



December 3, 2021

Urotronic, Inc.  
% Sew-Wah Tay, Ph.D.  
Regulatory Consultant  
Libra Medical, Inc.  
8401 73rd Avenue North  
Minneapolis, MN 55423

Re: P210020  
Trade/Device Name: Optilume<sup>®</sup> Urethral Drug Coated Balloon  
Product Code: QRH  
Filed: May 11, 2021  
Amended: September 1, 2021

Dear Sew-Wah Tay:

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) for the Optilume<sup>®</sup> Urethral Drug Coated Balloon (DCB). The Optilume<sup>®</sup> Urethral Drug Coated Balloon is used to treat patients with obstructive urinary symptoms associated with anterior urethral stricture. It is designed to be used in adult males for urethral strictures of  $\leq 3$  cm in length. We are pleased to inform you that the PMA 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). 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 1 year when the device is stored at room temperature in a dry location in its original packaging. 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.

You must obtain approval of your PAS protocol(s) within 60 days from the date of this order. Within 30 days of your receipt of this letter, you must submit PMA supplements that include complete protocols of your post-approval studies described below. Your PMA supplements should be clearly labeled as a "PMA Post-Approval Study Protocol" as noted below and submitted to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

1. The ROBUST-LT post-approval study (PR1277-001rA, received in a November 8, 2021 email) is a continuation of the ROBUST clinical program and is designed to verify the continued safety and effectiveness for the Optilume<sup>®</sup> Urethral Drug-Coated Balloon (DCB). It is intended to assess durability of outcomes after 6-months follow-up of the 194 patients currently enrolled in the ROBUST clinical program. Each patient's follow-up will be continued out to 5 years post-treatment. Each of the studies in the ROBUST clinical program defined various endpoints within the study protocol and statistical analysis plan for each study. Individual study reports will continue to be generated and written in accordance with the endpoint definitions specified in their respective protocols and statistical analysis plans. In addition, the analysis plan will harmonize endpoint definitions and data handling rules that will be utilized in program wide analyses and reported in a separate summary report. The harmonized primary effectiveness endpoint is defined as a patient experiencing a  $\geq 30\%$  improvement in International Prostate Symptom Score (IPSS) from baseline without the need for additional intervention. Additional harmonized endpoints include freedom from repeat intervention, uroflowmetry, IPSS, adverse event summary, and International Index of Erectile Function (IIEF). The primary safety endpoint is mortality rate that will be calculated for each study and reported as the number of deaths per 100 patient years. All adverse event (AE) data will be collected. Progress reports will be submitted to the FDA annually after PMA approval.
2. The "Post-market Study Evaluating the Safety and Efficacy of the Optilume<sup>®</sup> Urethral Drug Coated Balloon in a Real-World Setting" study (PR1276, v 0.2, received in a November 8, 2021 email) is a prospective, single arm, multi-center, post market clinical trial evaluating the continued safety and effectiveness for Optilume<sup>®</sup> Urethral DCB in a real-world clinical use. The study will enroll 150 patients at up to 15 sites in the European Union. The study will be open to men 18 years of age or

older who meet the selection criteria. Clinical follow-up will be conducted at 3-, 6- and 12-months post-procedure, and annually thereafter through 5 years. The primary effectiveness endpoint is the responder rate, defined as the proportion of subjects experiencing a  $\geq 30\%$  improvement in symptom scores without repeat intervention, at 12 months. The responder rate will be compared against a performance goal of 60% at 1 year. Ancillary endpoints include freedom from repeat intervention, improvement in IPSS over time, and improvement in urethral stricture surgery patient-reported outcome measure (USS-PROM) over time. The primary safety endpoint is freedom from treatment-related serious adverse events (SAE) through 3 months post-treatment. The ancillary safety endpoints include frequency and severity of device/procedure-related adverse events (AE).

3. The “Evaluation of the Impact of the Optilume<sup>®</sup> Urethral Drug Coated Balloon on Semen Characteristics Post-Treatment” study (PR1275 v0.1, received in a November 8, 2021 email) is a single-arm, prospective study assessing semen quality after treatment with the Optilume<sup>®</sup> Urethral DCB in men younger than 55 years of age. The objective of the study is to determine if treatment with the Optilume<sup>®</sup> Urethral DCB negatively impacts semen characteristics in men with normal baseline semen characteristics. The study will enroll 34 patients at up to 5 sites in the United States and will be open to male subjects between 22 and 55 years of age who meet the selection criteria. Semen quality parameters will be assessed at baseline, 3 months, and 6 months post-treatment. Parameters will include ejaculate volume (mL), sperm concentration (million/mL), total sperm per ejaculate (million), motility (% of sperm that is motile), progressive motility (%), and morphology (% normal). Values at each timepoint will be the average of two samples collected within 1-2 weeks of each other. Clinical follow-up will be conducted at 30 days, 3 months, 6 months, and 12 months post-treatment evaluating Lower Urinary Tract Symptoms (LUTS), sexual function, and voiding function. There is no hypothesis tested effectiveness endpoint. Ancillary effectiveness endpoints include improvement in International Prostate Symptom Score (IPSS) over time, and improvement in maximal flow rate (Q<sub>max</sub>) and post-void residual volume (PVR) over time. The primary safety endpoint is the average change in sperm concentration from baseline. Secondary safety endpoints include proportion of subjects experiencing  $\geq 50\%$  decrease in sperm concentration from baseline, change in semen characteristics from baseline, change in erectile function and overall satisfaction IIEF sub-scores, and device/procedure-related adverse events.

From the time of study protocol approval, you must meet the following timelines for the “Post-market Study Evaluating the Safety and Efficacy of the Optilume<sup>®</sup> Urethral Drug Coated Balloon in a Real-World Setting” and “Evaluation of the Impact of the Optilume<sup>®</sup> Urethral Drug Coated Balloon on Semen Characteristics Post-Treatment” studies:

- First subject enrolled within 6 months
- 20% of subjects enrolled within 12 months
- 50% of subjects enrolled within 18 months
- 100% of subjects enrolled within 24 months
- Submission of Final study report: 3 months from study completion (i.e. last subject, last follow-up date)

In addition, you must submit separate periodic reports on the progress of the “Post-market Study Evaluating the Safety and Efficacy of the Optilume® Drug-Coated Balloon in a Real-World Setting” and “Evaluation of the Impact of the Optilume® Urethral Drug Coated Balloon on Semen Characteristics Post-Treatment” studies, as follows:

- PAS Progress Reports every six (6) months until subject enrollment has been completed, and annually thereafter.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports (i.e., every 3 months), in addition to your periodic (6-months) PAS Progress Reports, until FDA notifies you otherwise.

For all other condition of approval studies, you must submit separate PAS Progress Reports for each study, every six (6) months for the first two (years) and annually thereafter, unless otherwise specified by FDA.

Please note that labeling should be updated on a yearly basis, after each yearly interval of follow up is completed for each PAS.

Each PAS report should be submitted to the address below identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable PMA reference number.

Be advised that failure to comply with any post-approval requirement, including initiation, enrollment, and completion requirements outlined above, constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 814.46(a)(2).

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 in accordance with 21 CFR 814.46(a)(3)-(4).

Be advised that protocol information, interim and final results will be published on the Post Approval Study Webpage [https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma\\_pas.cfm](https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm).

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" (<https://www.fda.gov/media/71327/download>).

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final Unique Device Identification (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, <https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-udi-system>.

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" <https://www.fda.gov/media/81431/download>.

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 post-marketing 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 <https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems> and on combination product post-marketing safety reporting is available at (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the post-marketing 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 <https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/industry-guidance-recalls>.

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 Home Page located at

<https://www.fda.gov/medical-devices/device-approvals-denials-and-clearances/pma-approvals>. 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 Mark Kreitz, Ph.D. at (301) 796-7019 or [Mark.Kreitz@fda.hhs.gov](mailto:Mark.Kreitz@fda.hhs.gov).

Sincerely,

**Sharon M. Andrews -S**

Sharon M. Andrews  
Director  
DHT3B: Division of Reproductive,  
Gynecology and Urology Devices  
OHT3: Office of GastroRenal, ObGyn,  
General Hospital and Urology Devices  
Office of Product Evaluation and Quality  
Center for Devices and Radiological Health