

Nerivio™

A drug-free, prescribed wearable therapeutic device
for the acute treatment of migraine



FDA clearance with DE NOVO Classification

* PLEASE SEE IMPORTANT SAFETY INFORMATION
AND ACCOMPANYING FULL PRESCRIBING INFORMATION

theranica
REDEFINE PAIN RELIEF

Nerivio™ Device



Nerivio™ is indicated for acute treatment of migraine with or without aura in patients 18 years of age or older who do not have chronic migraine. It is a prescription use, self-administered device for use in the home environment at the onset of migraine headache or aura.

PRESCRIPTION AND IMPORTANT SAFETY INFORMATION

Before using this device, please review the Nerivio User Guide and visit Theranica's website at theranica.com for complete indication, contraindications, warnings, precautions, adverse events, and directions for use.

Indication

Nerivio™ is indicated for acute treatment of migraine with or without aura in patients 18 years of age or older who do not have chronic migraine. It is a prescription use, self-administered device for use in the home environment at the onset of migraine headache or aura.

Contraindications

The device should not be used by people with:

- Congestive heart failure (CHF), severe cardiac or cerebrovascular disease
- Uncontrolled epilepsy
- An active implantable medical device, such as a pacemaker, hearing aid implant, or any implanted electronic device. Such use could cause electric shock, electrical interference or serious injuries or medical conditions.

Warnings

Do not:

- Attempt to perform any procedure before carefully reading all the instructions
- Use the device on the heart, chest, neck, head or any other body location other than the upper arm
- Use the device over skin conditions, such as open wounds or rashes, or over swollen, red, infected or inflamed areas or skin eruptions or fragile skin on your upper arm at the treatment location
- Share the device with other people
- Disassemble, crush, incinerate or short-circuit the battery

Precautions:

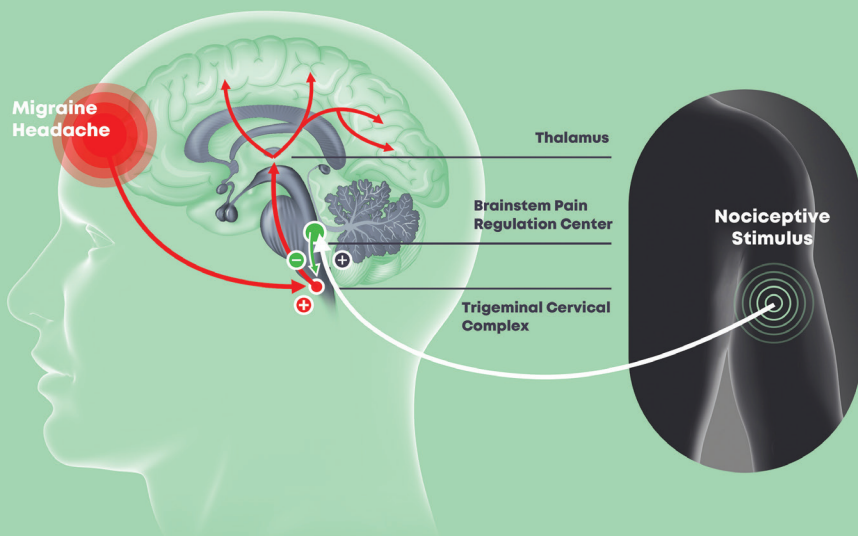
- Nerivio should only be applied on the upper arm over dry, healthy skin with normal physical sensation and without any metallic implants or in proximity to cancerous lesions.
- Nerivio has not been evaluated for use in pregnant women and people less than 18 years of age.
- The safety and effectiveness of the device have not been evaluated in people with chronic migraine and have not been evaluated for the preventive treatment of migraine headache.

Adverse reactions:

During the treatment you might experience a temporary sensation of warmth, local tingling, numbness in the arm or redness of the skin, which should disappear shortly after the end of the treatment.

Mode of Action

Conditioned Pain Modulation (CPM)



- Migraine pain signals travel along the trigeminal nerve to the trigeminal cervical complex and then along ascending pain pathways to the thalamus and cortex
- Nociceptive stimulation from Nerivio travels from the upper arm via pain fibers to pain regulation centers in the brainstem
- Stimulation of brainstem pain regulation centers activates descending serotonergic and noradrenergic pain inhibitory pathways
- Descending inhibitory signals travel to the trigeminal cervical complex

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REN* vs TENS

Parameter	Remote Electrical Neuromodulation (REN) Conditioned Pain Modulation (CPM)	Transcutaneous Electrical Nerve Stimulation (TENS) Gate Theory
MOA	Descending Pain Inhibition	Ascending Pain Inhibition
Nerve Fibers	C and Aδ Fibers	Aβ Fibers
Stimulated Sensory Tract	Nociceptive	Touch
Location	Remote from Pain Location	At Pain Location
Typical Pulse Frequency	100 - 120 Hz	40 - 80 Hz
Typical Pulse Width	400 μs	50 - 300 μs
Impact	Global	Local

- REN is distinct from Gate Theory/TENS mechanism
- CPM is a brainstem-mediated descending pain inhibition mechanism¹
- The Remote Electrical stimulus must activate nociceptive fibers but can be below the perceived pain threshold²
- The CPM stimulus must be remote from original pain location³
- CPM results in a global pain relief effect that lasts a few minutes beyond stimulation³

SOURCE: ¹Nir & Yarnitsky, 2015; ²Lautenbacher et al, 2001; ³Le Bars et al, 1979

* Remote Electrical Neuromodulation

Pivotal Study

Design: Randomized, double-blind, sham-controlled, multicenter study conducted at 7 sites in the United States and 5 sites in Israel

Subjects: Adults meeting the International Classification of Headache Disorders criteria for migraine with or without aura with 2 to 8 migraine attacks per month and fewer than 12 headache days/month

Disposition:

252 were randomized on a 1:1 ratio to active or sham stimulation (ITT population)

237 treated the first (training) attack

203 treated the primary or test attack (Final Analysis population)

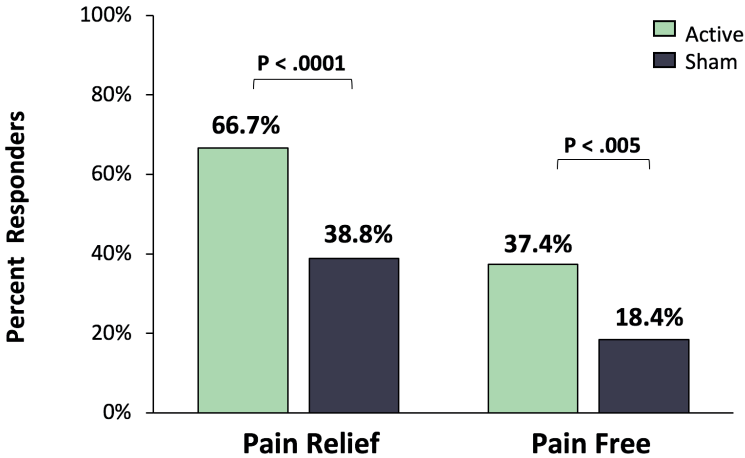
Parameter	Nervio	Sham Device
Waveform	Modulated symmetrical quad-phasic pulse	
Intensity scale (0% - 100%) (Self-tuned by user)	0-40 mA	
Pulse frequency	100-120 Hz (modulated)	~ 0.083 Hz
Pulse width	400 μ s	40-550 μ s (modulated)
Treatment duration	45 minutes	

The sham device aimed to induce a solid and perceptible sensation similar to the active device, but with a sufficiently low frequency to prevent any modulation of nociceptive nerve fibers.

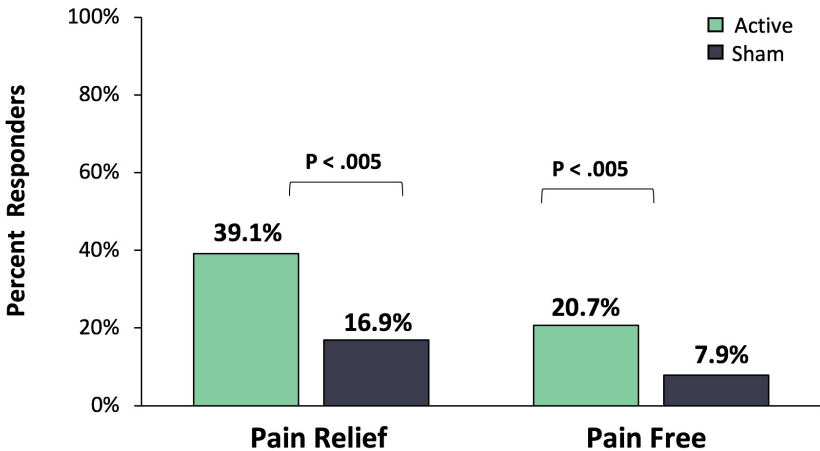
The Breslow-Day test was used to assess whether the difference between active and sham groups varied by what group participants thought they were in ($P = .911$). The nonsignificant P value of this analysis indicates that the difference between the active and sham groups was not affected by participant perception.

Source: Yarnitsky, 2019

2-Hour Pain Response Post-Treatment

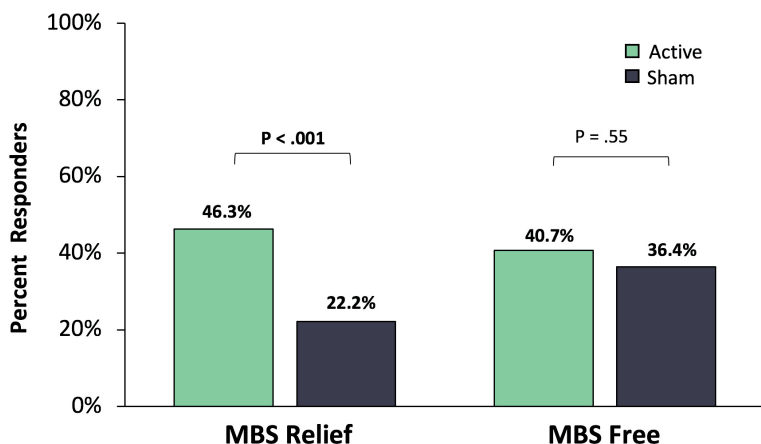


48-Hour Sustained Pain Response



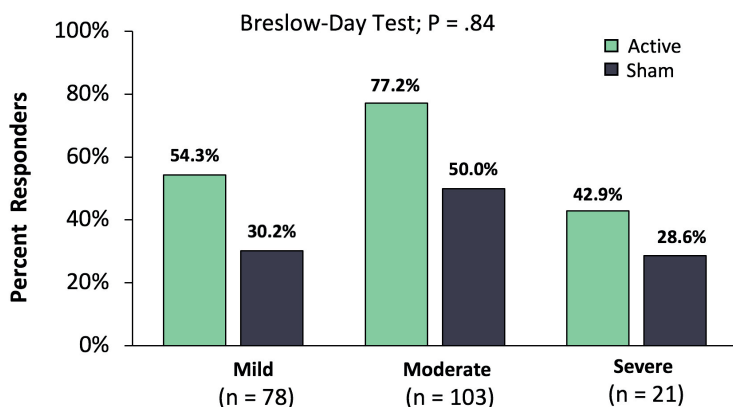
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2-Hour Most Bothersome Symptom Response



MBS = Most Bothersome Symptom

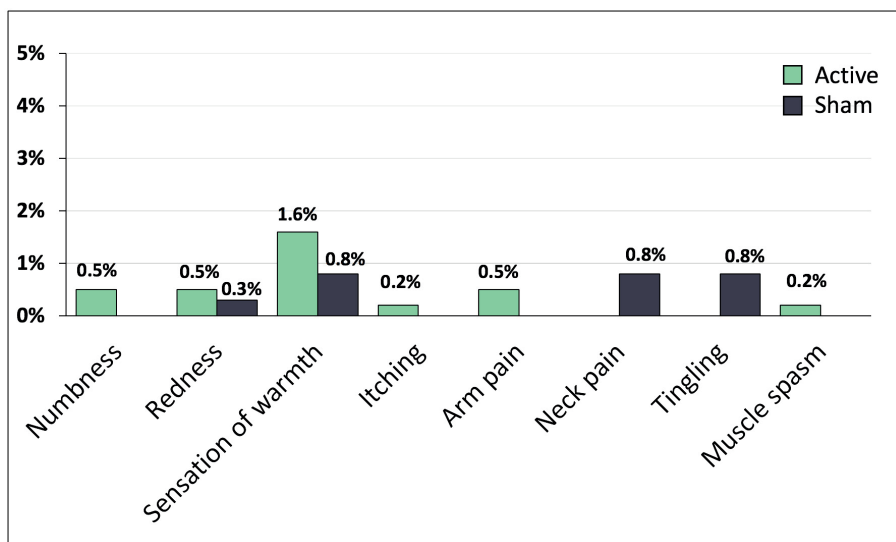
2-Hour Pain Relief as Function of Baseline Pain



The primary end-point was evaluated as a function of baseline pain intensity. The interaction between baseline pain intensity and response rate was not significant ($P = .84$), indicating that the treatment effect was similar across baseline pain intensity levels.

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Device-Related Adverse Events



Percent of All Treatment Episodes (N=773)

- 96.4% (243/252) of participants did not report any device-related adverse events
- There were no serious adverse events
- No participant discontinued due to adverse events
- All device-related adverse events were mild, did not require treatment, and resolved shortly after the device use ended

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Using Nerivio™

For effective treatments, ensure the following:

- Start the treatment within 1 hour of onset of migraine (headache pain or aura)
- Position Nerivio on upper arm, midway between the elbow and shoulder
- Securely fasten the device to the arm using the armband provided
- Gradually increase stimulus intensity to a level that feels strong but not painful
- See www.Nerivio.com for helpful instructional videos

About the app

- Available for free on Apple App store and Google Play store
- User must sign up for an account and be logged-in to be able to run a treatment (one time set up, automatic login is used thereafter)
- App connects to Nerivio using low-energy Bluetooth
- On first use, app walks user through onboarding sequence
- **Treatment screen:**
 - Start, stop, pause and stop a treatment
 - Adjust intensity
 - View connection to device and how many treatments left
- **Diary screen:**
 - View past migraine episodes
 - Accessible also via Web browser

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App Screenshots





Clinically proven



Drug-free



Connected device



Non-invasive



Easy-to-use



Smartphone-controlled



Nerivio™ is a novel, clinically proven device for the acute treatment of migraine, which utilizes innovative neuroscience research to provide migraine relief.

For instructional videos and treatment guides

- www.nerivio.com/support
- Nerivio App (choose Help from the More menu)
- YouTube videos
 - Nerivio Instructional Video
 - Nerivio - How to Ensure an Effective Treatment

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Nerivio Customer Support: 1-937-NERIVIO (637-4846)
or 1-866-NERIVIO (637-4846) support@nerivio.com

