DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 77732

MEETING MINUTES

Dow Pharmaceutical Sciences (DPS)
Attention: Charity Abelardo, RAC
Acting Senior Director, Regulatory Affairs
1330 Redwood Way
Petaluma, CA 94954-7121

Dear Ms. Abelardo:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for IDP-108 (efinaconazole) Solution, 10%.

We also refer to the meeting scheduled on April 17, 2012 between representatives of your firm and the FDA. The purpose of the meeting was to gain agreement that the information contained in the technical data sections are adequate for a 505(b)(1) NDA filing and to gain feedback for questions related to content/format of the NDA. Your premeeting briefing package (submitted February 22, 2012) provides background and questions for discussion.

We acknowledge email with Barbara Gould on April 15, 2012, notifying us that after receipt and review of the premeeting communication consisting of Agency responses to your questions, you have determined that the responses to your questions are sufficient and additional discussion is not necessary.

This letter and the enclosed final responses represent the official record.

If you have any questions, call Barbara Gould, Chief, Project Staff Management, at (301) 796-4224.

Sincerely,

{See appended electronic signature page}

Susan J. Walker, M.D., F.A.A.D.
Director
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure – Final Responses

FINAL RESPONSES

IND 077732

Product: (efinaconazole) Solution, 10%

Regulatory Path: 505(b)(1)

Sponsor: Dow Pharmaceutical Sciences

Proposed Indication: Topical treatment of [redacted] (b) (4) onychomycosis in patients 18 years or older

Type of Meeting: Type B

Meeting Date: April 18, 2012

Introductory Comment:

This material includes the Agency's final responses to the questions submitted for your meeting scheduled for April 18, 2012, at 10:00 am in White Oak Building 22 between Dow Pharmaceutical Sciences and the Division of Dermatology and Dental Products. This material was shared to promote a collaborative and successful discussion at the meeting. After receipt of the preliminary responses, you had two options:

- If these answers and comments were clear to you and you determined that further discussions were not required, you had the option of canceling the meeting.

- If you determined that discussion was needed for only some of the original questions, you had the option of reducing the agenda and/or changing the format of the meeting (e.g., from face-to-face to telecon).

You conveyed to Barbara Gould via email on April 15, 2012 that the responses to your questions were sufficient and additional discussion was not necessary. However, you requested clarification with regard to the responses provided under Question 2 and the additional information requested by FDA for inclusion in the NDA submission. As such, the below responses represent our final responses to your questions.

Purpose of the Meeting:
To gain agreement that the information contained in the technical data sections are adequate for a 505(b)(1) NDA filing and to gain feedback for questions related to content/format of the NDA.

Regulatory Correspondence History

We have had the following meetings with you:

- 8/17/2009 – End of Phase 2 Meeting

We have sent the following correspondences:

- 11/24/2009 – Advice
- 4/14/2010 – Advice/Information Request
- 4/14/2010 – Advice/Information Request
- 4/14/2010 – Advice/Information Request
- 8/30/2010 – Advice
- 2/14/2011 – Advice/Information Request
- 2/25/2011 – Advice
- 3/16/2011 – Advice
- 4/18/2011 – Advice

Regulatory

Question [1]:

Does the Agency agree that efinaconazole solution meets the regulatory standards for priority review?

Response:

No, the Agency does not agree that efinaconazole solution for the treatment of onychomycosis qualifies for priority review. You have not provided an adequate rationale that your proposed product provides for a significant improvement over existing therapies for a non-life threatening disease.

In order to qualify for priority review, you will need to provide an adequate rationale that your proposed product has the potential to provide significant advances in the treatment of onychomycosis. There are several currently approved therapies for onychomycosis. The preliminary efficacy analysis for your proposed product claims to show a primary efficacy response rate of about 16%, which is similar to at least one currently approved therapy. Approximately 84% of subjects would fail to respond to your proposed treatment.

Chemistry, Manufacturing and Controls (CMC)

No CMC questions were submitted in the briefing package for this meeting. After reviewing the limited CMC information provided in the briefing package, we have the following comments:

1. The proposed drug substance specification should include tests on chiral purity and residual solvents with appropriate acceptance criteria.

2. Address the issues of (b) (4) carried over from excipients for drug product in the proposed NDA.

3. To support the proposed container/closure system for the drug product, provide test results of USP<661> for each formulation-contacting packaging component. Additionally, due to the high level (b) (4) in the proposed formulation, provide the results of the extractables study (b) (4) (b) (4) and your investigation on leachables in the registration stability studies.

Pharmacology/Toxicology

Question [1]:
Does the Agency agree that the completed nonclinical program, as detailed in Section 8, is sufficient to characterize efinaconaozle toxicity for the NDA and that no other studies are required?

Response:
Yes.

Question [2]:
Does the Agency agree that the toxicity evaluation of the impurities have been fully addressed and no further studies will be required?

Response:
Yes.

Question [3] (microbiology question [1]):
Does the Agency agree with the proposed format and location for the specified studies and respective CTD sections described above?

Response:
Yes, the Agency agrees with the proposed format and location of clinical microbiology summaries and study reports.

Clinical

Question [1]:
Does the Agency agree to waive phototoxicity and photoallergy studies?

Response:
Yes, a waiver is likely to be appropriate at the time of NDA review. The submitted spectra for IDP-108A solutions, 5% and 10% w/w, and the IDP-108 (b) (4) solutions, 1% and 10%, and their excipients do not demonstrate any absorbance in the wavelength range of 290 to 700nm.

Question [2]:
Based on the completion of the clinical program as detailed in Section 9, does the agency agree that the clinical program is adequate to support approval of efinaconazole solution

with an indication for the topical treatment of (b) (4) onychomycosis in patients 18 years or older?

Response:
The clinical program presented in Section 9 appears to be adequate to meet NDA filing requirements; however, the adequacy of data and NDA approval will be the subject of the Agency NDA review.

Question [3]:
Does the Agency agree that the total patient exposure is adequate to support approval of the NDA?

Response:
It does appear that sufficient exposure to efinaconazole solution has been established to satisfy the ICH E1A guidelines. The adequacy of the safety data will be reviewed during the NDA review process, and supplementary safety information may be requested should additional safety issues be identified.

Question [4]:
Does the Agency agree that (b) (4) based upon the conditions described?

Response:
A (b) (4)

Biostatistics

Question [1]:
The complete list of efinaconazole clinical studies (IND and non-IND) is presented in Table 17. The datasets for the following clinical trials will be included in the NDA in CDISC format:

- DPSI-IDP-108-P3-01 (Phase 3 safety and efficacy)
- DPSI-IDP-108-P3-02 (Phase 3 safety and efficacy)
- DPSI-IDP-108-P2-01 (Phase 2 safety and efficacy)
- DPSI-IDP-108-P1-03 (Phase 1 PK)

The datasets for all other IND studies (DPSI-IDP-108-P1-01 and DPSI-IDP-108-P1-02) will be included in the NDA as SAS transport files. Datasets for the remaining two clinical studies not conducted under IND 077732 will not be included.

Does the Agency agree with the provision of the files in this format?

Response:
1. The electronic datasets for clinical studies in should be submitted in SAS transport form (.xpt).

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