

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

207589Orig1s000

Trade Name: Enstilar®

Generic Name: calcipotriene and betamethasone dipropionate

Sponsor: LEO Pharma Inc.

Approval Date: October 16, 2015

Indications: For the topical treatment of plaque psoriasis in patients 18 years of age and older..

CENTER FOR DRUG EVALUATION AND RESEARCH

207589Orig1s000

CONTENTS

Reviews / Information Included in this NDA Review.

| | |
|---|----------|
| Approval Letter | X |
| Other Action Letters | |
| Labeling | X |
| REMS | |
| Summary Review | X |
| Officer/Employee List | X |
| Office Director Memo | |
| Cross Discipline Team Leader Review | X |
| Medical Review(s) | X |
| Chemistry Review(s) | X |
| Environmental Assessment | |
| Pharmacology Review(s) | X |
| Statistical Review(s) | X |
| Microbiology / Virology Review(s) | |
| Clinical Pharmacology/Biopharmaceutics Review(s) | X |
| Other Reviews | X |
| Risk Assessment and Risk Mitigation Review(s) | |
| Proprietary Name Review(s) | X |
| Administrative/Correspondence Document(s) | X |

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

207589Orig1s000

APPROVAL LETTER



NDA 207589

NDA APPROVAL

LEO Pharma A/S
C/o LEO Pharma Inc.
Attention: Lori A. Palmer
Senior Director, US Regulatory Affairs
1 Sylvan Way
Parsippany, NJ 07054

Dear Ms. Palmer:

Please refer to your New Drug Application (NDA) dated and received December 18, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Enstilar[®] (calcipotriene and betamethasone dipropionate) Foam, 0.005%/0.064%.

We acknowledge receipt of your amendments dated March 27, April 17, 28, 30, May 13, 28, 29, June 16, 30, September 8, 15, 29, and October 12, 2015.

This new drug application provides for the use of Enstilar[®] (calcipotriene and betamethasone dipropionate) Foam, 0.005%/0.064% for the topical treatment of plaque psoriasis in patients 18 years of age and older.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text and with the minor editorial revision listed below and indicated in the enclosed labeling.

- In the third bullet of the WARNINGS AND PRECAUTIONS section of the HIGHLIGHTS OF PRESCRIBING INFORMATION, the word “to” was changed to “on.”

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, instructions for use). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs*

and As, available at

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels and carton and immediate container labels submitted on October 12, 2015, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008). Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 207589.**” Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to 11 years 11 months because there is evidence strongly suggesting that the drug product would be unsafe in this pediatric group.

We are deferring submission of your pediatric study for ages 12 to 16 years 11 months for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required under section 505B(a) of the FDCA is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(C) of the FDCA. This required study is listed below.

- 2958-1 An open-label study to assess the effect of Enstilar[®] (calcipotriene and betamethasone dipropionate) Foam, 0.005%/0.064% on calcium metabolism in 100 evaluable pediatric subjects aged 12 years to 16 years and 11 months with plaque psoriasis of the scalp and body. Pharmacokinetics (PK) of Enstilar[®] Foam and assessment of hypothalamic-pituitary axis (HPA)

suppression will be conducted in a sub-set of 30 subjects with at least moderate plaque psoriasis under maximal use conditions.

| | |
|----------------------------|---------------------|
| Final Protocol Submission: | 03/2015 (completed) |
| Study Completion: | 03/2017 |
| Final Report Submission: | 06/2018 |

Report of this required pediatric postmarketing study must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from this study. When submitting the report, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

- 2958-2 Conduct a single point vasoconstriction assay (VCA) trial in healthy subjects with adequate bracketing using visual assessment to determine the topical corticosteroid potency classification for Enstilar[®] (calcipotriene and betamethasone dipropionate) Foam, 0.005%/0.064%.

The timetable you submitted on September 15, 2015, states that you will conduct this trial according to the following schedule:

| | |
|----------------------------|---------|
| Final Protocol Submission: | 03/2016 |
| Trial Completion: | 01/2017 |
| Final Report Submission: | 09/2017 |

Submit clinical protocols to your IND 114063 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol,**" "**Postmarketing Commitment Final Report,**" or "**Postmarketing Commitment Correspondence.**"

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. 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, 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 20705-1266

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:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf>).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>.

Information and Instructions for completing the form can be found at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Dawn Williams, Regulatory Project Manager, at (301) 796-5376.

Sincerely,

{See appended electronic signature page}

Jill A. Lindstrom, MD, FAAD
Deputy Director
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosures:

Content of Labeling
Carton and Container Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JILL A LINDSTROM
10/16/2015