January 22, 2021

Theranica Bio-Electronics LTD
% Janice Hogan
Hogan Lovells US LLP
1735 Market Street
Suite 2300
Philadelphia, Pennsylvania 19103

Re: K203181
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: October 26, 2020
Received: October 26, 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,

Patrick Antkowiak
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: 06/30/2023
See PRA Statement below

510(k) Number *(if known)*

Device Name

Nerivio

Indications for Use *(Describe)*

The Nerivio is indicated for acute treatment of migraine with or without aura in patients 12 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.

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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

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Contact Person: Dagan Harris

Date Prepared: October 26, 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

Manufacturer: Theranica Bio-Electronics LTD.

510(K) Number: K201824

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 Nerivio is identical to the previously cleared Nerivio device with a modification to the indications for use to allow treatment in patients aged 12 years and older.

The device is composed of a pair of UltraStim® electrodes (K130987) covered with hydrogel and removable protective film, an electronic circuitry that includes firmware, LED indicator and a power button for activating the device and for wireless connection with Android and iOS mobile platforms and a battery contained in a plastic case situated within thermoplastic elastomers ("TPE") shell. In addition, an armband that is wrapped over the device to secure the Nerivio position on the user's arm is included.

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, stimulation duration, remaining number of treatments, and user notifications.

The patient is instructed to adjust the intensity to the strongest stimulation level just 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 12 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 subject 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.

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	N/A
Device Name	Nerivio	Nerivio	Same
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 12 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 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.	Modified to 12 years or older
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

Characteristic	Subject Device	Predicate Device	Comparison
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	12 treatments	Same
Power source	LiMnO2 cell battery	LiMnO2 cell battery	Same.
On/off button	Power push-button	Power push-button	Same
Dimensions	Device – 12.0x7.5x1.5 cm Armband – 48.0x10.0x0.3 cm	Device – 12.0x7.5x1.5 cm Armband – 48.0x10.0x0.3 cm	Same
Weight	Device - 50 gr Armband – 33 gr	Device - 50 gr Armband – 33 gr	Same
Shelf life	24 months	24 months	Same
Mobile Application software	Yes	Yes	Same
Biocompatibility	Yes	Yes	Same
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:

Prior testing conducted on the cleared Nerivio (K201824) addressed verification of the hardware and software, as well as performance. The subject device is identical to the cleared Nerivio (K201824); therefore, the previously completed non-clinical tests remain applicable.

Clinical Investigations:

A clinical study of the Nerivio device in adolescents with migraine (ages 12-17 years old) was performed to assess the safety and clinical efficacy of Nerivio in adolescents with migraine. Specifically, it assessed the safety of the device, the capability of the Nerivio device to relieve migraine headache pain and associated migraine symptoms, and the tolerability to the Nerivio device in patients aged 12-17 years. The study was conducted in compliance with 21 CFR parts 50, 56, and 812.

The study was a prospective, open-label, single arm, multicenter study conducted at 12 sites in the USA. Eligible participants were adolescents (12–17 years old, inclusive) who met the International Classification of Headache Disorders (ICHD-3) criteria for migraine, all the inclusion criteria and none of the exclusion criteria.

Following a 4 week “run-in” phase, eligible participants were asked to treat 4 qualifying migraine attacks at home with their optimal stimulation intensity, as soon as possible after migraine headache began and always within one hour of attack onset, during a period of up to 8-week. 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. Improvement in migraine-related disability following the treatment phase was assessed using the Pediatric Migraine Disability Assessment (PedMIDAS) questionnaire.

The primary safety endpoint was assessed by the incidence of adverse events in general and by seriousness, severity and association to the device. Treatment tolerability was assessed by the percent of subjects who fail to complete the study because of adverse events.

The secondary endpoints were related to device efficacy and included the proportion of participants who achieved pain relief at 2 hours post-treatment, defined as improvement from severe or moderate pain to mild or none, or improvement from mild pain to none; proportion of participants who achieved pain-free (improvement from mild, moderate, or severe pain to none) at 2 hours, and disappearance of associated symptoms (nausea/vomiting, photophobia, and phonophobia) at 2 hours post-treatment. Exploratory endpoints included sustained pain relief at 24 hours, sustained pain-free at 24 hours, and improvement in functional ability at 2 hours and at 24 hours. Within-subject consistency of pain relief and pain-free responses, defined as the proportion of participants achieving pain relief/pain-free at 2 hours post-treatment in at least 50% of their treated headaches, were also assessed.

Among the 45 participants who entered the treatment phase, all participants completed at least one treatment (the training treatment) and 39 participants completed the test treatment, forming the final analysis set (two participants had missing data at 2 hours post-treatment, three participants did not have migraine headaches and one participant was a lost to follow-up).

A total of 159 qualifying migraine headaches were treated with Nerivio for which pain data was recorded at baseline and at 2 hours post-treatment (average of 3.5 treatments per participant). Pain levels at baseline were 15.7% mild (25/159), 48.4% moderate (77/159) and 35.8% severe (57/159).

Safety analyses were performed on all 45 participants who used the device at least once. 10 participants (22.2%) reported at least one adverse event. There was one device-related adverse event reported (2.2%) in which a temporary pain in the arm was felt. This adverse event was mild and resolved after the treatment without requiring medication or any other intervention. The other adverse events which were deemed unrelated to the device included common cold (1 participant), chest congestion (2 participants), influenza (2 patients), leg pain (1 patient), streptococcus pharyngitis (1 participant), and upper respiratory infection (1 patient). One (1) patient suffered from a migraine attack that was not treated by the device where the migraine presented as severe and the patient was treated in the ER \ There were no device-related serious adverse events and none of the participants withdrew from the study due to device-related adverse events.

The efficacy endpoints were conducted on the test treatment of the final analysis set of 39 participants. Pain relief and pain-free at 2 hours were achieved by 71.8% (28/39) and 35.9% (14/39) participants, respectively. For the primary efficacy endpoint, missing data was imputed using a worst-case scenario, in which all treatments with missing pain level data were considered failures. According to this sensitivity analysis, pain relief was achieved by 68.3% (28/41) of the participants.

Pain relief was sustained for 24 hours in 90.9% (20/22) of the participants, and pain freedom was sustained for 24 hours in 90.9% (10/11) of the participants (only subjects achieving relief/freedom at 2 hours were included in the analyses; 6 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 54.5% (12/22), 41.9% (13/31), and 40.0% (10/25) participants, respectively. Furthermore, 69.7% (23/33) participants experienced improvement in functional ability at 2 hours (only participants with functional disability at baseline were included in the analysis) and 69.0% (20/29) participants experienced improvement in functional ability at 24 hours (only participants with functional disability at baseline were included in the analysis; 4 participants with missing data at 24 hours were excluded from the analysis).

In order to assess long-term response to the treatment, a consistency analyses was conducted across all treated attacks (excluding the training treatment). This analysis demonstrated that 66.7% (26/39) of the participants experienced pain relief in at least 50% of their treated attacks, and 33.3% (13/39) of the participants experienced pain-free in at least 50% of their treated attacks.

Headache disability as determined by the impact of recurrent headaches on a patient’s quality of life was assessed using the Pediatric Migraine Disability Assessment (PedMIDAS) questionnaire. 42 participants who completed the questionnaire both at baseline and at the end of treatment phase were included in the analysis. The change between the PedMIDASs at enrollment (37.1±30.4) and the end of the treatment phase (18.5±26.8) was 18.6 ± 23.4. These results indicate that treating migraine headaches with Nerivio significantly decreases migraine disability. Interestingly, the average decrease observed in the current study is similar to the reduction shown for migraine preventive treatments in the pediatric population [21]. These findings suggest that Nerivio is effective for improving patients’ quality of life.

The perceived usability of Nerivio was assessed using the system usability scale (SUS). 42 participants who completed the questionnaire at the end of treatment phase were included in the analysis. The mean SUS score was 85.1±12.7. These results indicate high levels of acceptability, ease of use, learnability and confidence when using Nerivio.

The results of the study show that Nerivio is safe and effective for the acute treatment of migraine in adolescents.

Conclusions:

The Nerivio has the same intended use and similar indications (with the addition of adolescent users), 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. Performance data demonstrate that the Nerivio is safe and effective for acute treatment of migraine in adolescents as it is in adult patients.