CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-087

SUMMARY REVIEW

Division Director Review for Regulatory Action

Date	23Jan09
From	Susan J. Walker, M.D.
Subject	Division Director Summary Review
NDA	22-087
Applicant Name	Galderma
Date of Submission	21 Dec 07; Amendment 17Oct08
PDUFA Goal Date	27Jan09
Proprietary Name / Established (USAN) Name	Vectical/Calcitriol
Dosage Forms / Strength	Topical ointment – 3 mcg/g
Proposed Indication(s)	Treatment of mild to moderate psoriasis in adults
Action	Approval

1. Introduction

Vectical (calcitriol) Ointment, 0.003%, is a topical vitamin D analogue for which the sponsor seeks approval under Section 505 (b) (1) of the Federal Food Drug and Cosmetic Act for the topical treatment of psoriasis in adult patients. This memo will summarize the findings of the multi-disciplinary review team and provide my recommendations for approval.

2. Background

Calcitriol Ointment 3mcg/g is currently marketed in 42 countries for the treatment of psoriasis. The active moiety, calcitriol, is available in the U.S. as an oral tablet, oral solution, and solution for injection, for treatment of other diseases.

3. CMC/Device

Calcitriol ointment 3 mcg/g is a translucent ointment containing 3mcg/g (0.0003% w/w) of calcitriol for the topical treatment of psoriasis. It is packaged in aluminum tubes——— ——— with an ——————— closed with ——————— screw caps. Tube sizes proposed for marketing are ——— 00 gram; a 5g size is intended for samples. b(4)

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. 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 for this application.

7. Clinical/Statistical-Efficacy

The applicant provided two identically designed multi-centered, randomized, double-blind, vehicle controlled, parallel group studies conducted in the United States. Subjects with mild to moderate psoriasis were randomized to calcitriol ointment or vehicle, and applied the product twice daily for 8 weeks. Study 18053 enrolled 418 subjects in 25 centers and study 18054 enrolled 421 subjects in 25 centers.

The applicant demonstrated the effectiveness of their product in the treatment of mild to moderate psoriasis when used twice daily for 8 weeks. The label should reflect efficacy results for each of the two phase 3 trials, with success defined as the proportion of subjects demonstrating "clear" or "almost clear" with a two grade improvement by week 8. The results for the intent-to-treat population in Study 18053 demonstrated 23.4% success for the active and 14.4% success for the vehicle. Success was replicated in the second study, 18054, with 20.5% success for the active and 6.6% success for the vehicle.

The applicant has demonstrated that the drug product is effective for the treatment of mild to moderate plaque psoriasis in adult patients.

8. Safety

Calcium homeostasis parameters were monitored in approximately 80 subjects in calcitriol and vehicle arms of two studies. Clinical symptoms of hypercalcemia were not noted. The multidisciplinary review team has extensively reviewed the adverse event profile for this product, with particular focus on the potential for the drug product to affect calcium homeostasis. I concur with the conclusion that the product has demonstrated safety for use as labeled.

Three subjects from the open-label long term safety study (2663) reported urinary stones (confirmed in two subjects); all three subjects had elevated 24-hr urine calcium at baseline. No subjects developed stones in the controlled pivotal trials. Elevations of serum calcium observed during the clinical studies were generally sporadic and there were no persistent alterations in measures of calcium homeostasis.

9. Advisory Committee Meeting

Calcitriol is not a new molecular entity and no Advisory Committee meeting was convened.

10. Pediatrics

The applicant requested a partial waiver for the pediatric age group less than 2 years of age because the necessary studies would be highly impractical based on the small number and geographical dispersion of patients with psoriasis in that age group. The applicant requested a deferral for those 2 to 17 years of age. The applicant completed studies in adults. I concur that the waivers and deferrals requested should be granted.

11. Other Relevant Regulatory Issues

There are no other unresolved relevant regulatory issues.

12. Labeling

Labeling discussions were concluded with the sponsor and the final approved labeling is attached to the approval letter.

13. Decision/Action/Risk Benefit Assessment

I concur with the recommendations of the multidisciplinary review team that the product should be approved.

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

/s/

Susan Walker
1/23/2009 04:42:13 PM
DIRECTOR

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