August 10, 2023

Nurami Medical Ltd.
℅ Janice Hogan
Partner
Hogan Lovells US LLP
1735 Market Street, Suite 2300
Philadelphia, Pennsylvania 19103

Re: K223445
Trade/Device Name: ArtiFascia
Regulation Number: 21 CFR 882.5910
Regulation Name: Dura Substitute
Regulatory Class: Class II
Product Code: GXQ
Dated: July 11, 2023
Received: July 11, 2023

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,

Adam D. Pierce -S

Digitally signed by Adam D. Pierce -S
Date: 2023.08.10 20:56:18 -04'00'

Adam D. Pierce, Ph.D.
Assistant Director
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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)*

K223445

Device Name

ArtiFascia

Indications for Use *(Describe)*

ArtiFascia is indicated as dura substitute for the repair of dura mater. ArtiFascia is indicated for defects of 25cm^2 (3.87 in^2) or less in area. For example, 6 cm X 4 cm (24 cm^2) would be an acceptable defect size.

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)

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K223445
510(k) SUMMARY
Nurami Medical Ltd.'s ArtiFascia Device

Submitter:

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Date Prepared: August 7, 2023

Name of Device: ArtiFascia

Common or Usual Name: Dural Substitute

Classification Name: Dura Substitute

Predicate Devices: Cerafix Dura Substitute (K161278) Acera Surgical, Inc.

Reference Devices: DuraGen Plus Dural Regeneration Matrix (K092388)

Codman Ethisorb Dura Patch (K991413)

Intended Use / Indications for Use:

ArtiFascia is indicated as dura substitute for the repair of dura mater. ArtiFascia is indicated for defects of 25cm^2 (3.87 in^2) or less in area. For example, 6 cm X 4 cm (24 cm^2) would be an acceptable defect size.

Technological Characteristics

ArtiFascia is an absorbable dural repair graft for the repair of cranial dural defects. ArtiFascia is a highly flexible, easy to handle, non-friable soft matrix composed of synthetic non-woven fibers and a non-porous film. ArtiFascia is packaged in a single-use peelable package and is provided sterile, non-pyrogenic. ArtiFascia readily conforms to the surface of the wound area and is applied to the dural defect by using sutures.

Performance Data

Comprehensive bench testing has been performed to confirm that the ArtiFascia has appropriate mechanical attributes for its intended use and performs in an equivalent manner to the predicate device. These tests include the following:

Test	Test Method Summary	Results
Morphological Evaluation	All the test articles underwent a visual examination for any morphological irregularities, thickness was measured, and the edges of each patch were visually examined to verify that the layers are not separated.	All evaluated test articles were found to comply with the predefined acceptance criteria set per the morphology test protocol.
Tensile Strength	A "Dog-bone" shaped test articles were cut from each article and tensile test was performed at a constant speed of 50mm/min. The maximal force and displacement for each test article was recorded.	The ArtiFascia patch can withstand tensile forces [Mpa] that are far greater than the predefined acceptance criteria,
Burst Pressure	A burst pressure test was performed in accordance with ASTM F2392-04 - "Standard Test Method for Burst Strength of Surgical Sealants," with some modifications. A custom-made testing apparatus was built according to the ASTM standard. Each evaluated test article was mounted upon a test fixture base and secured with an o-ring. Saline was injected into the test fixture at a flow rate of 2mL/min and burst strength was calculated for each sample as the peak pressure that allowed fluid leakage from the sample.	The ArtiFascia patch can withstand applied pressure [PSI] that is far greater than the predefined acceptance criteria (twice the expected intracranial pressures).
	Suture retention tests were adapted from the method described in ANSI/AAMI/ISO	The ArtiFascia patch can withstand suture retention forces [N] that are (on average)

Suture Retention Strength	7198:1998/2001/(R) 2004 standard and ASTM D882-12: Standard test method for tensile properties of thin plastic sheeting. The sample was then placed between the tensile testing machine grippers, by connecting the patch to the first grip and the suture to the other and tested to failure under tensile conditions.	greater than the predefined acceptance criteria, i.e., the average results as obtained for predicate device.
Shrinkage	The ArtiFascia 5cm X 5cm test articles were submerged in a saline solution heated to 37ºC for a period of 15min. Two of each articles' edge were measured (length and width) before and after the hydration process.	When some form of suspension, such as suturing, is utilized when applying the device, no shrinkage is noted.
In-Vitro Degradation	In-vitro degradation properties were assessed per ISO 13781. 96 samples were evaluated (overall) for this test procedure. Testing was performed to compare gamma and e-beam irradiated samples.	The results show that, after 126 days, the physical properties of the e-beam are equivalent to gamma- sterilized ArtiFascia.

Biocompatibility

The ArtiFascia device was evaluated per ISO 10993-1:2018 and found to comply with the requirements of the standard thus biocompatible for human use.

Study type (standard in effect at the time the study was initiated)	**Result**
Cytotoxicity - MEM elution (ISO 10993-5:2009)	Non-cytotoxic
Sensitization - GPMT (ISO 10993-10:2010)	Non- sensitizing
Irritation - Intracutaneous Reactivity (ISO 10993-10:2010)	Non-irritating
Systemic Toxicity - Acute (ISO 10993-11:2017)	Non-toxic

Study type (standard in effect at the time the study was initiated)	Result
Systemic Toxicity - Material-mediated pyrogenicity (ISO 10993-11:2017)	Non-pyrogenic
Implantation in rabbits (ISO 10993-6:2007)	No treatment-related adverse effects observed up to 12 months although there is still an ongoing, minor inflammatory response (see animal study section for more detail). Substantially resorbed by 12 months with remnants of the implanted mesh remaining, whereas the predicate control is resorbed by 6 months.
Implantation in rabbits (ISO 10993-6:2016)	No treatment-related adverse effects observed
Hemocompatibility – Hemolysis (ISO 10993-4:2017)	Non-hemolytic
Genotoxicity - Bacterial reverse mutation (Ames assay) (ISO 10993-3:2014)	Non-mutagenic
Genotoxicity – Mouse lymphoma assay (ISO 10993-3:2014)	Non-genotoxic

In addition, chemical analysis of all compounds contained in the final device were chemically analyzed and their toxicological risk was assessed under worst-case assumptions. All identified compounds exhibited safe margins of safety.

Animal Study Data

Two animal studies were conducted under Good Laboratory Practices (GLP): first a controlled experiment in which the biological response and in vivo degradation of the subject (ArtiFascia) and the reference devices (DuraGen Plus) were evaluated at 1, 6, and 12 months (19 animals in total) and a second bridging, 1-month study (9 animals in total). Both studies used a rabbit model, in which a craniotomy, durotomy, and subsequent repair were performed. Assessments included clinical assessments of animal well-being as well as histological examination of the treatment area. The control for the first study was DuraGen Plus, whereas e-beam sterilized ArtiFascia was compared to gamma sterilized ArtiFascia as the control in the second study. The first animal study was conducted on gamma sterilized ArtiFascia grafts as this was the sterilization method used at the time of testing. During product development, the sterilization method was changed to e-beam. Therefore, the company conducted a second bridging in-vivo study in which the biological response and degradation profile of e-beam sterilized subject devices vs. reference devices (DuraGen Plus) were compared up to 1 month. The one-month timepoint was selected because the only difference between devices due to the sterilization method was the starting molecular weight.

Results from the studies showed excellent local tissue response and tolerability to the 3 types of patches, ArtiFascia (e-beam), ArtiFascia (gamma), and DuraGen Plus. The results of both studies demonstrated that the ArtiFascia device was well-tolerated throughout its degradation process. Although minor inflammation was observed at 12 months in the first animal study, consistent with the longer resorption period, overall, the nature and severity of the biological response was comparable to that of the DuraGen device, which was fully degraded and without an associated inflammatory response by 6 months. ArtiFascia was mostly resorbed by 12 months with only sporadic ghost remnants of the implanted mesh remaining. It should be noted that the macrophage reaction was not accompanied with any other type of inflammation, or necrosis, and therefore it was judged to reflect

expected absorptive reaction of well tolerated biodegradable materials. No difference in tissue response was observed between the e-beam and gamma sterilized devices.

Clinical Study

The NEOART study, a prospective, randomized, controlled, multi-center, single-blinded, parallel group study, collected clinical data to evaluate the safety and effectiveness of ArtiFascia in comparison with commercially available dural substitutes in subjects requiring dural repair following neurosurgery. The basic hypothesis was that ArtiFascia is non-inferior in terms of effectiveness and safety to commercially available dural grafts.

A total of 85 subjects were enrolled randomized and treated, of which 78 received either Artifascia or an FDA-cleared control (58 in the investigational ArtiFascia treatment group and 20 in the control commercially dural substitutes group) at 7 clinical sites outside-of-the-US. Subjects were evaluated intra-operatively and immediate post operatively followed by evaluation at 4-6 weeks and at 6 months.

At each evaluation time-point, physical examination of the surgical site and a standard assessment of general neurological health were evaluated. Magnetic Resonance Imaging (MRI) was performed at 6 months. Adverse events were assessed on a continuous basis from the baseline through the study completion at 6 months.

The primary endpoint was the absence of CSF fistula (drainage from wound or sinus) and pseudo-meningocele within 6 months post-operative as evaluated by MRI imaging. Secondary endpoints were the following:

1. Wound healing assessment
2. Device handling Characteristics (i.e., Ease of Use, strength suturability, Seal Quality)
3. Magnetic Resonance Imaging at the 6-month follow-up, to determine the presence or absence of the following measures: adhesion formation, new tissue formation, and brain edema adjacent to device implant site.

Inclusion Criteria:
1. Subject between the ages of 18-75
2. Subject is scheduled for an elective cranial surgery with a dural damage that can be completely repaired/closed by a suturable dural substitute (ArtiFascia device or other commercially available dural substitutes)
3. Subject has undergone imaging (such as, MRI) in the past 6 months before enrolment
4. Surgical wound is expected to be Class I/clean
5. Subject understands the study requirements and the treatment procedures and provides written Informed Consent before any study-specific tests or procedures are performed
6. Subject is able and willing to adhere to the required follow-up visits and testing

Exclusion Criteria:
1. Pregnant women or interest in becoming pregnant during the duration of the study
2. Subject has known hydrocephalus
3. Subject is unable to undergo MRI after the surgery
4. Subject's life expectancy is less than 12 months
5. Subject has a local or systemic infection (e.g. urinary tract infection (UTI), active pneumonia) or evidence of any surgical site infection, fever > 38.3°C, positive blood culture and/or a positive chest x-ray for acute infectious process
6. Subject will require use of dural adhesive or sealant
7. Subject is intended to undergo craniectomy wherein bone flap will not be returned
8. Subject with suspected low success in wound healing due to past treatments (e.g. chemotherapy, radiation therapy, severe diabetes etc.) or other conditions (e.g. severe peripheral vascular disease, long standing steroids treatment)
9. Subject has been clinically diagnosed with malignancy (other than basal cell carcinoma or low-grade glioma), uncontrolled diabetes (A1C>6.5%), sepsis, systemic collagen disease.
10. Subject had chemotherapy and/or radiotherapy in the past 12 weeks before surgery or is planned to have chemotherapy or radiotherapy less than 12 weeks after surgery.

11. Subject is an acute cranial trauma surgical case
12. Subjects with a concurrent disease that would place the patient in excessive risk to the planned surgery
13. Subject had a previous neurosurgery in the same anatomical site
14. Subject with other undesirable symptoms defined by the principal investigator
15. Patient has clinically significant coagulopathy as determined by the surgeon
16. Subject is participating in another clinical study using similar investigational devices/drugs.

There were no reported cases of CSF fistula in either ArtiFascia or Control patients during the entire follow-up period. There was only a single case of CSF pseudomeningocele in the Control group at the 6 months visit. There were no cases of CSF pseudomeningocele in ArtiFascia patients during the entire follow-up period, so that at 6 months, 100% of patients implanted with ArtiFascia did not have CSF fistula and pseudomeningocele.

The company collected additional long-term data from the study subjects who participated in the study. Collected data included neurological change of status and/or MRI imaging at least 1 year or longer after implantation of a dural graft in patients who participated in the study. Both MRI and neurological assessment were collected if available. Out of the 63 subjects screened, a total of 32 subjects, underwent MRI and/or neurological assessment, rendering them eligible for inclusion in the data collection study. 25 of the eligible subjects were implanted with ArtiFascia, whereas 7 were implanted with control grafts.

In all subjects implanted with ArtiFascia or control grafts, no cases of pseudomeningocele, edema or other abnormal findings were observed in the MRI assessment, which was confirmed in an assessment of a blinded, independent radiologist. All subjects who completed a neurological assessment, (n=29) showed no changes in neurological status or other neurological symptoms were observed at least 12 months post-surgery. There was only one case of neurological status change in a Control subject which was not related to the device or the procedure. No abnormal findings at the surgical site were observed.

The results indicate that the clinical study met all primary, secondary and safety endpoints and that ArtiFascia is non-inferior to dural grafts in the control group. Longer term follow-up demonstrated the safety of the product for periods of >12 months after implantation.

Substantial Equivalence Discussion

The ArtiFascia Dura Substitute is as safe and effective as the Cerafix Dura Substitute. ArtiFascia has the same intended uses and similar indications, technological characteristics, and principles of operation as its predicate device. The minor technological differences between the ArtiFascia and its predicate devices raise no new issues of safety or effectiveness. Performance data demonstrate that the ArtiFascia is as safe and effective as Cerafix Dura Substitute Thus, the ArtiFascia is substantially equivalent.

A table comparing the key features of the subject device and the predicate device is provided below:

Specification/ Characterization	ArtiFascia	Cerafix Dura Substitute (K161278)
Indications for Use	ArtiFascia is indicated as a dura substitute for the repair of dura mater. ArtiFascia is indicated for defects of 25cm^2 (3.87 in^2) or less in area. For example, 6 cm X 4 cm (24 cm^2) would be an acceptable defect size.	The Cerafix Dura Substitute is indicated as a dura substitute for the repair of dura mater. This device is indicated for defects of 4.4in^2 (28.3cm^2) or less in area. For example, 4.0 in x 1.1 in (10.1cm x 2.8cm) would be an acceptable defect size.
Principle of operation	Device can be cut by surgeon and placed on dural defect by suturing technique. Suture line should be 2–3mm from edge of implant.	Device can be cut by surgeon and placed on dural defect via onlay or tensionless suturing technique. Suture line should be 2–3mm from edge of implant. Implant should be large enough to overlap edge of the remaining dura by at least one (1) centimeter.
Material of construction	Porous polymer matrix and a film layer	Porous polymer matrix
Sizing	3x4, 5x5, 7x7cm	1”x1”, 1”x3”, 2”x2”, 3”x3”, 4”x5”, 5”x7”
Material composition	Synthetic polymer	Synthetic polymer
Surgical application restrictions	Device does not have requirement for specific orientation	Device does not have requirement for specific orientation
Resorbable	Yes	Yes
Pliable	Pliable	Pliable
Sterility	Sterile, SAL 10^{-6}	Sterile, SAL 10^{-6}
Pyrogenicity	Non-pyrogenic	Non-pyrogenic
Biocompatibility	Biocompatible	Biocompatible

Conclusions

The ArtiFascia performs in a manner that is substantially equivalent to the predicate Cerafix Dura Substitute. The ArtiFascia has the same intended uses and similar indications, technological characteristics, and principles of operation as its predicate device. The minor differences do not alter the intended surgical use of the ArtiFascia device and do not raise different questions of safety or effectiveness. Thus, the ArtiFascia is substantially equivalent to the predicate device.