CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

212379Orig1s000

PRODUCT QUALITY REVIEW(S)

U.S. FOOD & DRUG ADMINISTRATION

RECOMMENDATION

☒ Approval
☐ Approval with Post-Marketing Commitment
☐ Complete Response

NDA 212379
Assessment # 1

Drug Product Name	AMZEEQ (minocycline)
Dosage Form	Foam
Strength	4%
Route of Administration	Topical
Rx/OTC Dispensed	Rx
Applicant	Foamix Pharmaceuticals Inc.
US agent, if applicable	N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original NDA Submission	12/20/2018	All
User Fee Coversheet	01/07/2019	Administrative – All
Labeling-Package Insert Draft	02/01/2019	All
Clinical Study Report	02/14/2019	Clinical
BIMO information	02/15/2019	Clinical
Response to Quality Information Request	02/21/2019	ONDP – Drug Substance and Drug Product
Clinical Study Report	03/04/2019	Clinical
Clinical Study Report	03/13/2019	Clinical
Clinical Study Report	03/22/2019	Clinical
Response to Quality Information Request	04/19/2019	ONDP – Drug Product
Clinical Study Report	04/29/2019	Clinical
Quality Information	O5/06/2019	ONDP- Drug Substance
Container and Carton Labels Physician Samples)	05/09/2019	All
Clinical Study Report	05/28/2019	Clinical
Response to Quality Information Request	06/03/2019	OPQ – ONDP and OPF
Clinical Study Report	06/19/2019	Clinical
Clinical Safety Update	06/20/2019	Clinical
Patent Exclusivity	06/24/2019	Administrative - All

Clinical Study Report (Biometrics)	08/07/2019	Clinical
Response to Quality Information Request	08/08/2019	OPQ – ONDP and OPF
Response to Quality Information Request	08/16/2019	OPQ – OPF
General Correspondence (patent Information Verification)	08/16/2019	Administrative - All
Response to Quality Information Request	08/19/2019	ONDP – Drug Product and Biopharmaceutics
Patent Exclusivity Certification	08/22/2019	Administrative - All
Patent Exclusivity - Patent Information	08/26/2019	Administrative - All
Response to Quality Information Request	08/28/2019	OPQ – ONDP and OPF
Response to Quality Information Request	08/30/2019	ONDP – Drug Product
PI Labeling and Container and Carton Labels	09/18/2019	All
PI Labeling and Container and Carton Labels	09/23/2019	All

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessment	Secondary Assessment
Drug Substance	Joseph Leginus, Ph.D.	Donna Christner, Ph.D.
Drug Product	Hailin Wang, Ph.D.	Mo-Jhong Rhee, Ph.D.
Manufacturing	Youmin Wang, Ph.D.	Yubing Tang, Ph.D.
Microbiology	Julia Marre, Ph.D.	Denise Miller, Ph.D.
Biopharmaceutics	Kalpana Paudel, Ph.D.	Vidula Kolhatkar, Ph.D.
Regulatory Business Process Manager	Bamidele (Florence) Aisida, Pharm. D., BCPS	
Application Technical Lead	Hamid Shafiei, Ph.D.	
Laboratory (OTR)	N/A	N/A
Environmental	Hailin Wang, Ph.D.	Moo-Jhong Rhee, Ph.D.

U.S. FOOD & DRUG ADMINISTRATION

QUALITY ASSESSMENT DATA SHEET

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	II	(b) (4)	Minocycline Hydrochloride - Micronized	Adequate	02/07/2019	Joseph Leginus, Ph.D.
	II		Minocycline Hydrochloride (dihydrate) - Micronized	Adequate	04/18/2019	Joseph Leginus, Ph.D.

B. OTHER DOCUMENTS: *IND, RLD, RS, Approved NDA*

Document	Application Number	Description
Commercial IND	122770	IND for the drug product, FMX-101
NDA	50808	SOLODYN (minocycline hydrochloride) Extended Release Tablets used as LD for nonclinical toxicology

2. CONSULTS

Discipline	Status	Recommendation	Date	Assessor
Biostatistics	N/A			
Pharmacology/Toxicology	N/A			
CDRH-ODE	N/A			
CDRH-OC	N/A			
Clinical	N/A			
Other	N/A			

U.S. FOOD & DRUG ADMINISTRATION

EXECUTIVE SUMMARY

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

- The applicant of this 505(b)(2) new drug application has provided **sufficient CMC information** to assure the identity, purity, strength, and quality of the drug substance (minocycline) and the drug product, AMZEEQ (minocycline) Topical Foam, 4%.

- Labels/labeling issues have been **satisfactorily** addressed.

- The Office of Process and Facility has made an overall "**Acceptable**" recommendation regarding the facilities involved in this NDA.

- The claim for categorical exclusion of the environmental assessment is granted.

Therefore, from the OPQ perspective, this NDA is recommended for **APPROVAL** with expiration dating period of **18 months**.

II. SUMMARY OF QUALITY ASSESSMENTS

A. Product Overview

Foamix Pharmaceuticals Inc. has submitted this 505(b)(2) new drug application for AMZEEQ (minocycline) Topical Foam, 4% indicated for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 9 years of age and older.

The active ingredient, minocycline, is a semi-synthetic derivative of tetracycline antibiotic that has been approved as its hydrochloride salt, minocycline hydrochloride, since 1971. Multiple drug products containing minocycline have been approved and are currently being marketed as capsules, tablets, extended-release tablets, oral suspensions, injections, and periodontal systems. Although the applicant, Foamix Pharmaceuticals Inc., has not obtained the right to cross reference SOLODYN® (minocycline hydrochloride) Extended-Release Tablets (NDA 50808), the applicant is relying on nonclinical toxicology safety provided in the prescribing information (PI) for SOLODYN® as the listed drug (LD).

AMZEEQ (minocycline) Topical Foam, 4% contains 40mg of minocycline provided as 43mg of micronized minocycline hydrochloride per gram, formulated as a suspension in a non-aqueous pre-foam formulation (b) (4) containing soybean oil, coconut oil, light mineral oil, cyclomethicone cetostearyl alcohol, stearic acid, myristyl alcohol, hydrogenated castor oil,

white wax (beeswax), stearyl alcohol, and docosanol (b) (4) (b) (4) as inactive ingredients. The pre-foam formulation is packaged as 7g (physician sample) and 30g (commercial drug product) in pressurized aerosol aluminum upright canisters with the propellant, (b) (4) (b) (4) (butane, isobutane, and propane) that will discharge the drug product as a foam for topical use. The physician sample canisters are filled with (b) (4) of pre-foam formulation and (b) (4) of propellant to ensure delivery of 7g of foam and the commercial drug product canisters are filled with (b) (4) of pre-foam formulation and (b) (4) of propellant to ensure delivery of 30g of foam.

The applicant has stated that the proposed foam formulation will allow for delivery of the drug product to the site of action with minimal systemic absorption which will reduce any side effect associated with systemic absorption of minocycline.

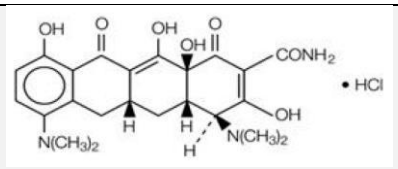
Proposed Indication(s) including Intended Patient Population	Treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 9 years of age and older
Duration of Treatment	As prescribed by physicians
Maximum Daily Dose	Small amount of foam gently applied to the affected skin area on a day at the same time one hour before bedtime
Alternative Methods of Administration	N/A

B. Quality Assessment Overview

Drug Substance: Adequate

Minocycline hydrochloride is a hydrochloride salt of minocycline, a semi synthetic tetracycline antibiotic derivative. Oral drug products containing minocycline have shown to have antibacterial and anti-inflammatory effects. The currently marketed drug product, SOLODYN® extended-release tablets has shown to be effective in the treatment of acne vulgaris.

Minocycline hydrochloride has the chemical name of 2-napthacenecarboxamide, 4,7-bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro- 3,10,12,12a-tetrahydroxy-1,11-dioxo-, monohydrochloride, molecular formula of $C_{23}H_{27}N_3O_7 \cdot HCl$, molecular weight of 493.94, and molecular structure below:



Minocycline hydrochloride is a (b) (4) (b) (4)

(b) (4) (b) (4)

(b) (4) (b) (4)

regarding the manufacture of micronized minocycline hydrochloride by (b) (4) is provided in DMF (b) (4) and the information regarding the manufacture of micronized minocycline hydrochloride (b) (4) (b) (4)

Minocycline hydrochloride is a compendial drug substance with USP and Eur monographs. It is tested and released according specification that complies with the compendial requirements. The release specification of minocycline hydrochloride intended for this application also includes testing and acceptance criteria for description, (b) (4) additional specific impurities, and particle size. It is packaged in (b) (4) (b) (4)

The information provided in DMF (b) (4) was reviewed by the Drug Substance reviewer, Dr. Joseph Leginus, on 02/07/2019 and 04/18/2019, respectively. Dr. Leginus has found both DMFs adequate to support this new drug application. Additionally, Dr. Leginus has found the information provided in the drug substance section of this application and (b) (4) review is provided in the Drug Substance Chapter of the IQA.

Drug Product: Adequate

AMZEEQ (minocycline) Topical Foam, 4% has been developed as a first in class topical drug product for the treatment of moderate to severe acne vulgaris.

It is formulated as non-aqueous, [redacted] pre-foam suspension formulation containing micronized minocycline hydrochloride equivalent to 40mg of minocycline per gram of pre-foam formulation. The pre-foam formulation is packaged as 7g for physician sample and 30g for commercial use in aluminum canisters pressurized with propellant to discharge the product as a foam. Minocycline hydrochloride has been approved as an active ingredient since 1971. Since original approval, multiple drug products containing minocycline hydrochloride such as capsules, tablets, extended-release tablets, oral suspensions, injections, and periodontal systems have been approved and are currently being marketed in the United States. SOLODYN® extended-release tablets are used as LD for this drug product.

The micronized minocycline hydrochloride pre-foam suspension formulation also contains soybean oil, coconut oil, light mineral oil, cyclomethicone [redacted] cetostearyl alcohol, stearic acid, myristyl alcohol, hydrogenated castor oil, white wax (beeswax), stearyl alcohol, and docosanol [redacted] as inactive ingredients. Aluminum canisters containing the drug product pre-foam formulation is pressurized with the propellant, [redacted] butane, isobutane, and propane. The inactive ingredients use in the composition AMZEEQ Topical Foam are compendial materials with the exception of docosanol and [redacted] propellant. Sufficient CMC information and certificates of analysis in support of the use of non-compendial excipients have been provided.

The drug product is tested and released according to a specification that includes testing and acceptance criteria for all physical and chemical attributes essential for assuring the identity, strength, purity, and quality of the drug product at release and throughout its proposed expiration dating period of 18 months. The applicant has provided sufficient stability data in support of the proposed drug product expiration dating period.

The drug product section of this application including the applicant's request for categorical exclusion from preparation of the environmental assessment has been reviewed by the Drug Product Reviewer, Dr. Hailin Wang. Dr. Wang has recommended the approval of this application with an expiration dating period of 18 months from the drug product perspective. Dr. Wang has also recommended granting the categorical exclusion for the preparation of environmental assessment for this

application. Dr. Wang's review is provided in the Drug Product Chapter of the IQA.

Labeling: Adequate

The CMC sections of the Prescribing Information (PI) as well as the immediate container and carton labels have been reviewed by the Drug Product Reviewer, Dr. Hailin Wang. Dr. Wang has found the final PI as well as immediate container and carton labels have been satisfactorily resolved for all outstanding issues noted in her Labeling Review #1, and therefore, she has recommended approval of this application from the CMC labeling/labels perspective (see Dr. Wang's addendum dated September 26, 2019 to her Labeling Review # 1).

(b) (4)

The Biopharmaceutic review of this application was mainly focused on the proposed IVRT method using Franz diffusion cell apparatus, method validation, and the proposed IVRT acceptance criterion. It was concluded that the proposed IVRT method and acceptance criterion of (b) (4) (b) (4) for testing of AMZEEQ foam are adequate.

All Phase 3 clinical studies, pharmacokinetic (PK) study, and Phase 1 safety studies were conducted using the formulation proposed for the commercial drug product. The applicant has stated that the commercial pre-foam formulation at (b) (4) scale will be manufactured using (b) (4) (b) (4) while the pre-foam formulation at (b) (4) scale used for the Phase 3 clinical trial material was manufactured using (b) (4). The applicant has provided comparative IVRT data that shows that sameness of pre-foam formulations manufactured by (b) (4) There were also some manufacturing process differences for the pre-foam formulation used in Adult Max and in Pediatric Max studies. The differences in the manufacturing process were reviewed by the process reviewer and determined to be minor (level (b) (4) change). Therefore, based on the principle outlined in SUPAC SS, it was concluded no bridging study is needed.

The Biopharmaceutics section of this application has been reviewed by the Biopharm Reviewer, Dr. Kalpana Paudel. Dr. Paudel has found the information provided in the biopharmaceutics section of this application to be adequate to support the approval of this application. Dr. Paudel's review is provided in the Biopharmaceutics Chapter of the IQA.

Microbiology (if applicable): Adequate

AMZEEQ (minocycline) Topical Foam, 4% is a non-aqueous, i- a e (b) (4) suspension formulation filled in an aluminum canister with propellant that discharges the drug product as a foam. It is non-sterile drug product and is tested for bioburden according to USP <61> and USP<62>.

The applicant has also provided sufficient information in support of bulk formulation hold-time as well as release and stability of the drug product. The microbiological attributes of this drug product have been reviewed by the Microbiology Reviewer Dr. Julia Marre, who has concluded that the information provided in the application regarding the microbiological attributes and bioburden testing of the drug product is adequate to support this application. Dr. Marre's review is provided in the Microbiology Chapter of the IQA.

C. Risk Assessment:

From Initial Risk Identification			Assessment		
Attribute/ CQA	**Factors that can impact the CQA**	**Initial Risk Ranking**	**Risk Mitigation Approach**	**Final Risk Evaluation**	**Lifecycle Considerations/ Comments**
Intra-container content uniformity	Homogenization and/or mixing of micronized minocycline hydrochloride into a uniform pre-foam suspension formulation	M	Uniformity is tested during release and stability (top, middle, and bottom of the container)	Acceptable	None

D. List of Deficiencies: None

Application Technical Lead:

Hamid R. Shafiei, Ph.D.
Brach V/DNDP II/ONDP/OPQ

Hamid Shafiei

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CHAPTER IV: LABELING

IQA NDA Assessment Guide Reference

1.0 PRESCRIBIN INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information:

1.1 HIGHLIGHTS O PRESCRIBING INFORMATION

AMZEEQTM (minocycline (b) (4)) Foam, (b) (4)
Initial U.S. Approval: 1971

	Information Provided in	Assessor's Comments
Product Title in Highlights		
Proprietary name	AMZEEQ™	ranted by DMEPA per review by M. Patel on 3/12/2019
Established name(s)	minocycline r r (b) (4) e Foam, (b) (4)	**Not Adequate** Recommended change: "minocycline topical foam". OPPQ (PQL mailbox) has been consulted on the established name determination. Active moiety is recommended per USP Salt Policy, all marketed minocycline-containing products examples and their monograph tittles. Reference email from Jibril Abdus-Samad is provided below.  RE_ Established name Minocycline HCl in a T
Route(s) of administration	Topical	Adequate
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system.	Foam, 4%	Adequate
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	N/A

For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.	N/A	N/A

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

For topical use only, not for oral, ophthalmic or intravaginal use [*see Clinical Studies (14)*]. After shaking the can well, a small amount of foam (a cherry-sized amount) should be expressed from the can onto the fingertips of the hand and then rubbed into acne-affected parts of the face. This should be repeated as needed until all acne-affected parts of the face are treated. If acne is present on other parts of the patient's body (neck, shoulders, arms, back or chest) additional amounts of foam should also be applied to these areas. The foam should be applied at approximately the same time each day at least 1 hour before bedtime. The patient should not bathe, shower or swim for at least 1 hour after application of the product.

Item	Information Provided in the NDA	Assessor's Comments
DOSAGE AND ADMINISTRATION section		
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents, storage conditions needed to maintain the stability of the reconstituted or diluted product)		dequate from CMC perspective

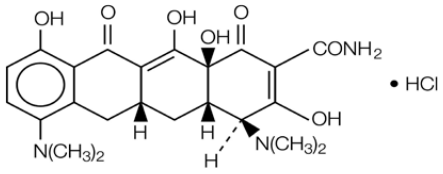
1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

Foam, 4% (3)

Item	Information Provided in the NDA	Assessor's Comments
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Foam	**Adequate**
Strength(s) in metric system	4%	**Adequate**
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance	Each gram of AMZEEQ contains (b) (4) minocycline (b) (4) equivalent to (b) (4) mg of (b) (4) minocycline.	**Not Adequate** Recommended change: Each gram of AMZEEQ contains 40 mg of minocycline equivalent to 43 mg of minocycline hydrochloride
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting	Not provided	**Adequate** The following revision has been made by OND labeling reviewer: Each gram of AMZEEQ contains minocycline hydrochloride equivalent to 40 mg of minocycline, and is supplied as a yellow suspension in a pressurized aluminum aerosol container.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	/A
For injectable drug products for parental administration, use appropriate labeling term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package.	N/A	/A

1.2.4 Section 11 (DESCRIPTION)

Minocycline hydrochloride, a semi-synthetic derivative of tetracycline, is [4S(4α,4aα,5aα,12aα)]-4,7-Bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12atetrahydroxy-1,11-dioxo-2-naphthacenecarboxamide mono hydrochloride. The structural formula is represented below:

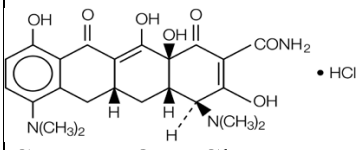


$C_{23}H_{27}N_3O_7$•HCl M. W. 493.94

Each gram of AMZEEQ contains micronized minocycline hydrochloride equivalent to 40 mg minocycline in a yellow suspension foam.

In addition, the 4% AMZEEQ Foam contains the following inactive ingredients: soybean oil, coconut oil, light mineral oil, cyclomethicone, cetostearyl alcohol, stearic acid, myristyl alcohol, hydrogenated castor oil, white wax (beeswax), stearyl alcohol, docosanol, and propellant (butane + isobutane + propane).

Item	Information Provided in the NDA	Assessor's Comments
DESCRIPTION section		
Proprietary and established name(s)	AMZEEQ™, Minocycline h (b) (4) Foam, (b) (4)	**Adequate**
Dosage form(s) and route(s) of administration	Foam topical use only	
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per FDA Guidance.	(b) (4) equivalent to 40 mg minocycline in a yellow suspension foam.	**Not Adequate** contains cr minocycline 40 mg equivalent to 43 mg minocycline hydrochloride in a yellow suspension foam.
List names of all inactive ingredients. Use USP/NF names. Avoid Brand names.	soybean oil, coconut oil, light mineral oil, cyclomethicone, cetostearyl alcohol, stearic acid, myristyl alcohol, hydrogenated castor oil, white wax (beeswax), stearyl alcohol, docosanol, and propellant (butane + isobutane + propane).	**Adequate** Includes 11 inactive ingredients for the suspension formulation, and 3 ingredients for the propellant mix. The sequence is arranged by function followed by amount.
For parenteral injectable dosage forms, include the name and	N/A	N/A

quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.		
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	N/A
Statement of being sterile (if applicable)	N/A	N/A
Pharmacological/ Therapeutic class	Derivative of tetracycline	**Adequate** from CMC perspective
Chemical name, structural formula, molecular weight	Minocycline hydrochloride, a semi-synthetic derivative of tetracycline, is [4S-(4α,4aα,5aα,12aα)]-4,7-Bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-2-naphthacenecarboxamide mono hydrochloride. The structural formula is represented below:  $C_{23}H_{27}N_3O_7$•HCl M.W. 493.94	**Adequate**
If radioactive, statement of important nuclear characteristics.	N/A	N/A
Other important chemical or physical properties (such as pKa or pH)	None	**Adequate**

Section 11 (DESCRIPTION) Continued

Item	Information Provided in the NDA	Assessor's Comments
For oral prescription drug products, include gluten statement if applicable	N/A	N/A
Remove statements that may be misleading or promotional	(b) (4)	**Not Adequate**

(e.g., “synthesized and developed by Drug Company X,” “structurally unique molecular entity”		The [redacted] (b) (4) should be deleted due to potential promotional implication.

1.2.5 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

16.1 How supplied

AMZEEQTM (minocycline [redacted] (b) (4)) Foam 4% is a yellow suspension supplied in a pressurized aluminum aerosol container (can), and is supplied as follows:
NDC 72356-101-03 30 g Can

16.2 Storage

AMZEEQ must be stored at 2ºC - 8ºC (36ºF - 46ºF) until dispensed to the patient.
Once dispensed, the patient is to store AMZEEQ at room temperature below 25ºC (77ºF) for 90 days. Do not store in the refrigerator.

16.3 Handling

Allow the can to warm to room temperature before first use.
Shake can well before use.
WARNING: Flammable. Avoid fire, flame, or smoking during and immediately following application. Contents under pressure. Do not puncture or incinerate. Do not expose to heat or temperatures above 49oC (120oF).

Item	Information Provided in the NDA	Assessor’s Comments
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s)	foam	**Not Adequate** Recommended change: topical foam
Strength(s) in metric system	4%	**Adequate**
Available units (e.g., bottles of 100 tablets)	30g	**Adequate**
Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number	Yellow suspension foam NDC 72356-101-03 30g Can	**Adequate**
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state “functionally scored”	N/A	/A
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.	N/A	/A

Section 16 (HOW SUPPLIED/STORAGE AND HANDLING) (Continued)

Item	Information Provided in the NDA	Assessor's Comments
Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to "Dispense in original container," provide reason why (e.g. to protect from light or moisture, to maintain stability, etc.)	WARNING: Flammable. Avoid fire, flame, or smoking during and immediately following application. Contents under pressure. Do not puncture or incinerate. Do not expose to heat or temperatures above 49°C (120°F).	**Adequate** Warning information is provided due to presences of propellant in the formulation. This is consistent with propellant properties and is deemed adequate.
If the product contains a desiccant, ensure the size and shape differ from the dosage form and desiccant has a warning such as "Do not eat."	N/A	N/A
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	AMZEEQ must be stored at 2ºC - 8ºC (36ºF - 46ºF) until dispensed to the patient. Once dispensed, the patient is to store AMZEEQ at room temperature below 25ºC (77ºF) for 90 days. Do not store in the refrigerator.	**Adequate** Storage condition and in-use condition is supported by stability data.
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: "Not made with natural rubber latex. Avoid statements such as "latex-free."	N/A	/A
Include information about child-resistant packaging	N/A	/A

1.2.6 Other Sections of Labeling

None

1.2.7 Manufacturing Information After Section 17 (for drug products)

Item	Information Provided in the NDA	Assessor's Comments
Manufacturing Information After Section 17		
Name and location of business (street address, city, state and zip code) of the manufacturer, distributor, and/or packer	Manufactured by: **ASM Aerosol-Service AG** Mohlin, Switzerland Manufactured for: **Foamix Pharmaceuticals, Inc.** Bridgewater, NJ 08807 Product of Portugal or Switzerland	Adequate

2.0 PATIENT LABELING

The patient labeling comply with all regulatory requirements from a CMC perspective.

3.0 CARTON AND CONTAINER LABELING

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Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Proprietary name, established name, and dosage form (font size and prominence	AMZEEQ™, AMZEEQ™ (Minocycline (b) (4)) Foam (b) (4)	**Not Adequate** Recommended change: AMZEEQ™ (minocycline) topical foam (b) (4) The font of the Established name appears to be at least half as large as the letters comprising the proprietary name. Both propriety name and established name are contrasted with different font color (black vs grey) and appear to have same prominence.
Dosage strength	%	**Adequate**
Route of administration	opical	**Adequate**
If the active ingredient is a salt, include the equivalency statement per FDA Guidance	Each gram of AMZEEQ contains (b) (4)	**Not Adequate** Recommended change: Each gram of AMZEEQ contains minocycline 40 mg equivalent to 43 mg minocycline
Net contents (e.g. tablet count)	30 g, 7g (physician sample)	**Adequate**
"Rx only" displayed on the principal display	Yes	**Adequate**
NDC number	DC 72356-101-03 NDC 72356-101-90	**Adequate**
Lot number and expiration date	Yes (bottom of carton)	**Adequate**

Storage conditions. If applicable, include a space on the carton labeling for the user to write the new BUD.	**Commercial Can 30g** Store at 2°C - 8°C (36°F - 46°F) until dispensed to the patient. Once dispensed, the patient is to store AMZEEQ at room temperature below 25ºC (77ºF) for 90 days. Do not store in the refrigerator. Allow the can to warm to room temperature before first use. Shake can well before use. WARNING: Flammable. Avoid fire, flame, or smoking during and immediately following application. Contents under pressure. Do not puncture or incinerate. Do not expose to heat or temperatures above 49°C (120°F). **Physician's can 7g** Store AMZEEQ at room temperature 68-77°F (20-25°C). Do not store in the refrigerator. Shake can well before use. WARNING: Flammable. Avoid fire, flame, or smoking during and immediately following application. Contents under pressure. Do not puncture or incinerate. Do not expose to heat or temperatures above 120°F (49°C).	Consistent with PI and supported by stability data. **Adequate**
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use)	N/A	/A
Other package terms include pharmacy bulk package and imaging bulk package which require "Not for direct infusion" statement.	N/A	/A

If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	N/A	
Bar code	Yes	

Item	Information Provided in the NDA	Assessor's Comments about Carton Labeling
Name of manufacturer/distributor	Manufactured by: ASM Aerosol-Service AG Mohlin, Switzerland Manufactured for: Foamix Pharmaceuticals Inc. Bridgewater, NJ 08807	**Adequate**
Medication Guide (if applicable)	N/A	/A
No text on Ferrule and Cap overseal	None	**Adequate**
When a drug product differs from the relevant USP standard of strength, quality, or purity, as determined by the application of the tests, procedures, and acceptance criteria set forth in the relevant compendium, its difference shall be plainly stated on its label.	N/A	/A
And others, if space is available	N/A	/A

Assessment of Carton and Container Labeling: ***{Not Adequate}***

The container and carton labels comply with all regulatory requirements from a CMC perspective.

ITEMS FOR ADDITIONAL ASSESSMENT

Overall Assessment and Recommendation: Not Adequate

List of Deficiencies:

A. Regarding Prescribing Information

1. The established name in the proposed product title, "AMZEEQ™ (minocycline hydrochloride) Foam", is not acceptable. It should be revised to,

   "AMZEEQ™ (minocycline) topical foam"

2. The equivalency statement, "Each gram of AMZEEQ contains 40 mg of minocycline equivalent to 43 mg of minocycline hydrochloride" should be added in the "**Dosage and Strength**", "**Description**" as well as **How Supplied/Storage and Handling** sections.

B. Container and Carton Labels

1. The the drug name, "AMZEEQ (minocycline (b) (4)) foam", in the labels should be revised to,

   "AMZEEQ™ (minocycline) topical foam"

2. The following equivalency statement in the carton label should be revised to:

   "Each gram of AMZEEQ contains 40 mg of minocycline equivalent to 43 mg of minocycline hydrochloride"

Primary Labeling Assessor Name and Date: Hailin (Sheena) Wang, Ph.D. 08/29/2019
This application is not deemed ready for approval in its present form per 21 CFR314.125(b)(6) until the labeling/labels deficiencies delineated in the **List of Deficiencies** above are resolved satisfactorily.

Secondary Assessor Name and Date (and Secondary Summary, as needed):

I agree with Dr. Wang's assessment on the labeling and labels and concur with her recommendation that this application is not ready for approval in its present form until the deficiencies delineated in the **List of Deficiencies** are satisfactorily resolved.

Moo-Jhong Rhee, Ph.D.
Chief, Branch V
DNDP II/ONDP

Sheena Hailin Wang

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Date: 9/10/2019 08:39:04AM
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Moo Jhong Rhee

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Date: 9/10/2019 08:49:49AM
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MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: September 26, 2019

TO: Review #1 of NDA 212379 Quality Assessment - Labeling

FROM: Hailin (Sheena) Wang, Ph.D.
Chemist, ONDP/DNDP II/OPQ

THROUGH Moo-Jhong Rhee, Ph.D.
Chief, Branch V
DNDP II/ONDP/OPQ

SUBJECT: **Final Recommendation on Labeling/Labels**

SUMMARY

The previous Quality Labeling Review #1 dated 09/10/2019, made a recommendation of not ready for approval of this NDA because of labeling deficiencies (see N212379 IQA Labeling R1). These labeling issues have been satisfactorily resolved based on the revisions made in SD 31 and SD 32.

RECOMMENDATION:
This application is now recommended for **Approval** from the Quality labeling/label perspective.

Assessment Notes

FDA labeling request along with additional labeling comments (including those identified by OND-labeling and CMC) were communicated to the applicant on 09/10/2019 and 09/19/2019. Subsequently, the following amendments were submitted and assessed.

List Submissions being reviewed:

Document Reviewed (eCTD #)	Date Received
eCTD-0031 (SD-31)	09/18/2019
eCTD-0032 (SD-32)	09/23/2019

Review of the applicant's IR response is provided below:

List of Deficiencies sent to the applicant on 09/10/2019:

1. The established name in the proposed product title, "AMZEEQ™ (minocycline (b) (4) Foam", is not acceptable. It should be revised to, "AMZEEQ™ (minocycline) topical foam"
2. The equivalency statement, "Each gram of AMZEEQ contains 40 mg of minocycline equivalent to 43 mg of minocycline hydrochloride" should be added in the "**Dosage and Strength**", "**Description**" as well as **How Supplied/Storage and Handling** sections.

Applicant response in SD 31 on 09/18/2019:

Foamix has updated all documents with the requested change in the established name and added the equivalency statement to the sections in the PI as requested.

Related information/revisions provided in SD 31

HIGHLIGHTS OF PRESCRIBING INFORMATION

AMZEEQ™ (minocycline) topical foam (b) (4)

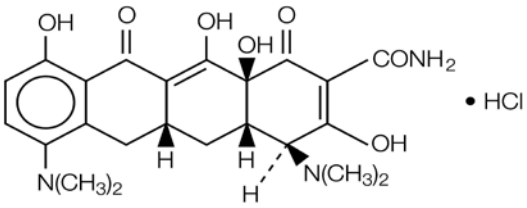
SECTION 3 (DOSAGE FORMS AND STRENGTHS)

Topical foam, 4%
Each gram of AMZEEQ contains minocycline 40 mg of minocycline equivalent to 43 mg of minocycline hydrochloride, and is supplied as a yellow suspension in a pressurized aluminum aerosol container (can).

SECTION 11 (DESCRIPTION)

Minocycline hydrochloride, a semi-synthetic derivative of tetracycline, is [4S-(4α,4aα,5aα,12aα)]-4,7-Bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-

tetrahydroxy-1,11-dioxo-2-naphthacenecarboxamide mono hydrochloride. The structural formula is represented below:



$C_{23}H_{27}N_3O_7$•HCl M. W. 493.94

Each gram of AMZEEQ contains micronized minocycline 40 mg equivalent to 43 mg minocycline hydrochloride in a yellow suspension foam.

In addition, the 4% AMZEEQ topical foam contains the following inactive ingredients: soybean oil, coconut oil, light mineral oil, cyclomethicone, cetostearyl alcohol, stearic acid, myristyl alcohol, hydrogenated castor oil, white wax (beeswax), stearyl alcohol, docosanol. AMZEEQ topical foam is dispensed from an aluminum container (can) pressurized with propellant (butane + isobutane + propane).

SECTION 16 (HOW SUPPLIED/STORAGE AND HANDLING)

How Supplied
AMZEEQ™ (minocycline) topical foam, 4% is a yellow suspension supplied in a pressurized aluminum aerosol container (can). Each gram of AMZEEQ contains 40 mg of minocycline equivalent to 43 mg of minocycline hydrochloride, and is supplied as follows:

NDC 72356-101-03 30 g Can

Reviewer's Assessment: Adequate

The applicant has revised the established name to include only the minocycline base per IR request. This is in line with USP salt policy.

As shown above, the equivalency statement (see yellow highlight) has been added to **"Dosage and Strength**", "**Description**" as well as **How Supplied/Storage and Handling** sections.

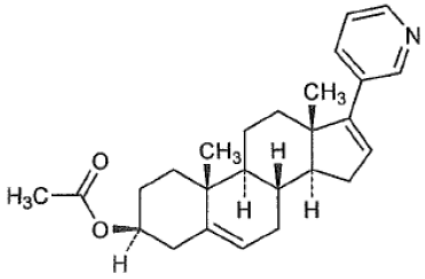
The applicant deleted the word "micronized" (b) (4) (b) (4) but kept it in Section 11 Description as recommended. Although there is no direct evidence to indicate micronized drug substance is required for product efficacy, "micronized" is a scientifically correct description of the drug substance characteristics. Laurie Buonaccorsi from OPDP confirmed that there are no concerns from a promotional perspective with using micronized as part of the description in

Section 11 if it is an accurate statement. This description appears in many other drug products, including recent approved examples: NDA 210308 and NDA 202236 (see excerpt below).

NDA 210308:

11 DESCRIPTION

Abiraterone acetate, the active ingredient of YONSA tablet is the acetyl ester of abiraterone. Abiraterone is an inhibitor of CYP17 (17α-hydroxylase/C17,20-lyase). Each YONSA Tablet contains 125 mg of abiraterone acetate. Abiraterone acetate is designated chemically as (3β)17-(3-pyridinyl) androsta-5,16-dien-3-yl acetate and its structure is:



Abiraterone acetate is micronized (smaller particle size) white to off-white, non-hygroscopic, crystalline powder. Its molecular formula is $C_{26}H_{33}NO_2$ and it has a molecular weight of 391.55. Abiraterone acetate is a lipophilic compound with an octanol-water partition coefficient of 5.12 (Log P) and is practically insoluble in water. The pKa of the aromatic nitrogen is 5.19.

Inactive ingredients in the tablets are lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, sodium lauryl sulfate, sodium stearyl fumarate, butylated hydroxyanisole, butylated hydroxytoluene.

NDA 202236:

Dymista (azelastine hydrochloride and fluticasone propionate) nasal spray, 137 mcg/50 mcg contains 0.1% solution of azelastine hydrochloride and 0.037% suspension of micronized fluticasone propionate in an isotonic aqueous suspension containing glycerin, microcrystalline cellulose and carboxymethylcellulose sodium, phenylethyl alcohol (2.5 mg/g), edetate disodium, benzalkonium chloride (0.1 mg/g), polysorbate 80, and purified water. It has a pH of approximately 6.0.

List of Deficiencies sent to the applicant on 09/19/2019:

A. Container and Carton Labels

1. The drug name, "AMZEEQ (minocycline (b) (4)) foam", in the labels should be revised to,
   "AMZEEQ™ (minocycline) topical foam"
2. The following equivalency statement in the carton label should be revised to:

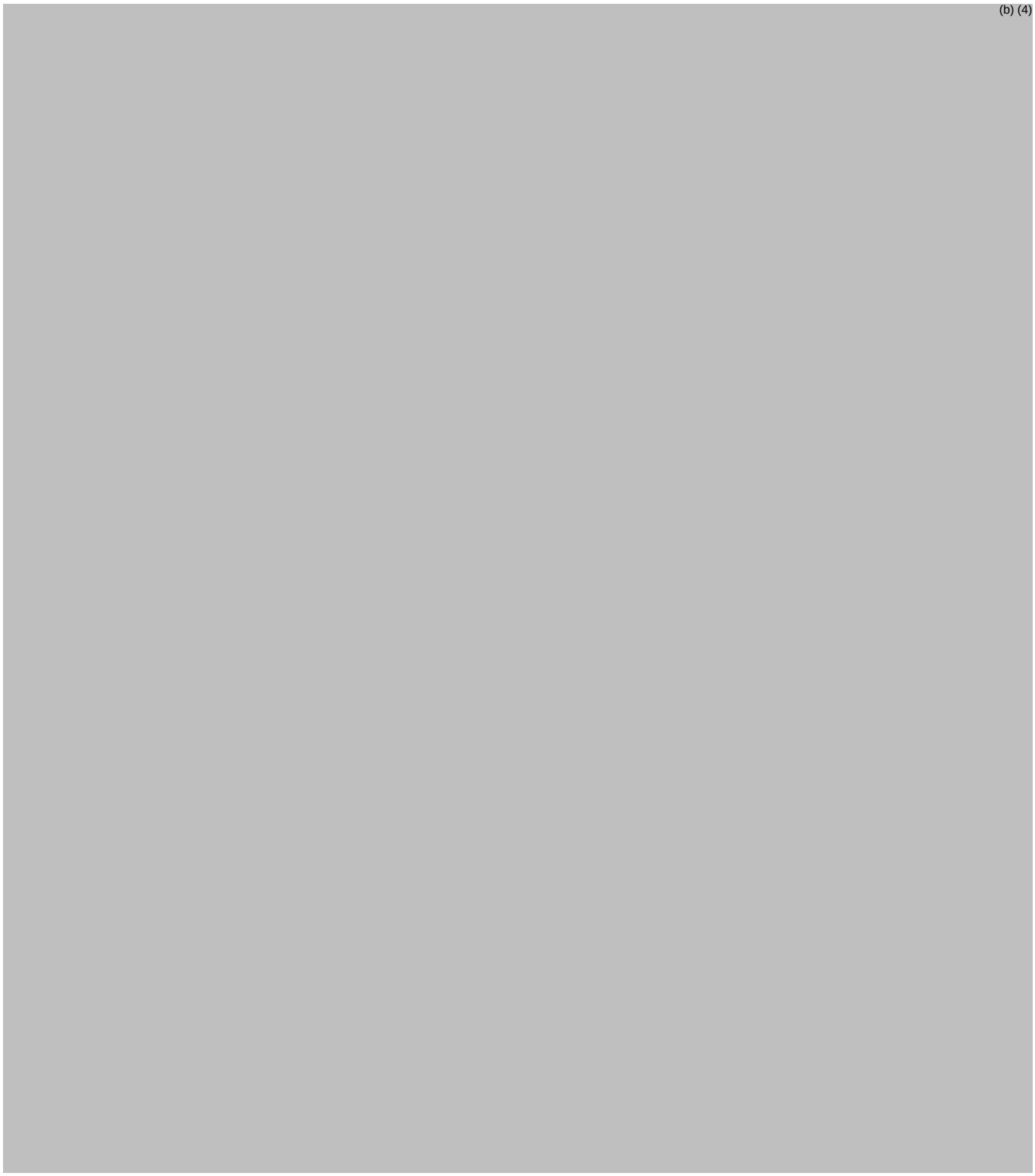
   "Each gram of AMZEEQ contains 40 mg of minocycline equivalent to 43 mg of minocycline hydrochloride"

Applicant response in SD 32 on 09/23/2019:

Foamix has made the requested revisions to the 30 g Trade Carton (72356-101-03-Trade Carton); the 7 g Physician Sample Carton and Sample Tray (72356-101-90-Sample Carton; and 72356-101-90-Sample Tray).

Related information/revisions provided in SD 31 and SD 32

CONTAINER LABEL



(b) (4)

Reviewer's Assessment: Adequate

As shown above, the applicant has revised the established name on the container label and revised the equivalency statement on the AMZEEQ 30 g Trade and 7 g Physician Sample Cartons in accordance with the change in the PI.

Sheena Hailin Wang

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Moo Jhong Rhee

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BIOPHARMACEUTICS

NDA: NDA 212379-ORIG-1

FMX101 4% is topical, aerosol foam product containing minocycline hydrochloride (HCl) as the active ingredient. The product is manufactured by producing a bulk pre-foam formulation (PFF or bulk PFF). The PFF is a (b) (4) non-aqueous, (b) (4) dispersion of minocycline HCl that is filled into canisters and pressurized with a propellant. FMX101 is supplied in aerosol canisters to deliver 7 g and 30 g of FMX101 4% foam.

Drug Product Name / Strength: Minocycline foam (FMX 101)/4%

Indication: Treatment of moderate to severe acne vulgaris

Route of Administration: Topical

Applicant Name: Foamix Pharmaceuticals Inc.

Review Recommendation: **ADEQUATE**

Review Summary:

In Vitro Release Test (IVRT) and Acceptance Criterion*:* ADEQUATE

The Applicant has developed and validated an IVRT method using a Franz diffusion cell apparatus. The following IVRT method and in vitro release acceptance criterion are approved:

Apparatus	Speed (RPMs)	Medium/Temperature	Volume (mL)	Recommended Acceptance criterion
Franz cell	600	DMSO:IPA (10:90 v/v) /32.0°C ± 0.5°C	12ml	(b) (4)

Bridging to the Proposed To-Be-Marketed Drug Product: ADEQUATE

All clinical Phase 3 studies, the pharmacokinetic (PK) study (FX2016-21) and Phase 1 safety studies used formulation MCH-330 (also known as FMX101 4% Foam), the final formulation for commercialization. However, per the Applicant commercial manufacture of the bulk PFF at the (b) (4) scale will be undertaken in the (b) (4) whereas all Phase 3 clinical studies formulation (330) were manufactured using (b) (4) at the (b) (4) scale. Comparative IVRT data submitted by the Applicant demonstrates sameness of the drug product manufactured using (b) (4) (pre-change) and (b) (4) (post change). In addition, there were some changes in manufacturing process between formulations used in Adult Max study and Pediatric Max study, which were determined by Process reviewer to be minor (Level (b) (4) changes). Hence, per the

principle outlined in SUPAC SS, bridging this manufacturing process change with IVRT data is not needed.

Biowaiver Request: Not requested
Only one strength is developed.

List of Submissions being reviewed:

Application 212379 - Sequence 0001 - 0001 (1) 12/20/2018 ORIG-1 /Multiple Categories/Subcategories

Application 212379 - Sequence 0006 - 0006 (6) 02/21/2019 ORIG-1 /Quality/Response To Information Request

Application 212379 - Sequence 0016 - 0016 (16) 06/03/2019 ORIG-1 /Quality/Response To Information Request

Application 212379 - Sequence 0021 - 0021 (21) 08/08/2019 ORIG-1 /Quality/Response To Information Request

Application 212379 - Sequence 0024 - 0024 (24) 08/19/2019 ORIG-1 /Quality/Response To Information Request

Highlight Key Outstanding Issues from Last Cycle: The Applicant was requested to revise in vitro release acceptance criterion.

Concise Description Outstanding Issues Remaining: None.

BCS Designation

Reviewer's Assessment: N/A

Solubility: N/A

Permeability: N/A

Dissolution: N/A

1. Composition of proposed drug product:
FMX101 4% Foam is a non-aqueous (b) (4) topical formulation which was chosen as minocycline hydrochloride is unstable in the presence of water. The micronized crystalline particles of minocycline HCl are dispersed and homogeneously distributed in the vehicle, with (b) (4) of the API dissolved in the supernatant of the formulation.

The quantitative composition of each component of FMX101 4% Foam is listed in Table 1.

Table 1: Minocycline foam (FMX 101) 4% formulation

Component	Quality Standard	Composition (%w/w)	Function
Minocycline HCl (micronized) [1]	USP	4.00	Active ingredient
Soybean Oil	USP	(b) (4)	
Coconut Oil	USP		
Light Mineral Oil [1]	NF		
Cyclomethicone (b) (4)	NF		
Cetostearyl Alcohol	NF		
Stearic Acid 50	NF		
Myristyl Alcohol	NF		
Hydrogenated Castor Oil	NF		
White Wax (Beeswax)	NF		
Stearyl Alcohol	NF		
Docosanol [2]	(b) (4)		
Total PFF		**100.00**	**Bulk PFF product**

(b) (4)

Abbreviations: #=number; CAS= Chemical Abstracts Service; HCl=hydrochloride; NF=National Formulary; PhEur=European Pharmacopeia; PFF=pre-foam formulation; USP=United States Pharmacopeia.

(b) (4)

(b) (4)

Membrane:	(b) (4)
Receptor medium:	DMSO: IPA (10:90 v/v)
Temperature (˚C):	32˚C±0.5˚C
Stirring speed:	600 rpm
Pre-soaking of membrane:	(b) (4)
Medium volume:	12 mL
Aliquot volume:	(b) (4)
Number of aliquots withdrawn:	
Sampling intervals:	

(b) (4)

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(b) (4)

nit r results during sta ilit

Reviewer's Assessment:

- The Applicant has developed and validated an IVRT method using a Franz diffusion cell apparatus. The Applicant has provided method development report. The IVRT method is acceptable.
- The proposed product is non-aqueous, (b) (4) dispersion of minocycline HCl. Particle size distribution was identified as one of the critical quality attributes. Minocycline particle size is controlled, and the Applicant has proposed following particle size specification to be tested at release and stability:

Particle size Number of particles in range	
(b) (4)	

The applicant provided in vitro release data obtained from batch manufactured with un-micronized particles. Based on this data, the in vitro release method has limited discriminating ability with respect to particle size. Particle size is controlled as described above. There are no additional concerns from biopharmaceutics perspective.

- The Applicant's in vitro release acceptance criterion was wide based on the submitted data. The Applicant accepted the following Agency recommended acceptance criterion:

(b) (4)

Phase 3 clinical batches

The Applicant was requested to provide drug product batch numbers used for each of the Phase 3 clinical studies in a tabular format and to identify each clinical study (See IR1.2 in Appendix 1). The following table was provided in response.

Batches used for Phase 3 clinical studies:

Drug product Batch No	Clinical Study No
6012101	FX2014-04 & FX2014-05
6012501	FX2014-04 & FX2014-05
6031601	FX2014-04 & FX2014-05
6040701	FX2014-04 & FX2014-05
6051201	FX2014-04 & FX2014-05
6080801	FX2014-04 & FX2014-05
6112201	FX2014-04 & FX2014-05
7011001	FX2014-04 & FX2014-05
7011901	FX2014-04 & FX2014-05
7032801	FX2014-04 & FX2014-05
7011201	FX2017-22
7011601	FX2017-22
7042601	FX2017-22

Bridging of formulations used in Phase 3 clinical studies and proposed commercial formulation

All clinical Phase 3 studies (FX2014-04, FX2014-05, and FX2017-22), the pharmacokinetic (PK) study (FX2016-21) and Phase 1 safety studies (FX2016-06, FX2016-07, FX2016-08 and FX2016-09) used formulation MCH-330 (also known as FMX101 4% Foam), the proposed final formulation for commercialization. The composition of MCH-330 is presented in Table 1.

Formulation MCH-244 (b) (4) was used in a Phase 2 clinical study (FX2010-03). The formulation was also used in an in-vitro skin delivery study to evaluate the degree of penetration and rate of permeation of these two strengths of foam formulation over 24 hours. It is the same formulation as FMX101 4% Foam (formulation MCH-330) except that it also contained (b) (4) (b) (4) Per the Applicant, formulation MCH-244 underwent changes in foam color from yellow (b) (4) in long-term stability study which was attributed to the presence of (b) (4) (b) (4)

Formulation MCH-330, the final formulation for commercialization, is identical to formulation MCH- 244A (4%), except for the (b) (4) (b) (4) This change in the ingredients is (b) (4)

(b) (4)

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(b) (4)

[redacted]

Primary Biopharmaceutics Reviewer Name and Date: Kalpana Paudel, Ph.D.

***Secondary Reviewer Name and Date (and Secondary Summary, as needed*:**

Kalpana Paudel

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Vidula Kolhatkar

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MICROBIOLOGY

(b) (4) (b) (4)

hydrocarbon propellant-driven aerosol
This drug product is indicated in the tr
drug product produces a smooth, stable, foam dispensed fro an
container that collapses when rubbed into skin.

NDA: 212-379

Drug Product Name / Strength: 4% Minocycline (b) (4) suspended as micronized minocycline hydrochloride foam in final drug product FMX101 4% (proprietary name: AMZEEQ). The same composition drug product is present in the 30 g patient-use aerosol canister and in the 7 g physician sample aerosol canister.

Route of Administration: Topical

Applicant Name: Foamix Pharmaceuticals, Inc.

Manufacturing Site:

MX 0 c n
semi-finished aerosol foam product for secondary packaging in the US,
a g in e t t s g ex i ie t e ea es in
ASM Aerosol-Service AG
(b) (4) h in,
(b) (4) Switzerland
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(b) (4)

elease of

Foamix Pharmaceuticals, Inc.
(b) (4)
Bridgewater, NJ 08807, USA
FEI: Establishment registration to be completed with NDA submission
(b) (4)

Method of Sterilization: nonsterile, non-aqueous drug product

Review Recommendation: Adequate

Review Summary: This drug product is a (b) (4) non-aqueous, nonsterile, (b) (4) hydrocarbon propellant-driven aerosol foam. The applicant has provided adequate information to support bulk drug hold times during manufacturing, routine release testing of the drug product, and stability testing of the drug product.

List Submissions Being Reviewed:

Submit	Received	Assigned to Reviewer
20 December 2018	20 December 2018	3 January 2019

Highlight Key Outstanding Issues from Last Cycle: NA

Remarks: NA

Concise Description Outstanding Issues Remaining: NA

Supporting Documents: NA

List Number of Comparability Protocols (ANDA only): NA

(b) (4)

(b) (4)

Description of drug product – The FMX101 drug product is a (b) (4) non-aqueous (b) (4) (b) (4) hydrocarbon propellant-driven aerosol foam containing 4% w/w minocycline in an aerosol canister. A smooth, stable, yellow foam is produced upon actuation from the aerosol canister, which collapses when rubbed onto the skin, delivering the minocycline. The product is to be provided in two configurations, a commercial package and a physician sample. The commercial package has a fill volume of (b) (4) and the physician sample has a fill volume of (b) (4)

Drug product composition – The composition of the drug product is provided in the table below from p. 5 of *Section 2.3.P Quality Overall Summary* of the applicant's submission.

Table 1: FMX101 4% Composition

Component	Quality Standard	Composition (%w/w)	Function
Minocycline HCl (micronized) [1]	USP	4.00	Active ingredient
Soybean Oil	USP	(b) (4)	
Coconut Oil	USP		
Light Mineral Oil [1]	NF		
Cyclomethicone (b) (4)	NF		
Cetostearyl Alcohol	NF		
Stearic Acid 50	NF		
Myristyl Alcohol	NF		
Hydrogenated Castor Oil	NF		
White Wax (Beeswax)	NF		
Stearyl Alcohol	NF		
Docosanol [2]	(b) (4)		
Total PFF		**100.00**	**Bulk PFF product**
(b) (4)			

Abbreviations: #=number; CAS= Chemical Abstracts Service; HCl=hydrochloride; NF=National Formulary; PhEur=European Pharmacopeia; PFF=pre-foam formulation; USP=United States Pharmacopeia.

(b) (4)

Description of container closure system – The drug product suspension is packaged in individual aluminum canisters with a valve/actuator assembly that is pressurized by the addition of a propellant. The FMX101 4% 30 g product (patient-use) is filled and crimped in a 35 x 88 mm aluminum canister while the FMX101 4% 7 g product is filled and crimped in a 35 x 65 mm aluminum canister. The canisters are supplied by

(b) (4)

The table below describes all components in contact with the foam product from p. 4 of *Section 3.2.P.2 Pharmaceutical Development, Att. 4*:

Component	Material
(b) (4)	

Reviewer's Assessment: ***Adequate***

The composition of the drug product and the container closure system were adequately described.

P.2 Pharmaceutical Development

P.2.5 Microbiological Attributes

(b) (4)

(b) (4)

[redacted]

Reviewer's Assessment: ***Adequate***

Comparability Protocols: NA

2. REVIEW OF COMMON TECHNICAL DOCUMENT – QUALITY (CTD-Q) MODULE 1

2.A. Package Insert: The 30 g canister of the drug product is stored at 2 – 8°C for up to 18 [redacted]nths until dispensed. The 7 g physician sample canister is stored at controlled room temperature [redacted] (b) (4) Following patient receipt, the drug product is to be stored at 25°C for up to 90 days.

Reviewer's Assessment: ***Adequate***
Storage conditions were listed on the drug product label.

Post-Approval Commitments: NA

List of Deficiencies: NA

Primary Microbiology Reviewer Name and Date: Julia Marré, PhD, Microbiologist, 4/16/2019

Secondary Reviewer Name and Date: Denise Miller, Sr. Microbiologist, 4/16/2019

Julia Marre

Digitally signed by Julia Marre
Date: 4/17/2019 08:50:39AM
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Denise Miller

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/s/

HAMID R SHAFIEI
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