

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
22-563

SUMMARY REVIEW

Summary Review for Regulatory Action

Date	October 6 th , 2010
From	Susan J. Walker, M.D., F.A.A.D. Director, Division of Dermatology and Dental Products
Subject	Summary Review
NDA/BLA # Supplement #	022563
Applicant Name	Stiefel Laboratories, Inc.
Date of Submission	December 18th, 2009
PDUFA Goal Date	October 21st, 2010
Proprietary Name / Established (USAN) Name	SORILUX (calcipotriene)
Dosage Forms / Strength	Foam, 0.005%
Proposed Indication(s)	Topical treatment of plaque psoriasis in patients aged 18 years and older
Action:	<i>Approval</i>

Material Reviewed/Consulted	Names of discipline reviewers
OND Action Package, including:	
Medical Officer Review	Melinda, McCord, M.D.
CDTL Review	Jill Lindstrom, M.D.
Statistical Review	Carin Kim, Ph.D.
Pharmacology Toxicology Review	Carmen Booker, Ph.D.
CMC Review	Rajiv Agarwal, Ph.D.
CMC Microbiology Review	Robert Mello, Ph.D.
Clinical Pharmacology Review	Julia Cho, Ph.D.
DDMAC	Lynn Panholzer Pharm. D. and Sheetal Patel, Pharm.D.
DSI	Roy Blay, Ph.D.
OSE/DMEPA	Zachary Oleszczuk Pharm. D. and Felicia Duffy, R.N.
OSE/DRISK	Sharon Mills, R.N. and Latonia Ford, R.N.
OSE/DPV	Tracy Salaam, Pharm.D.
PMHS	Elizabeth Durowicz, M.D.
SEALD	Debbie Beitzell, R.N.

OND=Office of New Drugs
DDMAC=Division of Drug Marketing, Advertising and Communication
OSE= Office of Surveillance and Epidemiology
DMEPA=Division of Medication Error Prevention and Analysis
DSI=Division of Scientific Investigations
DRISK= Division of Drug Risk Evaluation
DPV=Division of Risk Management
CDTL=Cross-Discipline Team Leader
PMHS-Pediatric and Maternal Health Staff
SEALD-Study endpoint and Labeling Development

Signatory Authority Review

1. Introduction

SORILUX (calcipotriene) foam, 0.005%, is a topical drug product for which the applicant seeks approval under Section 505 (b) (2) of the Federal Food Drug and Cosmetic Act for the topical treatment of plaque psoriasis in patients [REDACTED] ^{(b) (4)}. The active ingredient, calcipotriene, is a vitamin D analog which is currently marketed in the US in various topical dosage forms (cream, ointment, and solution) and as fixed-dose combination (with betamethasone dipropionate, in ointment and suspension). I concur with the recommendation for approval provided by the review team and with the CDTL summary review.

2. Background

The applicant reached agreement with the agency on relevant aspects of their application during the development program.

3. CMC/Device

I concur with the conclusions reached by the chemistry reviewer regarding the acceptability of the manufacturing of the drug product and drug substance. Manufacturing site inspections were acceptable. Stability testing supports an expiry of 24 months. There are no outstanding issues.

4. Nonclinical Pharmacology/Toxicology

I concur with the conclusions reached by the pharmacology/toxicology reviewer that there are no outstanding pharm/tox issues that preclude approval.

5. Clinical Pharmacology/Biopharmaceutics

I concur with the conclusions reached by the clinical pharmacology/biopharmaceutics reviewer that there are no outstanding clinical pharmacology issues that preclude approval.

6. Clinical Microbiology

Not applicable

7. Clinical/Statistical-Efficacy

I concur with the conclusions reached by the biostatistical reviewer, clinical reviewer and cross discipline team leader that the applicant has provided adequate information to demonstrate safety and efficacy.

The sponsor submitted results from two (U0267-301 and U067-302) 8 week multi-centered, prospective, randomized, double blind vehicle-controlled phase 3 trials to support the safety and efficacy of their product. The enrolled population was subjects 12 years of age and older with plaque psoriasis, a score of mild or moderate on the investigator's static global assessment at baseline and between two and twenty percent body surface area of involvement (excluding the face and scalp). The primary efficacy analysis was based upon the proportion of subjects who achieved an investigator's static global assessment of "clear" or "almost clear" with at least a two grade improvement from baseline at week 8. The intent to treat analysis set included 659 subjects in phase 3 trials. The scope of the applicant's development program is acceptable, with adequate study numbers and study design.

I concur with the review team recommendation that the totality of the information provided supports the efficacy of calcipotriene 0.005% for treatment of plaque psoriasis.

8. Safety

The 120-day safety update was reviewed, and did not identify new safety signals.

The safety database is adequate. In the pooled safety analysis set, which included subjects from studies CAL.201, U0267-301, and U0267-302 (vehicle-controlled studies of 8-weeks duration), 473 subjects were exposed to SORILUX foam dosed BID, including 437 subjects in the pivotal trials.

There were no deaths and no serious adverse events (SAE) attributable to study drug. The most frequently reported adverse events in the SORILUX arm were application site erythema (2%) and application site irritation (2%). Collection of adverse event data and assessment of local tolerance did not reveal unexpected safety signals.

I concur with the conclusion of the cross-discipline team leader that no postmarketing commitments or requirements are necessary. PREA requirements are discussed below.

9. Advisory Committee Meeting

Calcipotriene is not a new molecular entity and there were no issues that required an advisory committee meeting.

10. Pediatrics

The application was presented to the Pediatric Review Committee (PeRC) on July 21st, 2010. The committee concurred with the Division's recommendation to grant a partial waiver for pediatric patients aged 0 to 2, and a deferral for pediatric patients aged 2 to 16. The committee agreed with the plan to conduct pharmacokinetic/pharmacodynamics (PK/PD) studies in children 2 through 11 and adolescents 12 through 16 with psoriasis, and a vehicle-controlled safety and efficacy study in subjects 2-11 years of age with psoriasis, detailed as follows:

1. The applicant should conduct a PK/PD study in a minimum of 20 evaluable pediatric subjects with psoriasis aged 12 through 16.
2. The applicant should conduct a PK/PD study in a minimum of 25 evaluable pediatric subjects with psoriasis aged 2 through 11.
3. The applicant should conduct a vehicle-controlled study of the safety and efficacy of their product in pediatric subjects with psoriasis aged 2 to 11 years of age with a minimum of 100 evaluable subjects exposed to active.

11. Other Relevant Regulatory Issues

There are no other unresolved relevant regulatory issues.

12. Labeling

- Proprietary name "SORILUX" was accepted by DMEPA on September 17th, 2010.
- Labeling agreements, including carton and container labeling, have been reached with the applicant and labeling is appended to the approval letter.

13. Decision/Action/Risk Benefit Assessment

- This application will be approved.
- Risk Benefit Assessment – the product presents an acceptable benefit/risk profile. There are no novel concerns for this product.
- Recommendation for Postmarketing Risk Evaluation and Mitigation Strategies - None
- Recommendation for other Postmarketing Requirements and Commitments – Postmarketing requirements under PREA include:

1684-1 Deferred pediatric study under PREA for the treatment of topical treatment of plaque psoriasis in pediatric patients ages 12 through 16. A pharmacokinetic/pharmacodynamic trial of calcipotriene foam under maximal use conditions in 20 evaluable pediatric subjects with plaque psoriasis age 12 through 16 years. Evaluate the effect of the product on calcium metabolism in all subjects.

Final Protocol Submission: April, 2011
Study/Trial Completion: June, 2013
Final Report Submission: January, 2014

1684-2 Deferred pediatric study under PREA for the treatment of topical treatment of plaque psoriasis in pediatric patients ages 2 through 11. A pharmacokinetic/pharmacodynamic trial of calcipotriene foam under maximal use conditions in 25 evaluable pediatric subjects with plaque psoriasis age 2 through 11 years. Evaluate the effect of the product on calcium metabolism in all subjects.

Final Protocol Submission: April, 2011
Study/Trial Completion: September, 2013
Final Report Submission: March, 2014

1684-3 Deferred pediatric study under PREA for the treatment of topical treatment of plaque psoriasis in pediatric patients ages 2 through 11. A vehicle-controlled trial of the safety and efficacy of calcipotriene foam in 100 evaluable pediatric subjects with plaque psoriasis age 2 through 11 years. Evaluate the effect of the product on calcium metabolism in all subjects.

Final Protocol Submission: Sept, 2011
Study/Trial Completion: June, 2013
Final Report Submission: January, 2014

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

/s/

SUSAN J WALKER
10/06/2010