



December 17, 2018

Micro Therapeutics, Inc. d/b/a ev3 Neurovascular  
Pratibha Lakshmanan  
Senior Specialist, Regulatory Affairs  
9775 Toledo Way  
Irvine, California 92618

Re: P100018/S015  
Trade/Device Name: Pipeline™ Flex Embolization Device

Dear Pratibha Lakshmanan:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) completed its review of your premarket approval application (PMA) supplement and issued an approval order on December 14, 2018. We inadvertently made an error in the placement of the trademark symbol in the “Trade/Device Name.”

We hope that this error has not inconvenienced you. If you have any questions about this corrective action, please contact Leigh Anderson at 301-796-5613 or [Leigh.Anderson@fda.hhs.gov](mailto:Leigh.Anderson@fda.hhs.gov).

Sincerely,

Carlos L. Peña -S Digitally signed by Carlos L. Peña -S  
Date: 2018.12.17 14:10:41 -05'00'

Carlos L. Peña, PhD, MS  
Director  
Division of Neurological  
and Physical Medicine Devices  
Office of Device Evaluation  
Center for Devices and Radiological Health



December 14, 2018

Micro Therapeutics, Inc. d/b/a ev3 Neurovascular  
Pratibha Lakshmanan  
Senior Specialist, Regulatory Affairs  
9775 Toledo Way  
Irvine, California 92618

Re: P100018/S015

Trade/Device Name: Pipeline Flex™ Embolization Device

Product Code: OUT

Filed: June 28, 2017

Amended: July 31, 2017, March 9, 2018, and September 17, 2018

Dear Pratibha Lakshmanan:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) supplement for the Pipeline Flex™ Embolization Device for expanding the indications to include the endovascular treatment of small and medium wide-necked intracranial aneurysms. The device is indicated for use in the internal carotid artery up to the terminus for the endovascular treatment of adults (22 years of age or older) with small and medium wide-necked (neck width  $\geq 4$  mm or dome-to-neck ratio  $< 2$ ) saccular or fusiform intracranial aneurysms (IAs) arising from a parent vessel with a diameter  $\geq 2.0$  mm and  $\leq 5.0$  mm.

We are pleased to inform you that the PMA supplement is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below. Although this letter refers to your product as a device, please be aware that some approved products may instead be combination products. The Premarket Approval Database located at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm> identifies combination product submissions.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 3 years. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of the PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. This report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the PMA device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below. Separate PAS Progress Reports must be submitted for each study every six (6) months during the first two (2) years of the study and annually thereafter, unless otherwise specified by FDA. Each report, identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified below and bearing the applicable PMA reference number, should be submitted to the address below.

The "Prospective Study on Embolization of Intracranial Aneurysms with the Pipeline™ Device (PREMIER)": The PREMIER study is a prospective, multi-center non-randomized pivotal study that was conducted under IDE G140084 and was initiated prior to device approval. The study subjects were consented to be followed for up to three (3) years post-procedure. The 1-year follow-up data from the PREMIER study was used to support the approval of the subject PMA supplement. As part of the PMA post-approval study, the long-term follow-up from the PREMIER study can provide safety and effectiveness information on the durability and safety of treatment using the Pipeline Flex™ Embolization Device up to 3 years post-procedure. The primary safety and effectiveness endpoints are the rate of major or disabling strokes or neurological deaths and the rate of patients who had complete (100%) Raymond-Roy Class I intracranial aneurysm occlusion without clinically significant parent artery stenosis or retreatment of the target aneurysm, respectively. Patients will be followed at 2 years and 3 years post-procedure with imaging assessment of intracranial aneurysm occlusion and parent artery stenosis performed at 2 and 3 years using the approved IDE G140084 clinical study protocol. In addition, all new and ongoing adverse events will be recorded and adjudicated by the Clinical Events Committee (CEC) per the approved G140084 clinical study protocol.

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA.

Be advised that protocol information, interim and final results will be published on the Post Approval Study Webpage <http://www.fda.gov/devicepostapproval>.

In addition, the results from any post approval study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm>).

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final UDI rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24, 2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report. It is not necessary to identify any device identifier discontinued prior to December 23, 2013. Combination Products may also be subject to UDI requirements (see 21 CFR 801.30). For more information on these requirements, please see the UDI website, <http://www.fda.gov/udi>.

Before making any change affecting the safety or effectiveness of the PMA device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" (<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm>).

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52 for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or
2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> and on combination product postmarketing safety reporting is available at (see <https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm>).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the postmarketing safety reporting requirements (21 CFR 4, Subpart B) for combination products, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at

<http://www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm>.

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at

<http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm>. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with a copy of all final labeling. Final labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final labeling is identical to the labeling approved in draft form. If the final labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

U.S. Food and Drug Administration  
Center for Devices and Radiological Health  
Document Control Center - WO66-G609  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Leigh Anderson at 301-796-5613 or [Leigh.Anderson@fda.hhs.gov](mailto:Leigh.Anderson@fda.hhs.gov).

Sincerely,

Carlos L. Peña -S Digitally signed by Carlos L. Peña -S  
Date: 2018.12.14 14:15:38 -05'00'

Carlos L. Peña, PhD, MS  
Director  
Division of Neurological  
and Physical Medicine Devices  
Office of Device Evaluation  
Center for Devices and Radiological Health