scores from baseline to 2 weeks post-surgery (p<0.0001), and also in the PROMIS pain interference scores from baseline to 6 weeks post-surgery (p<0.0001); however, the absolute values of the differences were not reported and there was overlap in the supplemental data. No significant results were noted in other outcomes. No complications were reported due to cryoneurolysis and the most common side effect was local bruising. There were several limitations to this study, including the retrospective, nonrandomized design, and lack of blinding. With the study being single-center and single-surgeon, there is limited generalizability of the results. Furthermore, no disclosure or denial of conflict of interest was reported.

Yoon and colleagues reported on a prospective study with the aim to evaluate the safety and efficacy of cryoneurolysis as a treatment for refractory peripheral neuropathic pain. The study was approved for 144 individuals; however, only 28 subjects were screened and 22 of those subjects were included in the study. All included individuals were treated with cryoneurolysis for peripheral neuropathy after failure of first- and second-line therapy. Results showed a significant decrease in self-reported pain using a visual analog scale (VAS) at 1 month (p=0.0001), 3 months (p=0.0002), 6 months (p=0.002), and 12 months (p=0.03) posttreatment. Cryoneurolysis had to be repeated for 11 (50%) individuals within 12 months of the original treatment. No complications were reported. While this study resulted in positive outcomes, the small sample size and lack of comparator group limits the applicability of the data. In addition, the authors did not disclose the reason for the large gap between the number of individuals approved for the study and the number of individuals screened for the study, which raises concerns of selection bias.

In 2017, Radnovich and colleagues released the results of multicenter, randomized, double-blind, sham-controlled trial that evaluated cryoneurolysis for the treatment of pain and symptoms of knee osteoarthritis. From April 2013 to June 2016, 180 individuals were recruited and enrolled into either the active treatment group (n=121) or the sham treatment group (n=59). No significant difference in demographic or clinical characteristics between the two groups was found. Prior to the baseline visit, all individuals discontinued all prescription and over-the-counter (OTC) pain medications, herbal supplements, and all other treatments for knee osteoarthritis for a duration of five times the half-life of the medication, and discontinued adjunctive therapies for knee pain for 72 hours. The sham treatment used a sham cryoneurolysis device that did not produce any freezing and had no therapeutic effect. After cryoneurolysis or sham treatment was administered, individuals were assessed at eight follow-up visits (Day 1, Day 7, Day 30, Day 60, Day 90, and Day 120; Days 150 and 180 were included if there was a continued effect reported at the previous visit as determined by WOMAC pain subscale score). "Compared to the sham group, patients who received active treatment had a statistically significant greater change from baseline in the WOMAC pain subscale score at Day 30 (p=0.0004), Day 60 (p=0.0176), and Day 90 (p=0.0061)" (Radnovich, 2017). While the evaluators focus their discussion of the results on the statistical significance in these self-reported outcomes, it should be noted that the least squares (LS) mean absolute differences are small. For example, the LS mean absolute difference from sham (95% confidence interval [CI]) for the WOMAC pain subscale score at Day 30 (primary endpoint) was −7.12 (−11.01 to −3.22). No significant difference in WOMAC pain response rate was noted at Day 120 and beyond. There was a significant difference found between the two groups in the WOMAC physical function and stiffness subscales at Day 30 (p=0.0012; p=0.0060), but not at later follow-up points. Also, a significant difference was noted in VAS responders when comparing the two groups at Day 30 (p=0.0124). "There

were no statistically significant differences in [VAS] response rates between the groups at Day 60 (p=0.180), Day 90 (p=0.400), and Day 120 (p=0.5060)" (Radnovich, 2017). Use of medications taken for knee pain during the treatment phase of the study was recorded 33 times in 15 (8.3%) individuals (10 [8.3%] active, 5 [8.4%] sham), and use of medications taken for pain other than knee pain was recorded 52 times in 48 (26.6%) individuals (32 [26.4%] active, 16 [27.1%] sham). Out of 243 recorded adverse events, 84 were deemed possibly or probably related to the cryoneurolysis device. All adverse events were mild to moderate except for one severe adverse event, which was altered sensation. There were four serious adverse events reported, which were all determined to be unrelated to the cryoneurolysis device. While individuals in this study were blinded, the evaluators noted that individuals began to accurately guess their assigned group over time, which could have affected self-reported outcomes and resulted in biased results. Cryoneurolysis for the treatment of knee osteoarthritis resulted in significant outcomes in this study; however, more randomized controlled trials are needed with comparisons to standard pain treatments to validate these findings.

The American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine published Practice Guidelines for Chronic Pain Management in 2010. These guidelines include cryoneurolysis and cryoablation in the discussion section; however, the recommendations only include cryoablation for the treatment of peripheral nerve pain and do not address cryoneurolysis (American Society of Anesthesiologists, 2010). Currently, other major authoritative organizations have not published recommendations on the use of cryoneurolysis for the treatment of peripheral nerve pain.

Background/Overview

Cryoneurolysis, also referred to as cryoanalgesia, is a surgical procedure that creates a reversible nerve block through application of extreme cold to the selected site for treatment of various peripheral nerve pain conditions. There are several cryogenic devices, such as the iovera° System (Myoscience, Inc., Fremont, CA), that have received U.S. Food and Drug Administration (FDA) 510k clearance to administer cryoneurolysis for this indication. The device uses cryogenic fluid to cool the cryoneurolysis probe, which is introduced percutaneously at the treatment site. Once the probe is under the skin, a localized cold zone is generated and it creates lesions in nervous tissue creating a temporary nerve block for up to 90 days.

Definitions

Osteoarthritis: A degenerative condition of the joints that causes destruction of the material in the joints that absorbs shock and allows proper movement.

Peripheral nervous system: The collection of nerves and ganglia outside the brain and spinal cord that connects the central nervous system to the rest of the body.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. 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.

When services are Investigational and Not Medically Necessary:
For the following procedure codes; or when the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT	
64999	Unlisted procedure, nervous system [when specified as cryoneurolysis] Note: other CPT codes when used to describe cryoneurolysis (for example destruction by neurolytic agent, such as 64640), are considered investigational and not medically necessary
ICD-10 Diagnosis	
	All diagnoses

References

Peer Reviewed Publications:

1. Dasa V, Lensing G, Parsons M, et al. Percutaneous freezing of sensory nerves prior to total knee arthroplasty. Knee. 2016; 23(3):523-528.
2. Radnovich R, Scott D, Patel AT, et al. Cryoneurolysis to treat the pain and symptoms of knee osteoarthritis: a multicenter, randomized, double-blind, sham-controlled trial. Osteoarthritis Cartilage. 2017; 25(8):1247-1256.
3. Yoon JH, Grechushkin V, Chaudhry A, et al. Cryoneurolysis in patients with refractory chronic peripheral neuropathic pain. J Vasc Interv Radiol. 2016; 27(2):239-243.

Government Agency, Medical Society, and Other Authoritative Publications:

1. American Society of Anesthesiologists. Practice guidelines for chronic pain management: an updated report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine. Anesthesiology. 2010; 112(4):810-833.
2. U.S. Food and Drug Administration 510(k) Premarket Notification Database. iovera° system 510(k) Summary. No. K173763. Rockville, MD: FDA. February 28, 2018. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf17/K173763.pdf. Accessed on January 9, 2020.

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The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action

New	02/20/2020	Medical Policy & Technology Assessment Committee (MPTAC) review. Initial document development.