ANDA 214688

ANDA APPROVAL

Glenmark Pharmaceuticals Inc., USA
U.S. Agent for Glenmark Pharmaceuticals Limited
750 Corporate Drive
Mahwah, NJ 07430
Attention: Thomas J. Callaghan
Executive Director - Regulatory Affairs

Dear Thomas J. Callaghan:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on June 22, 2020, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Calcipotriene and Betamethasone Dipropionate Foam, 0.005%/0.064%.

Your product is a combination product as defined by 21 CFR 3.2(e) and is comprised of drug and device constituent parts.

Reference is also made to the tentative approval letter issued by this office on May 6, 2022, the complete response letter issued by this office on November 28, 2022, and to any amendments thereafter.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug meets the requirements for approval under the FD&C Act. Accordingly the ANDA is **approved**, effective on the date of this letter. We have determined your Calcipotriene and Betamethasone Dipropionate Foam, 0.005%/0.064%, to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Enstilar Foam 0.005%/0.064%, of Leo Pharma AS (Leo Pharma).

Reference is also made to FDA's Competitive Generic Therapy Designation – Grant letter dated August 17, 2020.

The RLD upon which you have based your ANDA, Leo Pharma's Enstilar Foam 0.005%/0.064%, is subject to periods of patent protection. The following patents and expiration dates are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

U.S. Patent Number	Expiration Date
9,119,781 (the '781 patent)	December 10, 2031*
9,566,286 (the '286 patent)	June 10, 2031
10,130,640 (the '640 patent)	December 10, 2031*
10,617,698 (the '698 patent)	June 10, 2031
10,660,908 (the '908 patent)	June 10, 2031
10,682,364 (the '364 patent)	June 10, 2031
10,688,108 (the '108 patent)	June 10, 2031
10,716,799 (the '799 patent)	June 10, 2031

* with pediatric exclusivity added

Your ANDA contains paragraph IV certifications to each of the patents[1], under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Calcipotriene and Betamethasone Dipropionate Foam, 0.005%/0.064%, under this ANDA. You have notified the Agency that Glenmark Pharmaceuticals Limited (Glenmark) complied with the requirements of section 505(j)(2)(B) of the FD&C Act. Litigation was initiated within the statutory 45-day period against Glenmark for infringement of the '698 and '908 patents in the United States District Court for the District of Delaware [Leo Pharma A/S and Leo Pharma Inc. v. Glenmark Pharmaceuticals Ltd., Civil Action No. 20-01359]. You have also notified the Agency that this case was dismissed.

We note that Glenmark was granted a Competitive Generic Therapy (CGT) designation for Calcipotriene and Betamethasone Dipropionate Foam, 0.005%/0.064%. However, Glenmark is not a "first approved applicant" for such competitive generic therapy, as defined in section 505(j)(5)(B)(v)(III) of the FD&C Act, because this drug product is eligible for 180-day patent challenge exclusivity under section 505(j)(5)(B)(iv) of the FD&C Act. See section 505(j)(5)(B)(v)(III)(bb)(BB) of the FD&C Act. Therefore, this drug product is not eligible for CGT exclusivity under section 505(j)(5)(B)(v) of the FD&C Act.

With respect to 180-day generic drug exclusivity, we note that Glenmark was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification for Calcipotriene and Betamethasone Dipropionate Foam, 0.005%/0.064%. Therefore, with this approval, Glenmark is eligible for 180-days of generic drug exclusivity for Calcipotriene and Betamethasone Dipropionate Foam, 0.005%/0.064%. FDA notes that after issuance of this approval letter, eligibility for 180-day exclusivity is subject to future events that may result in forfeiture of exclusivity under section

505(j)(5)(D) of the FD&C Act. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the FD&C Act, will begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). Please submit correspondence to this ANDA notifying the Agency within 30 days of the date of the first commercial marketing of this drug product or the RLD. If you do not notify the Agency within 30 days, the date of first commercial marketing will be deemed to be the date of the drug product's approval. See 21 CFR 314.107(c)(2).

Under section 506A of the FD&C Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Please note that if FDA requires a Risk Evaluation and Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the FD&C Act.

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Agency should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Agency in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.

Your product is a combination product as defined by 21 CFR 3.2(e) and is comprised of drug and device constituent parts; therefore, we remind you that you must comply with the postmarketing safety reporting requirements for an approved combination product (21 CFR Part 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling materials prior to publication or dissemination. Please note that these submissions are voluntary. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert (PI), Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: https://www.fda.gov/media/128163/download).

You must also submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at https://www.fda.gov/media/73013/download. Information and Instructions for completing the form can be found at https://www.fda.gov/media/132152/download. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/opdp-ectd.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions[2] with respect to self-identification of facilities and payment of annual facility fees. ANDAs that identify at least one facility that is referenced in an approved ANDA are subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1st of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the *Federal Register* notice announcing facility fee amounts.

All finished dosage forms or active pharmaceutical ingredients manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

In addition, we note that GDUFA requires that certain non-manufacturing sites and organizations listed in generic drug submissions comply with the self-identification requirement. The failure of any facility, site, or organization to comply with its obligation to self-identify and/or to pay fees when due may raise significant concerns about that site or organization and is a factor that may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because facilities, sites, or organizations fail to comply with the law requiring self-identification or fee payment.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at https://www.fda.gov/media/71211/download. The SPL will be accessible via publicly available labeling repositories.

We remind you that you must continually monitor available labeling resources such as DRUGS@FDA for changes to your reference listed drug's labels and labeling and make any necessary revisions to your labels and labeling. More information on post-approval labeling changes may be found in the guidance for industry titled "Changes to an Approved NDA or ANDA" at https://www.fda.gov/media/71846/download.

Sincerely yours,

{See appended electronic signature page}

For Edward M. Sherwood
Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

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[1] The Agency notes that the '364, '108 and '799 patents were submitted to the Agency after submission of your ANDA. Litigation, if any, with respect to these patents would not create a statutory stay of approval.

[2] Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

Catherine Poole

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