10/23/2020

Theranica Bio-Electronics LTD.
% Janice Hogan
Hogan Lovells US LLP
1735 Market Street, Floor 23
Philadelphia, Pennsylvania 19103

Re: K201824
Trade/Device Name: Nerivio
Regulation Number: 21 CFR 882.5899
Regulation Name: Trunk and limb electrical stimulator to treat headache
Regulatory Class: Class II
Product Code: QGT
Dated: September 28, 2020
Received: September 28, 2020

Dear Janice Hogan:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Xiaorui Tang -S

Xiaorui Tang
Acting Assistant Director
DHT5B: Division of Neuromodulation
and Physical Medicine Devices
OHT5: Office of Neurological
and Physical Medicine Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K201824

Device Name

Nerivio

Indications for Use *(Describe)*

The Nerivio is intended for acute treatment of migraine with or without aura in patients 18 years of age or older. It is a prescription use, self-administered device for use in the home environment at the onset of migraine headache or aura.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

510(k) SUMMARY

Theranica Bio-Electronics LTD.'s Nerivio

Submitter
Theranica Bio-Electronics LTD.
4 Ha-Omanut St. Netanya, ISRAEL, 4250438

Phone: +972-72-3909755

Facsimile: +972-72-3909762

Contact Person: Dagan Harris

Date Prepared: October 22, 2020

Name of Device: Nerivio

Common or Usual Name: Nerivio

Classification Name: Trunk and limb electrical stimulator to treat headache

Regulatory Class: Class II

Product Code: QGT

Predicate Device:

Device Name: Nerivio Migra
Manufacturer: Theranica Bio-Electronics LTD.
510(K) Number: DEN180059

Device Description:

The Nerivio is a wearable, battery-powered device that is controlled by a mobile application. The system delivers low energy electrical pulses to the upper arm for 45 minutes per treatment, after which the device turns off automatically.

The device hardware consists of an armband intended to be worn on a user's upper arm. The armband contains the electronic circuitry and the battery in a plastic storage case as well as two electrodes that are attached to the interior of the armband and placed against the user's skin.

The device is operated and controlled via software that is installed and run on a user's personal mobile device such as a mobile phone or tablet. The device hardware communicates with the mobile application through a Bluetooth protocol. This mobile application software allows the user to control the stimulation intensity from 0 to 100% (representing intensity levels of 0- 40mA), to start or stop the stimulation program, and to view device status such as the device's connection state, a progress bar for stimulation duration, battery level, and user notifications.

The patient is instructed to adjust the intensity to the strongest stimulation level below the perceived pain level. Treatments with Nerivio are intended to be self-administered by the user immediately after the onset of migraine headache or aura.

Intended Use / Indications for Use

The Nerivio is intended for acute treatment of migraine with or without aura in patients 18 years of age or older. It is a prescription use, self-administered device for use in the home environment at the onset of migraine headache or aura.

Summary of Technological Characteristics

Both the device and the predicate device function as remote electrical neuromodulation (REN) devices that utilize electro-stimulation that relieves migraine headache, using equivalent output parameters. The basic pulse structure is biphasic, with symmetrical interleaving phases and rectangular shape. The amplitude shift signal alternates between a nominal maximum and a nominal minimum of the amplitude signal. The maximal output current is 40mA. The assumed impedance is 1K ohm +/- 500 ohms.

Characteristic	Subject Device	Predicate Device	Comparison
Submission Number	K201824	DEN180059	N/A
Device Name	Nerivio	Nerivio Migra	Minor modification for marketing
Manufacturer	Theranica Bio-Electronics LTD.	Theranica Bio-Electronics LTD.	Same
Indications for Use	The Nerivio is intended for acute treatment of migraine with or without aura in patients 18 years of age or older. It is a prescription use, self-administered device for use in the home environment at the onset of migraine headache or aura.	The Nerivio Migra 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.	Modified to remove limitation for the treatment of chronic migraine
Prescription or OTC	Prescription	Prescription	Same
Electrical waveform	Biphasic rectangular, modulated	Biphasic rectangular, modulated	Same
Electrical output			
Max output voltage 500 Ω 2 KΩ 10 KΩ	 20V (measured) 60V (measured) 60V (measured)	 20V (measured) 60V (measured) 60V (measured)	Same
Max output current 500 Ω 2 KΩ 10 KΩ	 40 mA 30 mA 6mA	 40 mA 30 mA 6mA	Same
Maximum phase charge (500Ω)	8μC	8μC	Same

Maximum average current (500Ω)	1.76mA	1.76mA	Same
Maximum current density (peak) (500Ω)	1.6mA/cm2	1.6mA/cm2	Same
Maximum current density (r.m.s) (500Ω)	0.34mA/cm	0.34mA/cm	Same
Maximum average current density (abs value) (500Ω)	0.07mA/cm2	0.07mA/cm2	Same
Maximum average power density (500Ω) Frequency	1.41mW/cm2	1.41mW/cm2	Same
Primary phase duration [µSec]	200	200	Same
Pulse Duration [µSec]	400	400	Same
Electrode Area	25 cm2	25 cm2	Same
Treatment location	Upper arm	Upper arm	Same
Treatment duration	45 min.	45 min.	Same
Reusable	Yes	Yes	Same
# of treatments per one device	12 treatments	8 treatments	Allows for more treatments prior to replacement. Does not raise different questions of safety and effectiveness.
Power source	LiMnO2 cell battery	Lithium-Ion battery	Does not raise different questions of safety and effectiveness.
On/off button	Power push-button	ON/OFF switch	Does not raise different questions of safety and effectiveness.
Dimensions	Device – 12.0 x 7.5 x 1.5 cm Armband – 48.0 x 10.0 x 0.3 cm	Device+Armband = 49.0 X 11.0 X 3.0 cm	Does not raise different questions of safety and effectiveness. Does not raise different questions of safety and effectiveness.
Weight	Device - 50 gr Armband – 33 gr	125 gr (device + armband)	Does not raise different questions of safety and effectiveness.
Shelf life	24 months	9 months	Does not raise different questions of safety and effectiveness.
Mobile Application software	Yes	Yes	Same function for treatment control.

			Different GUI. Does not raise different questions of safety and effectiveness.
Biocompatibility	Yes.	Yes	Different armband coating material. Does not raise different questions of safety and effectiveness.
Sterile	No	No	Same
Processor control	Yes.	Yes	Same
Wireless control	Yes.	Yes	Same
Automatic overload trip	Yes.	Yes	Same
Automatic no load trip	Yes.	Yes	Same
Automatic shut off	Yes.	Yes	Same
Stimulation intensity control	Yes.	Yes	Same

Table 1 provides a comparison between the key functional features of the Nerivio and predicate device.

Characteristic	Subject Device	Predicate Device	Comparison
Submission Number	K201824	DEN180059	N/A
Device Name	Nerivio	Nerivio Migra	Minor modification for marketing
Manufacturer	Theranica Bio-Electronics LTD.	Theranica Bio-Electronics LTD.	Same
Indications for Use	The Nerivio is intended for acute treatment of migraine with or without aura in patients 18 years of age or older. It is a prescription use, self-administered device for use in the home environment at the onset of migraine headache or aura.	The Nerivio Migra 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.	Modified to remove limitation for the treatment of chronic migraine
Prescription or OTC	Prescription	Prescription	Same
Electrical waveform	Biphasic rectangular, modulated	Biphasic rectangular, modulated	Same

Electrical output			
Max output voltage 500 Ω 2 KΩ 10 KΩ	 20V (measured) 60V (measured) 60V (measured)	 20V (measured) 60V (measured) 60V (measured)	Same
Max output current 500 Ω 2 KΩ 10 KΩ	 40 mA 30 mA 6mA	 40 mA 30 mA 6mA	Same
Maximum phase charge (500Ω)	8μC	8μC	Same
Maximum average current (500Ω)	1.76mA	1.76mA	Same
Maximum current density (peak) (500Ω)	1.6mA/cm2	1.6mA/cm2	Same
Maximum current density (r.m.s) (500Ω)	0.34mA/cm	0.34mA/cm	Same
Maximum average current density (abs value) (500Ω)	0.07mA/cm2	0.07mA/cm2	Same
Maximum average power density (500Ω) Frequency	1.41mW/cm2	1.41mW/cm2	Same
Primary phase duration [μSec]	200	200	Same
Pulse Duration [μSec]	400	400	Same
Electrode Area	25 cm^2	25 cm^2	Same
Treatment location	Upper arm	Upper arm	Same
Treatment duration	45 min.	45 min.	Same
Reusable	Yes	Yes	Same
# of treatments per one device	12 treatments	8 treatments	Allows for more treatments prior to replacement. Does not raise different questions of safety and effectiveness.
Power source	LiMnO2 cell battery	Lithium-Ion battery	Does not raise different questions of safety and effectiveness.
On/off button	Power push-button	ON/OFF switch	Does not raise different questions of safety and effectiveness.

Dimensions	Device – 12.0 x 7.5 x 1.5 cm Armband – 48.0 x 10.0 x 0.3 cm	Device+Armband = 49.0 X 11.0 X 3.0 cm	Does not raise different questions of safety and effectiveness. Does not raise different questions of safety and effectiveness.
Weight	Device - 50 gr Armband – 33 gr	125 gr (device + armband)	Does not raise different questions of safety and effectiveness.
Shelf life	24 months	9 months	Does not raise different questions of safety and effectiveness.
Mobile Application software	Yes	Yes	Same function for treatment control. Different GUI. Does not raise different questions of safety and effectiveness.
Biocompatibility	Yes.	Yes	Different armband coating material. Does not raise different questions of safety and effectiveness.
Sterile	No	No	Same
Processor control	Yes.	Yes	Same
Wireless control	Yes.	Yes	Same
Automatic overload trip	Yes.	Yes	Same
Automatic no load trip	Yes.	Yes	Same
Automatic shut off	Yes.	Yes	Same
Stimulation intensity control	Yes.	Yes	Same

Table 1 – Comparison between subject and predicate devices

Performance Data

Non-Clinical Tests:

Nerivio non-clinical bench tests addressed verification and validation of the hardware and software. Device performance testing is summarized in Table 2.

Test	Test description
Safety tests	According to ANSI AAMI ES60601-1, IEC 60601-1-11 and IEC60601-2-10
EMC and radio tests	According to EN IEC 60601-1-2
Wireless coexistence	According to ANSI C63.27
FCC	According to 47CFR part 15.347 part 15.205 part 15.207 part 15.209
Biocompatibility	According to ISO 10993

Table 2 – Nerivio non-clinical tests list

In addition, the company conducted internal bench tests to verify and validate the device battery's lifetime and safety, firmware testing, system testing, mobile application software testing and usability testing. In all instances, the Nerivio functioned as intended and expected.

Clinical Tests:

Two clinical studies of the Nerivio device in chronic migraine patients were performed to assess the Nerivio safety and clinical efficacy in the chronic migraine population. Specifically, it assessed the capability of the Nerivio device to relieve migraine headache pain and associated migraine symptoms in patients with chronic migraine. All studies were in compliance with 21 CFR parts 50, 56, and 812

The first study was a prospective, open-label, single arm, multicenter study conducted at 2 sites. 42 patients were recruited in this study. Eligible participants were adults (18–75 years old) who met the International Classification of Headache Disorders (ICHD-3) criteria for chronic migraine (at least 15 headache days a month, with at least eight days a month on which their headaches and associated symptoms meet diagnostic criteria for migraine).

Participants treated their migraine attacks at home for 4 weeks (treatment phase), within one hour from migraine symptom onset. Participants were instructed to avoid taking rescue medications prior or within two hours post-treatment. Pain scores, absence/presence of associated migraine symptoms, and functional disability were recorded at baseline, 2- and 24-hours post-treatment using the electronic diary application installed on the participants' smartphones.

The primary efficacy endpoint was the proportion of participants who achieved pain relief at 2 hours post-treatment in the test treatment, defined as improvement from severe or moderate pain to mild or none, or, improvement from mild pain to none.

38 participants completed at least one treatment in response to a migraine. A total of 296 qualifying migraine headaches were treated with Nerivio. Pain relief and pain-free at 2 hours were achieved by 50.0% (19/38; CI95% 33.4-66.6%) and 26.3% (10/38; CI95% 13.4-43.1%) participants, respectively. Pain relief was sustained for 24 hours in 83.3% (10/12; CI95% 51.6-97.9%) of the participants (7 participants did not report pain level at 24 hours and were thus excluded from the analysis). Nausea, photophobia, and phonophobia disappeared at 2 hours in 58.8% (10/17; CI95% 32.9-81.6%)), 37.5% (9/24; CI95% 18.8-59.4%), and 50.0% (8/16; CI95% 24.7-75.3%) participants, respectively. Furthermore, 46.7% (14/30; CI95% 28.3-65.7%) participants experienced improvement in functional

ability at 2 hours and 72.7% (16/22; CI95% 49.8-89.3%) participants experienced improvement in functional ability at 24 hours (8 participants with missing data at 24 hours were excluded from the analysis). Consistency analyses across all attacks (excluding the training treatment) demonstrated that 73.7% (28/38) of the participants experienced pain relief in at least 50% of their treated attacks

One device-related adverse event was reported (1.8% of patients [1/42] or 0.003% of treatments [1/296]). This adverse event included bilateral tingling in the temples, disturbed and double vision. The event resolved within 48 hours following drug therapy. There were no device-related serious adverse events and none of the participants withdrew from the study due to device-related adverse events.

The second study was also a prospective, open-label, single arm, multicenter study conducted at 9 sites in the USA. Eligible participants were adults (18–75 years old) who met the International Classification of Headache Disorders (ICHD-3) criteria for chronic migraine (at least 15 headache days a month, with at least eight days a month on which their headaches and associated symptoms meet diagnostic criteria for migraine).

Following a 4 weeks “Run-in” phase, eligible participants were asked to treat their migraine attacks at home for 4 weeks with their optimal stimulation intensity, as soon as possible after migraine headache began and always within one hour of attack onset. Participants were instructed to avoid taking rescue medications prior or within the first two hours post-treatment. Pain scores, absence/presence of migraine associated symptoms, and functional disability were recorded at baseline, 2- and 24-hours post-treatment using the electronic diary application.

The primary efficacy endpoint was the proportion of participants who achieved pain relief at 2 hours post-treatment in the test treatment, defined as improvement from severe or moderate pain to mild or none, or, improvement from mild pain to none.

97 participants completed at least one treatment of a qualifying migraine headache (the training treatment) and 91 participants completed the test treatment with evaluable data at baseline and at 2 hours, forming the final analysis set (5 participants did not have qualifying migraine headaches and 3 participants had missing data in the test treatment at baseline or at 2 hours).

A total of 493 evaluable treatments (excluding the training treatment) of qualifying migraine headaches were conducted by the 91 participants included in the analyses, with an average of 5.4±2.8 evaluable treatments per patient per 4 weeks.

The primary, secondary, and exploratory endpoints of a single attack were conducted on the test treatment of the final analysis set of 91 participants. Pain relief and pain-free at 2 hours were achieved by 59.3% (54/91; $CI_{95\%}$ 48.5-69.5%) and 20.9% (19/91; $CI_{95\%}$ 13.0-30.6%) of the participants, respectively. Pain relief was sustained for 24 hours in 71.1% (32/45; CI95% 51.6-97.9%) of the participants (9 participants did not report pain level at 24 hours and were thus excluded from the analysis). Nausea, photophobia, and phonophobia disappeared at 2 hours in 48.8% (20/41; $CI_{95\%}$ 32.8-64.8%), 40.5% (30/74; $CI_{95\%}$ 29.2-52.5%), and 44.6% (29/65; $CI_{95\%}$ 32.2-57.4%) participants, respectively.

Furthermore, 59.4% (19/32; $CI_{95\%}$ 40.6-76.3%) of the participants experienced improvement in functional ability at 2 hours (participants with missing data at baseline or at 2 hours were excluded

from the analysis) and 50.0% (7/14; $CI_{95\%}$ 23.0-76.9%) of the participants experienced improvement in functional ability at 24 hours (participants with missing data at baseline or at 24 hours were excluded from the analysis).

Consistency analyses across all attacks (excluding the training treatment) demonstrated that 57.1% (52/91) of the participants experienced pain relief in at least 50% of their treated attacks.

One device-related adverse event was reported (1.0% [1/99]) in which pain in the arm was felt following the use of the device on that arm. The device-related adverse event was mild, resolved within 24 hours without medication.

Based on the clinical performance that was documented in these studies, the Nerivio has a safety and effectiveness profile that is similar to the predicate device.

Conclusions

The Nerivio has the same intended use and similar indications (with the modification to remove the limitation for the treatment of chronic migraine patients), technological characteristics, and principles of operation as its predicate device. The minor differences in the indications do not alter the intended therapeutic use of the device and do not affect its safety and effectiveness when used as labeled. In addition, the minor technological differences between the Nerivio and its predicate devices raise no different questions of safety, efficacy, or usability. Performance data demonstrate that the Nerivio is as safe and effective as the Nerivio Migra. Thus, the Nerivio is substantially equivalent to its predicate.