

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**213690Orig1s000**

**OTHER REVIEW(S)**

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**MEMORANDUM**  
**REVIEW OF REVISED LABEL AND LABELING**  
Division of Medication Error Prevention and Analysis (DMEPA)  
Office of Medication Error Prevention and Risk Management (OMEPRM)  
Office of Surveillance and Epidemiology (OSE)  
Center for Drug Evaluation and Research (CDER)

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Date of This Memorandum: April 9, 2020  
Requesting Office or Division: Division of Dermatology and Dentistry (DDD)  
Application Type and Number: NDA 213690  
Product Name and Strength: Zilxi (minocycline hydrochloride) topical foam, 1.5%  
Applicant/Sponsor Name: Foamix Pharmaceuticals Inc.  
OSE RCM #: 2019-1662-1  
DMEPA Safety Evaluator: Madhuri R. Patel, PharmD  
DMEPA Team Leader: Sevan Kolejian, PharmD, MBA

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## 1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels and carton labeling received on April 6, 2020 for Zilxi. Division of Dermatology and Dentistry (DDD) requested that we review the revised container labels and carton labeling for Zilxi (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.<sup>a</sup>

## 2 CONCLUSION

The Applicant implemented all of our recommendations and the revised carton labeling and commercial container label are acceptable from a medication error perspective. However, there is a typo in the professional sample container label. we have no additional recommendations at this time. We provide our recommendation below in Section 3.

## 3 RECOMMENDATIONS FOR FOAMIX PHARMACEUTICALS INC.

We recommend the following be implemented prior to approval of this NDA:

- A. For the professional sample container label, revise "Usual Doage" to "Usual Dosage".

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<sup>a</sup> Patel M. Label and Labeling Review for minocycline (NDA 213690). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 JAN 31. RCM No.: 2019-1662.

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/s/

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MADHURI R PATEL  
04/09/2020 01:46:35 PM

SEVAN H KOLEJIAN  
04/09/2020 02:53:46 PM

**Department of Health and Human Services  
Public Health Service  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Medical Policy**

**PATIENT LABELING REVIEW**

Date: March 17, 2020

To: Jennifer Harmon, PharmD  
Regulatory Health Project Manager  
**Division of Dermatology and Denistry (DDD)**

Through: LaShawn Griffiths, MSHS-PH, BSN, RN  
Associate Director for Patient Labeling  
**Division of Medical Policy Programs (DMPP)**

Shawna Hutchins, MPH, BSN, RN  
Senior Patient Labeling Reviewer  
**Division of Medical Policy Programs (DMPP)**

From: Susan Redwood, MPH, BSN, RN  
Patient Labeling Reviewer  
**Division of Medical Policy Programs (DMPP)**

Laurie Buonaccorsi, PharmD  
Regulatory Review Officer  
**Office of Prescription Drug Promotion (OPDP)**

Subject: Review of Patient Labeling: Patient Package Insert (PPI)  
and Instructions for Use (IFU)

Drug Name (established name): TRADENAME (minocycline)

Dosage Form and Route: topical foam

Application Type/Number: NDA 213690

Applicant: Foamix Pharmaceuticals Inc.

## 1 INTRODUCTION

On August 2, 2019, Foamix Pharmaceuticals Inc., submitted for the Agency's review an original 505(b)(2) New Drug Application (NDA 213690) for TRADENAME (minocycline) topical foam, for the proposed indication of use for the treatment of [REDACTED] rosacea.

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Dermatology and Dentistry (DDD) on August 19, 2019 for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) and Instructions for Use (IFU) for TRADENAME (minocycline) topical foam.

DMPP conferred with the Division of Medication Error, Prevention, and Analysis (DMEPA) and a separate DMEPA review of the IFU will be forthcoming.

## 2 MATERIAL REVIEWED

- Draft TRADENAME (minocycline) topical foam PPI and IFU received on August 2, 2019, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on March 12, 2020.
- Draft TRADENAME (minocycline) topical foam Prescribing Information (PI) received on August 2, 2019, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on March 12, 2020.
- Approved AMZEEQ (minocycline) topical foam NDA 212379 labeling dated October 18, 2019.
- Approved SOLODYN (minocycline hydrochloride) Extended Release Tablets, NDA 050808 labeling dated October 21, 2013.

## 3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6<sup>th</sup> to 8<sup>th</sup> grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8<sup>th</sup> grade reading level.

Additionally, in 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss. We reformatted the PPI and IFU document using the Arial font, size 10.

In our collaborative review of the PPI and IFU we:

- simplified wording and clarified concepts where possible
- ensured that the PPI and IFU are consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information
- ensured that the PPI and IFU are free of promotional language or suggested revisions to ensure that they are free of promotional language
- ensured that the PPI and IFU meet the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)
- ensured that the PPI and IFU are consistent with the approved labeling where applicable.

## 4 CONCLUSIONS

The PPI and IFU are acceptable with our recommended changes.

## 5 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
- Our collaborative review of the PPI and IFU are appended to this memorandum. Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the PPI and IFU.

Please let us know if you have any questions.

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SUSAN W REDWOOD  
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LAURIE J BUONACCORSI  
03/17/2020 02:24:49 PM

SHAWNA L HUTCHINS  
03/18/2020 07:39:02 AM

LASHAWN M GRIFFITHS  
03/18/2020 07:44:01 AM

**FOOD AND DRUG ADMINISTRATION**  
**Center for Drug Evaluation and Research**  
**Office of Prescription Drug Promotion**

**\*\*\*Pre-decisional Agency Information\*\*\***

## Memorandum

**Date:** March 17, 2020

**To:** Kevin Clark/Clinical Reviewer, M.D.  
Division of Dermatology and Dental Products (DDDP)  
  
Jennifer, Harmon, Regulatory Project Manager, (DDDP)

**From:** Laurie Buonaccorsi, Regulatory Review Officer  
Office of Prescription Drug Promotion (OPDP)

**CC:** Matthew Falter, Team Leader, OPDP

**Subject:** OPDP Labeling Comments for minocycline topical foam

**NDA:** 213690

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In response to DDDP's consult request dated August 19, 2019, OPDP has reviewed the proposed product labeling (PI), patient package insert (PPI), Instructions for Use (IFU), and carton and container labeling for the original NDA submission for minocycline topical foam.

**PI and PPI:** OPDP's comments on the proposed labeling are based on the draft PI received by electronic mail from DDDP on March 12, 2020.

A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed, and comments on the PPI and IFU will be sent under separate cover.

**Carton and Container Labeling:** OPDP has reviewed the proposed carton and container labeling submitted by the Sponsor to the electronic document room on August 2, 2019, and our comments are provided below.

Thank you for your consult. If you have any questions, please contact Laurie Buonaccorsi at (240) 402-6297 or [laurie.buonaccorsi@fda.hhs.gov](mailto:laurie.buonaccorsi@fda.hhs.gov).

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LAURIE J BUONACCORSI  
03/17/2020 02:28:23 PM

Clinical Inspection Summary

Date	11 March 2020
From	Cheryl Grandinetti, PharmD, Clinical Pharmacologist Good Clinical Practice Assessment Branch Division of Clinical Compliance Evaluation Office of Scientific Investigations
To	Jennifer Harmon, RPM Gordana Diglisic, MD, Clinical Reviewer Kevin Clark, MD, Clinical Team Leader Kendall Marcus, MD, Division Director, Division of Dental and Dermatology Products
NDA #	213690
Applicant	Foamix Pharmaceuticals, Inc.
Drug	Minocycline HCl 1.5% Topical Foam
NME	No
Proposed Indication	Treatment of (b) (4) rosacea
Consultation Request Date	9 September 2019
Summary Goal Date	23 March 2020
Action Goal Date	15 May 2020
PDUFA Date	2 June 2020

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

The clinical sites of Drs. Hooper, Zaiac, Abson, and Kempers were inspected in support of this NDA. The inspections covered Protocols FX2016-11 and FX2016-12. Overall the studies appear to have been conducted adequately, and the data generated by these sites appear acceptable in support of the respective indication.

II. BACKGROUND

This application was submitted in support of the use of minocycline HCl 1.5% Topical Foam for the treatment of subjects with (b) (4) rosacea in adults 18 years of age or older. The key studies supporting the application were the following:

- FX2016-11, "A Randomized, Multicenter, Double-blind, Vehicle-controlled Study to Evaluate the Safety and Efficacy of FMX103 1.5% Topical Minocycline Foam Compared to Vehicle in the Treatment of Facial Papulopustular Rosacea"
- FX2016-12, "A Randomized, Multicenter, Double-blind, Vehicle-controlled Study to Evaluate the Safety and Efficacy of FMX103 1.5% Topical Minocycline Foam Compared to Vehicle in the Treatment of Facial Papulopustular Rosacea"

Protocol FX2016-11

- *Subjects:* A total of 751 subjects were enrolled (495 in the FMX103 1.5% group and 256 in the Vehicle Foam group), and 669 completed the study (437 in the FMX103 1.5% group and 232 in the Vehicle Foam group).
- *Sites:* 54 sites in the United States
- *Study Initiation and Completion Dates:* 2 Jun 2017 to 28 Sep 2018

### Protocol FX2016-12

- *Subjects:* A total of 771 subjects were enrolled (514 received FMX103 1.5% and 257 received Vehicle Foam), and 718 completed the study (479 in the FMX103 1.5% group and 239 in the Vehicle Foam group).
- *Sites:* 46 sites in the United States
- *Study Initiation and Completion Dates:* 01 June 2017 – 31 July 2018

Protocols FX2016-11 and FX2016-12 were identical in design. These were randomized, multicenter, double-blind, vehicle-controlled, 2-arm studies that evaluated the safety and efficacy of 1.5% minocycline HCl topical foam compared to vehicle in the treatment of subjects with moderate-to-severe facial papulopustular rosacea. The primary objectives were to determine the efficacy, tolerability, and safety of 1.5% minocycline HCl foam applied topically once daily for 12 weeks in the treatment of rosacea.

Subjects with qualifying lesion counts and Investigator Global Assessment (IGA) of rosacea severity were enrolled and randomized in a 2:1 ratio to receive minocycline HCl 1.5% foam or matching vehicle foam. Both the Investigator and subject were blinded to the study drug identity. Subjects applied the assigned study drug topically once daily for 12 weeks as directed. Subjects returned for visits at Weeks 2, 4, 8, and 12.

The co-primary efficacy endpoints were:

- The absolute change in the inflammatory lesion count from Baseline to Week 12
- Treatment Success (dichotomized as yes/no) at Week 12, where success was defined as an IGA score of 0 or 1, and at least a 2-grade improvement (decrease) from Baseline

Efficacy evaluations (inflammatory lesion counts and IGA score) were performed at Weeks 4, 8, and 12.

### Rationale for Site Selection

The clinical sites were chosen primarily based on numbers of enrolled subjects, site efficacy, and prior inspectional history.

### III. RESULTS (by site):

1. Deirdre Hooper, MD  
Site #115  
Inspection Dates: 19 – 21 November 2019  
DelRicht Research  
3525 Prytania Street, Suite 308 and 501  
New Orleans, LA 70115

At this site for Protocol FX2016-11, 75 subjects were screened, 59 were randomized, and 48 subjects completed the study. Per the sponsor's data listings reported to FDA, 4 subjects were lost to follow-up; 5 subjects withdrew from the study for various personal reasons; 1 subject withdrew due to an adverse event (influenza); and one subject withdrew for other reasons not identified by the sponsor. Records reviewed included, but were not limited to, the study protocol and amendments, IRB submissions and approvals, subject eligibility criteria, informed consent, randomization procedures, source data and records, electronic case report forms, electronic diary data and paper rescue medication diaries, drug accountability, adverse event reporting, protocol deviations, and monitor logs and follow-up letters. An audit of the study records for the 59 subjects who were randomized was conducted.

There was no evidence of under-reporting of adverse events. The source records for the co-primary efficacy endpoint data

were reviewed and verified against the data listings provided by the sponsor for all 59 randomized subjects; no discrepancies were noted.

2. Martin Zaiac, MD  
Site #144  
Inspection Dates: 12 – 18 November 2019  
Sweet Hope Research Specialty, Inc.  
14160 Palmetto Frontage Road , Suite 100  
Miami Lakes, FL 33016

At this site for Protocol FX2016-11, 52 subjects were screened, 49 were randomized, and 46 subjects completed the study. Three subjects withdrew from the study. Per the sponsor's data listings, one subject was lost to follow-up and 2 withdrew their participation in the study for personal reasons. Records reviewed included, but were not limited to, the study protocol and amendments, IRB submissions and approvals, subject eligibility criteria, informed consent, randomization procedures, source data and records, electronic case report forms, electronic diary data and paper rescue medication diaries, drug accountability, adverse event reporting, protocol deviations, and monitor logs and follow-up letters. An audit of the study records for all 49 randomized subjects was conducted.

There was no evidence of under-reporting of adverse events. The source records for the co-primary efficacy endpoint data were reviewed and verified against the data listings provided by the sponsor for all 49 randomized subjects; no discrepancies were noted.

3. Kim Abson, MD  
Site #203  
Inspection Dates: 18 – 20 November 2019  
The Polyclinic Madison Center  
904 7th Avenue  
Seattle, WA 98104

At this site for Protocol FX2016-12, 38 subjects were screened and 21 were randomized, all of whom completed the study. Records reviewed included, but were not limited to, the study protocol and amendments, IRB submissions and approvals, subject eligibility criteria, informed consent, randomization procedures, source data and records, electronic case report forms, electronic diary data and paper rescue medication diaries, drug accountability, adverse event reporting, protocol deviations, and monitor logs and follow-up letters. An audit of the study records for all 21 subjects who were randomized was conducted.

There was no evidence of under-reporting of adverse events. The source records for the co-primary efficacy endpoint data were reviewed and verified against the data listings provided by the sponsor for all 21 randomized subjects. A single transcription error was observed for subject (b) (6) (randomized to minocycline HCl). The total inflammatory lesion count at Week 12 was recorded as 1 on the source document while it was recorded as 0 in the sponsor's data listing.

*Reviewer's comment: This discrepancy is related to a variable (i.e., total inflammatory lesion count) and a timepoint (Visit 12) used in the assessment of the co-primary efficacy endpoint. Given that this discrepancy is minor and occurred in only one subject at this site, the inspection finding likely does not have a significant effect on overall efficacy results of the study.*

4. Steven Kempers, MD  
Site #232  
Inspection Dates: 18 – 20 November 2019

Minnesota Clinical Study Center  
7205 University Avenue NE  
Fridley, MN 55432

At this site for Protocol FX2016-12, 25 subjects were screened and 24 were randomized, all of whom completed the study. Records reviewed included, but were not limited to, the study protocol and amendments, IRB submissions and approvals, subject eligibility criteria, informed consent, randomization procedures, source data and records, electronic case report forms, electronic diary data and paper rescue medication diaries, drug accountability, adverse event reporting, protocol deviations, and monitor logs and follow-up letters. An audit of the study records for all 25 subjects who were screened was conducted.

There was no evidence of under-reporting of adverse events. The source records for the co-primary efficacy endpoint data were reviewed and verified against the data listings provided by the sponsor for all 24 randomized subjects; no discrepancies were noted.

{See appended electronic signature page}

Cheryl Grandinetti, Pharm.D.  
Clinical Pharmacologist  
Good Clinical Practice Assessment Branch  
Division of Clinical Compliance Evaluation  
Office of Scientific Investigations

CONCURRENCE:

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CONCURRENCE:

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Kassa Ayalew, M.D., M.P.H Branch Chief  
Good Clinical Practice Assessment Branch  
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cc:

Central Doc. Rm. NDA 213690  
DNP/Project Manager/ Jennifer Harmon  
DNP/Medical Officer/ Gordana Diglisic  
DNP/Clinical Team Leader/ Kevin Clark  
DNP/Division Director/ Kendall Marcus

OSI/DCCE/Branch Chief/Kassa Ayalew  
OSI/DCCE/Team Leader/Phillip Kronstein  
OSI/DCCE/GCP Reviewer/Cheryl Grandinetti  
OSI/ GCP Program Analysts/Yolanda Patague  
OSI/Database Project Manager/Dana Walters

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CHERYL A GRANDINETTI  
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03/12/2020 04:12:14 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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Food and Drug Administration

Center for Drug Evaluation and Research  
Office of New Drugs, ODE-IV  
Division of Pediatric and Maternal Health  
Silver Spring, MD 20993  
Telephone 301-796-2200  
FAX 301-796-9855

**MEMORANDUM TO FILE**

**Date of Consult Request:** August 19, 2019  
**From:** Division of Pediatric and Maternal Health (DPMH)  
Kerri-Ann Jennings, MS, BSN, RN  
Senior Regulatory Project Manager  
**To:** Division of Dermatology and Dental Products  
**NDA Number:** 213690  
**Drug:** minocycline hydrochloride foam, 1.5%  
**Applicant:** Foamix Pharmaceuticals Inc.  
**Indication:** Treatment of (b) (4) rosacea

The Division of Dermatology and Dental Products (DDDP) submitted a consult request to the Division of Pediatric and Maternal Health (DPMH) on August 19, 2019, requesting assistance in reviewing the labeling for compliance with PLLR format and provide recommendations regarding the proposed language, for applicable sections, for the above referenced NDA.

DPMH participated in applicable team and labeling internal meetings from September 16, 2019 through March 4, 2020 to discuss the application and provide labeling recommendations to DDDP.

DPMH- Maternal Health has no further comments at this time, thus, this memorandum will close out the consult request.

DPMH Maternal Health MO Reviewer- Jane Liedtka, MD  
DPMH Maternal Health Team Leader- Miriam Dinatale, DO  
DPMH Division Director- Lynne Yao, MD  
DPMH RPM- Kerri-Ann Jennings, MS, BSN, RN

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