CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

203567Orig1s000

MEDICAL REVIEW(S)

CLINICAL REVIEW RESUBMISSION

Application Type	505(b)(1)
Application Number(s)	203-567
Priority or Standard	Standard
Submit Date(s)	20-DEC-2013
Received Date(s)	20-DEC-2013
PDUFA Goal Date	20-JUN-2014
Division / Office	DDDP/ODE III
Reviewer Name(s)	Gary Chiang MD, MPH
Review Completion Date	8-MAY-2014
Established Name	efinaconazole
(Proposed) Trade Name	Julia™
Therapeutic Class	antifungal
Applicant	Dow Pharmaceutical Sciences
Formulation(s)	Topical solution 10%
Dosing Regimen	Once daily
Indication(s)	Onychomycosis
Intended Population(s)	Adults 18 years and older

Template Version: March 6, 2009

Table of Contents

Table of Tables

1 Recommendations/Risk Benefit Assessment

1.1 Recommendation on Regulatory Action

Dow Pharmaceutical Sciences has re-submitted a New Drug Application for JUBLIA™ (efinaconazole solution, 10%) with a proposed indication of once daily topical treatment of onychomycosis of the toenail (tinea unguium) in patients 18 years and older. The applicant successfully demonstrated safety and efficacy in two adequate and well controlled clinical trials for the treatment of onychomycosis in patients 18 years and older, when used once daily for 48 weeks.

The original NDA was submitted on July 26, 2012 and this submission received a complete response due to Chemistry Manufacturing and Control (CMC) deficiencies on May 13, 2013, principally related to leakage of the container closure system (b) (4) The nonclinical, clinical pharmacology and clinical programs submitted with the original application were found generally acceptable though labeling negotiations were not initiated once it became clear that the bottle leakage would preclude approval of the application.

On December 20, 2013 the applicant re-submitted their NDA to with a new container closure system to address the CMC deficiencies. The applicant has redesigned the container closure system and provided data that no leakage has occurred. No new nonclinical information was provided, and no new clinical pharmacology or clinical trials were conducted for this resubmission.

The critical CMC review issues that concluded with a Complete Response from the first review cycle have been resolved. The new container closure system has been found to be acceptable for marketing and the applicant has provided appropriate information to provide sufficient data to assure the identity, strength, purity, and quality of the drug product. The new bottle with a brush applicator dispenses drug product with similar quantity and distribution as the container/closure system used in the Phase 3 clinical trials so that additional clinical trials are not required.

This reviewer is in agreement with the CMC recommendation for approval, and the clinical recommendation is for approval of this application.

1.2 Risk Benefit Assessment

The risk to benefit assessment for this application is primarily based on the clinical trial results, which were extensively reviewed in the initial cycle and documented in the clinical review dated April 13, 2013. In the two pivotal Phase 3 clinical trials, the most common adverse events associated with the drug product were application site reactions (application site dermatitis and application site vesicles). There were no deaths or serious adverse events attributed to the drug product. In the two combined pivotal Phase 3 clinical trials, a greater percentage of subjects in the JUBLIA™ group relative to the Vehicle group achieved "Complete Cure" (clinical cure as well as mycological cure) at Week 52 (16.6% versus 4.3%, respectively), demonstrating that the drug product was effective in treating toenail onychomycosis.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.