July 9, 2026

Merz North America Inc
Karan Modi
Manager, Regulatory Affairs
6501 Six Forks Road
Raleigh, North Carolina 27615

Re: P250016
Trade/Device Name: Belotero® Intense (+) Lidocaine
Product Code: LMH
Filed: July 18, 2025
Amended: July 18, 2025; April 10, 2026

Dear Karan Modi:

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 Belotero® Intense (+) Lidocaine. This device is indicated for submucosal and/or subcutaneous implantation for lip augmentation in adults over the age of 21.

Based upon the information submitted, 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 available 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 all other applicable requirements, including those governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 24 months when stored at room temperature (up to 25°C/77°F).

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 must 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, under 21 CFR 814.82(a)(9), 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.

1. The PAS is a prospective, post-market, open-label, multicenter, single arm study investigating the safety and effectiveness of Belotero® Intense (+) for lip augmentation in participants with fitzpatrick skin types V or VI to further characterize the safety and effectiveness profile in this subpopulation.

    - **Study purpose/objectives:** This post-approval study is intended to expand the clinical evidence base in this underrepresented population and further characterize treatment-related safety.
    - **Study design (specify control, randomization, etc.):** Prospective, Post-market, Open-label, Multicenter, Single arm Study
    - **Total number of subjects:** Approximately 20 participants will be screened to achieve approximately 16 participants assigned to Belotero Intense (+) treatment.
    - **Length of follow-up and frequency of assessments:** The expected study duration per participant excluding visit window is up to 30 weeks (up to 10 days screening period + baseline treatment + optional touch-up at Week 4 + 24-week follow-up). After the screening period participants will be followed for 24 weeks post last treatment (initial or touch-up treatment). Participants who do not receive a touch-up treatment will have seven on-site visits (including the screening visit), and participants who receive a touch-up treatment will have nine on-site visits (including the screening visit). After the baseline visit, follow-up visits will occur at Weeks 2, 4, 8, 16, and 24 for participants without touch-up treatment and Weeks 2, 4, 6, 8, 16, 20, and 28 for participants with touch-up treatment.
    - **Endpoints:**

      Primary Safety Endpoint

      Occurrence of related TEAEs, as documented by the investigator throughout the study (i.e. device and/or procedure-related)

      Additional Safety Variables

      - Occurrence of TEAEs
      - Occurrence of serious TEAEs
      - Occurrence of TEAEs leading to discontinuation from the study
      - Occurrence of device deficiencies
      - Occurrence of prespecified CTRs as documented by the participant for 28 day

Effectiveness Endpoint

- Responder rate at Visit V3, according to the MLFAS, as assessed live by the treating investigator, where response is defined as ≥ 1-point improvement on participant's treated lips compared to baseline

Exploratory Effectiveness Endpoints

- Global Aesthetic Improvement Scale (GAIS) scores for treated participants at all post-baseline visits, as completed by the treating investigator (iGAIS).
- GAIS scores for treated participants post-baseline visit, as completed by the participant (pGAIS).

- **High-level description of the data analysis plan for the primary endpoints:** Adverse events (AEs) will be coded to a Preferred Term (PT) and a System Organ Class (SOC) according to the Medical Dictionary for Regulatory Activities (MedDRA) version in effect at the time of database lock. A treatment-emergent event (TEAE) is defined as an event that emerges during treatment having been absent from pre-treatment or worsens relative to the pre-treatment state.
  The number and percentage of participants experiencing at least one event, as well as the total number of events, will be summarized by SOC and PT for the following events: TEAEs, related TEAEs, and serious TEAEs. Listings will be provided for all AEs, related TEAEs, serious TEAEs, serious TEAEs with fatal outcome, and TEAEs leading to study discontinuation.
  Incidences of common treatment responses (CTRs) will be summarized by worst severity and maximum duration.
  Effectiveness endpoints will be analysis descriptively in an explorative manner without any confirmatory statistical hypothesis testing.
  In general, qualitative variables will be summarized using frequency tables including the number of values analyzed, absolute frequencies and percentages. Descriptive statistics for metric variables will include the number of values analyzed, mean, standard deviation, median, quartiles, minimum and maximum.
- **Reference to protocol:** Study outline received July 7, 2026 (version 0.3)
- **Plan for interim data release:** Interim safety data will be submitted to FDA as part of the 6-month PAS progress reports.

From the date of study protocol approval, you must meet the following timelines for the PAS:

- 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

In addition, you must submit separate periodic reports on the progress of the PAS as follows:

- PAS Progress Reports every six (6) months until subject enrollment has been completed, and annually thereafter, from the date of the PMA approval letter, unless otherwise specified by FDA.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports every 3 months in addition to your periodic (6-month) PAS Progress Reports, until FDA notifies you otherwise.
- Submit the Final PAS Report three (3) months from study completion (i.e., last subject's last follow-up date).

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 Studies Program Database Webpage, available at 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. Under 21 CFR 814.39, 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 Premarket Approval Application 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 Part 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 available at 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. Additional information about changes that may require a PMA supplement are provided in 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.

Your device is also subject to, among other requirements, the Quality Management System Regulation (QMSR) (21 CFR Part 820), which includes, but is not limited to, ISO 13485 clause 7.3 (Design controls),

ISO 13485 clause 8.3 (Nonconforming product), ISO 13485 clause 8.5.2 (Corrective action), and ISO 13485 clause 8.5.3 (Preventative action). Please note that regardless of whether a change requires premarket review, the QMSR requires device manufacturers to review and approve changes to device design and production (ISO 13485 clause 7.3 and ISO 13485 clause 7.5) and document changes and approvals in the Medical Device File (ISO 13485 clause 4.2.3).

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 Part 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 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 Part 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 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 to the CDRH Portal and should reference the above PMA number to facilitate processing. For more information on the CDRH Portal, please visit https://www.fda.gov/medical-devices/industry-medical-devices/send-and-track-medical-device-premarket-submissions-online-cdrh-portal.

If you have any questions concerning this approval order, please contact Scott Herting at 240-402-6148 or Scott.Herting@fda.hhs.gov.

Sincerely,

RACHANA VISARIA -S

Rachana Visaria, Ph.D.
Director
DHT4B: Division of Plastic and
Reconstructive Surgery Devices
OHT4: Office of Surgical and
Infection Control Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health