Backgrounder

About Myoscience, Inc.

Fremont, California-based Myoscience is a privately-held medical device company committed to making its platform technology, the iovera° system, the standard of care for managing pain without the need for opioids.

About iovera°

The iovera° system is a small, hand-held device that uses disposable tips to penetrate the skin in order to target the source nerve. The iovera° treatment provides immediate, long-lasting pain relief by blocking the nerve's ability to signal pain. The iovera° system is cleared by US FDA for the blocking of pain. It is also cleared for relieving pain and symptoms associated with osteoarthritis of the knee for up to 90 days.

The iovera° treatment

The iovera° treatment is typically performed by trained physicians, for example: orthopaedic surgeons, anaesthesiologists, rheumatologists, and pain management specialists. The treatment area is first cleaned and then marked. The iovera° Smart Tips are then used to deliver the treatment to the targeted area. While the treatment should not be painful, it is normal to experience pressure, a sensation of cold, warmth, tingling and/or tapping during treatment. The treatment can take as little as 8 minutes and may be comprised of multiple treatment cycles for each area, depending on patient anatomy. Results are immediate, so the patient and physician will know when the iovera° treatment has achieved the desired result. Duration of the pain relief varies (see the "Effectiveness and safety" section below for additional information).

The iovera° treatment is reimbursed by Medicare and several private insurers. Patients are encouraged to ask their physician or insurance provider for more information regarding their individual insurance reimbursement and payment options.

How it works

The iovera° system is a convenient and powerful handheld device that employs specially designed Smart Tips for various treatments. The iovera° system creates a precisely controlled, sub-dermal cold zone that allows doctors to selectively treat specific nerves for accurate and predictable results.

iovera° treatments provide immediate pain relief by drawing on the body's natural response to cold to temporarily disrupt pain signaling by peripheral nerves for a period of time. This signal disruption is followed by a restoration of function as the treated area regenerates in predictable fashion. The results are safe and effective.

The iovera° system uses liquid nitrous oxide (N_2O) that is contained within the handpiece. This highly pressurized liquid travels from the handpiece to the closed-end needles of the Smart Tips, where it undergoes a phase change and becomes very cold (below -20C). This phase change draws in heat energy from the surrounding tissue forming a precise zone of cold. The nitrous oxide is then expelled out of the handpiece as gas, leaving nothing behind the body.

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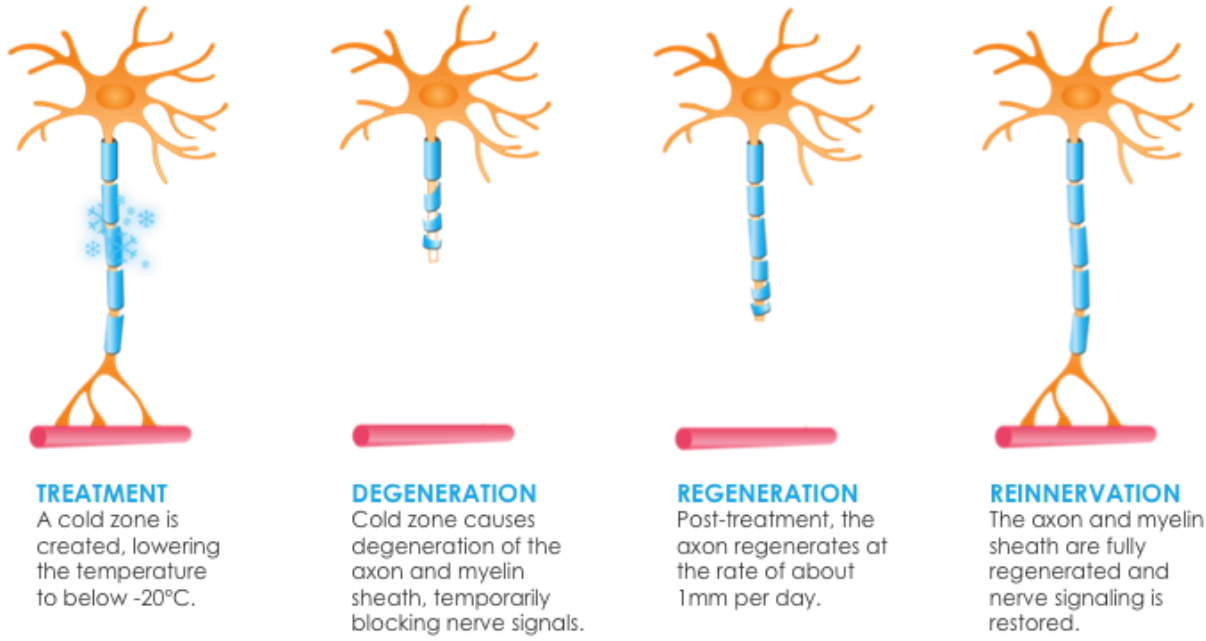
This precise application of cold creates a temporary nerve block based on a process called Wallerian degeneration (2nd degree nerve injury). This degeneration affects the axon and myelin sheath, leaving the surrounding nerve components intact. When sensory nerves (nerves that pass impulses from receptors toward or to the central nervous system) are treated, their ability to signal is interrupted, which immediately blocks pain signals. Post-treatment, the axon slowly regenerates until in reconnects (reinnervates) to the sensory receptor for a predictable restoration of nerve function.



Effectiveness and safety

The iovera° system has the following FDA clearance and indications in the United States:

The Myoscience iovera° system is used to destroy tissue during surgical procedures by applying freezing cold. It can also be used to produce lesions in peripheral nervous tissue by the application of cold to the selected site for the blocking of pain. . It is also indicated for the relief of pain and symptoms associated with osteoarthritis of the knee for up to 90 days. The iovera° system is not indicated for treatment of central nervous system tissue.

The iovera° system's "1x90" Smart Tip configuration (indicating one needle which is 90 mm long) can also facilitate target nerve location by conducting electrical nerve stimulation from a separate nerve stimulator.

Clinical Results:

- Compared to the sham group, patients who received iovera° 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). Patients deemed WOMAC pain responders at Day 120 continued to experience a statistically significant treatment effect at Day 150. [1]
- 94% of patients who received iovera° treatment prior to surgery had a hospital stay of less than two days compared to only 33% in the control group. [2]

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- 50% of patients who received iovera° treatment were discharged on the day of surgery compared to only 14% in the control group. [2]
- Over 80% of subjects reported ≥2 point improvement in pain score at 30 days[3].
- An average of 70% improvement in WOMAC functionality subscale at 7 days.
- 70% of subjects reported a treatment effect at 56 days.[1]
- No serious adverse events were reported related to the iovera° treatment.

Because the iovera° system uses Nitrous Oxide, it is incapable of reaching a temperature that would cause permanent nerve injury. As with any medical treatment, a doctor should always be consulted.

As with any surgical treatment that uses needle-based therapy, there is potential for *temporary* site-specific reactions, including but not limited to:

- Bruising (ecchymosis)
- Swelling (edema)
- Inflammation and/or redness (erythema)
- Pain and/or tenderness, including headache
- Altered sensation (localized dysesthesia)

Typically, these reactions resolve with no physician intervention. Patients may help the healing process by applying ice packs to the affected sites, and by taking over-the-counter analgesics.

Use of the iovera° treatment for post-surgical pain management

The iovera° treatment can pave the way for knee surgery recovery, when used as a pre-surgical treatment for post-surgical pain. In a clinical study[2], patients treated with iovera° prior to TKA surgery reported less knee pain and stiffness than patients not treated. In the same study, it was discovered that the iovera° treated patients requested only half the opioids as patients not treated, while reporting similar function and pain scores.

- **Knee pain after surgery**: iovera° patients reported KOOS Pain Scores that were statistically significantly higher ($p<0.05$) with a difference of 11.2 (6 weeks post) and 13.4 (12 weeks post) over non-iovera° patients
- **Stiffness after surgery**: iovera° patients reported KOOS Symptom Scores that were statistically significantly higher ($p<0.05$) with a difference of 12 (6 weeks post) and 13.4 (12 weeks post) over non-iovera° patients
- **Opioid use**: iovera° patients requested 1933.75mg average morphine equivalents (MME) compared to 3751.25 mg for non-iovera° patients ($p=0.0006$) over the 12 week post-surgical period

NOTE 1: The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is a widely used, proprietary set of standardized questionnaires used by health professionals to evaluate the condition of patients with osteoarthritis of the knee and hip, including pain, stiffness, and physical functioning of the joints. (Source: https://www.rheumatology.org/I-Am-A/Rheumatologist/Research/Clinician-Researchers/Western-Ontario-McMaster-Universities-Osteoarthritis-Index-WOMAC)
NOTE 2: KOOS is a patient-reported outcome measurement instrument, developed to assess the patient's opinion about their knee and associated problems. The score is a percentage score from 0 to 100, with 0 representing extreme problems and 100 representing no problems. (Source: http://www.koos.nu/koosfaq.html)

[1] Radnovich R., et al., Cryoneurolysis to treat the pain and symptoms of knee osteoarthritis: a multicenter, randomized, double-blind, sham-controlled trial. Osteoarthritis and Cartilage, 2017. 8: p. 1247-1256.
[2] Dasa V, Lensing G, Parsons M, Harris J, Volaufova J, Bliss R, Percutaneous freezing of sensory nerves prior to total knee arthroplasty. The Knee, 2016. 23(3): p. 523-528.

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