

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

207071Orig1s000

CHEMISTRY REVIEW(S)

MEMORANDUM

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

DATE: July 23, 2015

TO: NDA 207071 CMC Review # 1

FROM: Hamid R. Shafiei, Ph.D., CMC Reviewer
(ONDP/Division II/Branch V)

THROUGH: Moo-Jhong Rhee, Ph.D., Branch Chief
(ONDP/Division II/Branch V)

SUBJECT: Final CMC Recommendation

In the Review # 1 of NDA 207071 Finacea (azelaic acid) Foam, 15% , this NDA was not recommended for approval from the CMC perspective due to the following reasons:

- 1) CMC related label/labeling issues were **not** resolved
- 2) An overall recommendation of "Acceptable" from the Office of Process and Facilities regarding the facilities involved in this NDA was **not** yet issued

The CMC label/labeling issues have been resolved via the amendments dated July 15, 16, and 22, 2015 (see the review notes in the **Attachment**).

The Office of Process and Facilities has also made an overall recommendation of "Acceptable" for the facilities involved in this NDA on July 23, 2015 (see the overall recommendation of "Acceptable" from the Office of Process and Facilities in Panorama).

Recommendation:

This NDA is now recommended for **approval** from the ONDP perspective with the product expiration dating period of 24 months.

Hamid
Shafiei -S
Hamid R. Shafiei, Ph.D.
CMC Reviewer, Branch V, Division II, ONDP

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ou=HHS, ou=FDA, ou=People,
cn=Hamid Shafiei -S,
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Moojhong Rhee -S
Moo-Jhong Rhee, Ph.D.
Branch Chief, Branch V, Division II, ONDP

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Attachment: Final Labeling/Labels

A. Package Insert:

1) Highlights:

FINACEA[®] (azelaic acid) Foam, 15% for topical use

Reviewer Evaluation: The product name has been appropriately (b) (4) to Finacea (azelaic acid) Foam, 15% as requested. **Adequate**

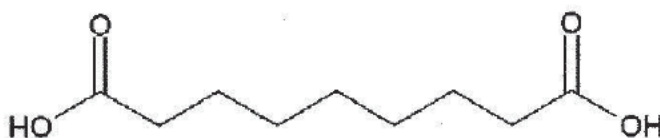
2) #3 Dosage Form and Strength:

Each gram of Finacea (azelaic acid) Foam contains 0.15 g of azelaic acid (15% w/w) in a white to off-white foam.

Reviewer Evaluation: The product name has been appropriately (b) (4) to Finacea (azelaic acid) Foam, 15% as requested. **Adequate**

3) #11 Description:

Finacea (azelaic acid) Foam contains 15% (w/w) azelaic acid, a naturally-occurring saturated dicarboxylic acid and is suspended in an oil-in-water emulsion vehicle for topical administration to affected skin area. Chemically, azelaic acid is 1,7-heptanedicarboxylic acid. The structural formula of azelaic acid is:



Azelaic acid has a molecular formula of C₉ H₁₆ O₄ and a molecular weight of 188.22.

The aluminum containers are filled with hydrophilic emulsion, crimped with a continuous spray valve, and pressurized with propellants consisting of propane, butane, and isobutane. Each gram of Finacea Foam contains 0.15 g of azelaic acid. Finacea Foam also contains benzoic acid, cetostearyl alcohol, dimethyl isosorbide, medium-chain triglycerides, methylcellulose, mono- and di-glycerides, polyoxyl 40 stearate, polysorbate 80, propylene glycol, purified water, sodium hydroxide, and xanthan gum as inactive ingredients.

Reviewer Evaluation: *As requested, the product name has been appropriately (b) (4) to Finacea (azelaic acid) Foam, 15% and the route of administration is provided. Pharmacological / therapeutic class is not specified. This reviewer has been informed by the clinical team that azelaic acid has never been assigned an official Pharmacological / therapeutic class and therefore, it is not required to be specified in the package insert for this product. Adequate*

4) #16 How Supplied:

Finacea (azelaic acid) Foam 15% is a white to off-white emulsion supplied in a pressurized 50 g (NDC 50419-825-05) aluminum can.

16.2 Storage and Handling

Store at 25°C (77°F); excursions permitted between 15–30°C (59–86°F) [See USP Controlled Room Temperature].

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 store at temperatures above 120°F (49°C).

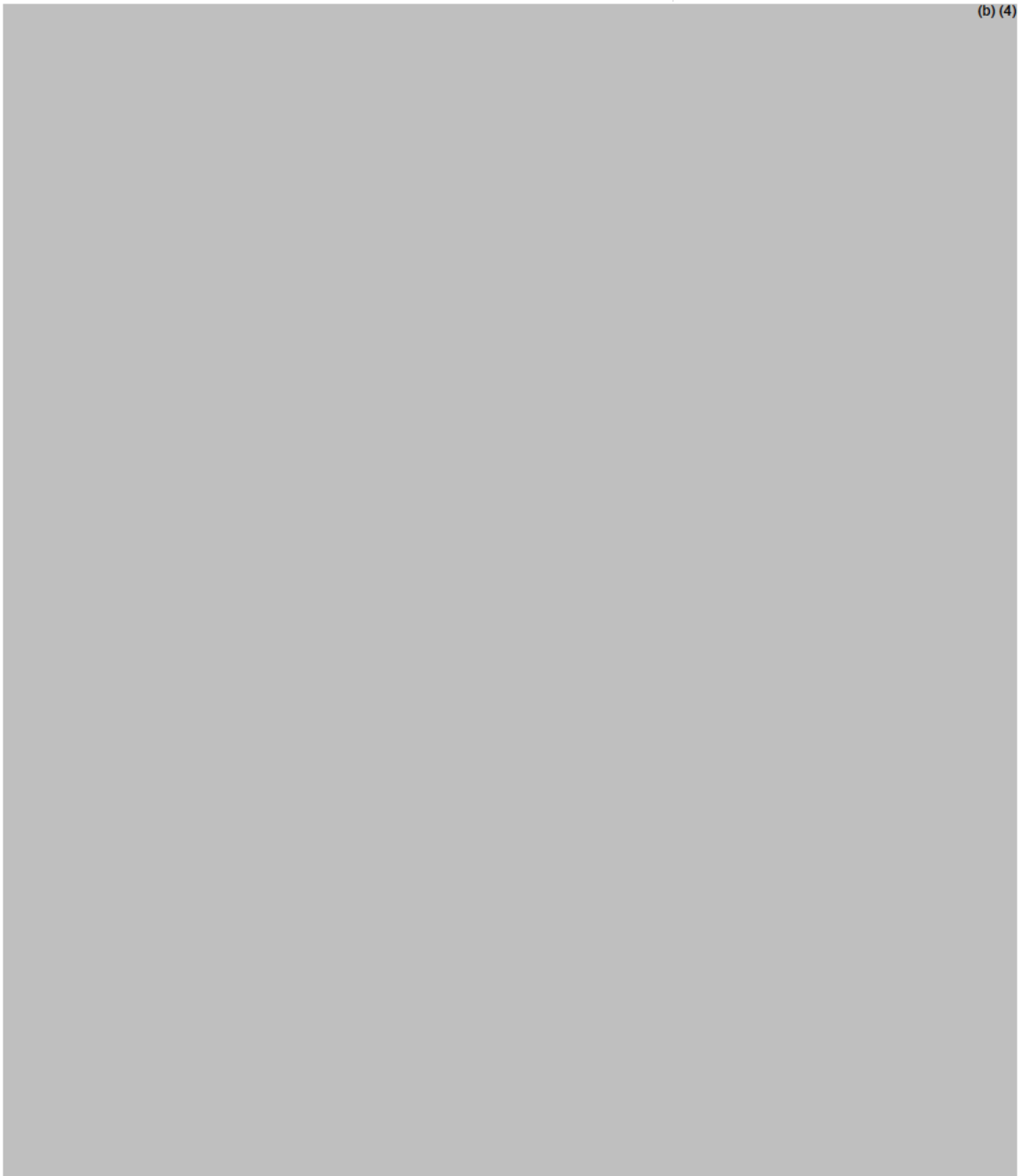
Reviewer Evaluation: *The product name has been appropriately (b) (4) to Finacea (azelaic acid) Foam, 15% as requested. Adequate*

B. Immediate Container Label:



Reviewer Evaluation: *As requested, the product name has been appropriately (b) (4) to Finacea (azelaic acid) Foam, 15%, and barcode, lot number, and expiration date are properly displayed. Adequate*

C. Carton Label:



Reviewer Evaluation: *As requested, the product name has been appropriately (b) (4) to Finacea (azelaic acid) Foam, 15%, and lot number and expiration date are properly displayed.*
Adequate



NDA 207071

Finacea (azelaic acid) Foam, 15%

Bayer HealthCare Pharmaceuticals Inc.

Hamid Shafiei, Ph.D.

Review Chemist

**Office of New Drug Products
Division II
Branch V**

**CMC REVIEW
For the Division of Dermatology and Dental Products**



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CMC Review Data Sheet

CMC Review Data Sheet

1. NDA 207071
2. REVIEW #: 1
3. REVIEW DATE: March, 31, 2015
4. REVIEWER: Hamid Shafiei, Ph.D.
5. PREVIOUS DOCUMENTS:
6. SUBMISSION(S) BEING REVIEWED:

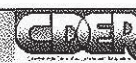
<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original Submission	09/30/2014
Correspondence (C)	
Amendment (BC)	11/03/2014
Amendment (BC)	10/31/2014
Amendment (BC)	11/10/2014
Amendment (BC)	12/19/2014

7. NAME & ADDRESS OF APPLICANT:

Name: Bayer HealthCare Pharmaceuticals, Inc.
Address: 100 Bayer Boulevard
P.O. Box 915
Whippany, New Jersey 07981-0915
Representative: Karen A Costa, M.S., Ph.D.;
Global Regulatory Affairs,
Specialty Medicine (Dermatology)
Telephone: (862) 404-3306

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Finacea
- b) Non-Proprietary Name: Azelaic Acid
- c) Code Name/# (ONDP only):
- d) Chem. Type/Submission Priority (ONDP only):
 - Chem. Type: 3



CMC Review Data Sheet

- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

10. PHARMACOL. CATEGORY: Treatment of papulopustular rosacea

11. DOSAGE FORM: Foam

12. STRENGTH/POTENCY: 15%

13. ROUTE OF ADMINISTRATION: Topical

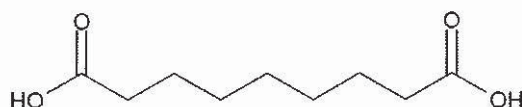
14. Rx/OTC DISPENSED: ☒ Rx ☐ OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

☐ SPOTS product – Form Completed

☒ Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



Azelaic Acid

Empirical Formula:

C₉H₁₆O₄

Molecular Mass:

188.22

CAS Number:

123-99-9

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
9289	II	Bayer Pharma AG	Drug Substance	1	Adequate	01/30/2015	Reviewed by Dr. Joel Hathaway



CMC Review Data Sheet

(b) (4)	II	(b) (4)	1	Adequate	02/02/2015	Reviewed by Dr. Joel Hathaway
	III		4			
	III		4			

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND		
NDA		



CMC Review Data Sheet

18. STATUS:

ONDP:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A		
EES	Pending		
Pharm/Tox	Approval	05/06/2015	Jianyong Wang, PhD
Biopharm			
LNC			
Methods Validation	N/A		
DMETS			
EA	Categorical exclusion is requested (see review)		
Microbiology	Adequate	04/02/2015	Jessica Cole, PhD



Executive Summary Section

The CMC Review for NDA 207071

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The applicant of this NDA has provided sufficient information to assure the identity, strength, purity, and quality of the drug product, Finacea (azelaic acid) Foam, 15%.

However, the Office of Compliance has **not** made an overall "Acceptable" recommendation regarding the facilities involved in this NDA.

Also label/labeling issues identified have **not** been satisfactorily resolved.

Therefore, from the ONDP perspective, this NDA is **not** ready for approval in its present form, per 21 CFR 314.125(b)(6) & (13).

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

II. Summary of CMC Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

(1) Drug Substance

Azelaic acid belongs to a class of medication called dicarboxylic acids. This API is used to treat mild to moderate acne both comedonal acne and inflammatory acne. It works by killing the bacteria that infect the skin pores. It is also used as topical gel in the treatment of rosacea because of its ability to reduce inflammation. Azelaic acid is a naturally-occurring saturated dicarboxylic acid which is found in wheat, rye, and barley and has been used as an ingredient in number of hair and skin conditioners. Azelaic acid is the active ingredient in number of brand name products such as Azepur 99, Azaclear, Azclear Action, Azelex, White Action Cream, Finevin, Melazepam, Skinoren, and Ezanic. It is also the active ingredient of the drug product, Finacea (azelaic acid) Gel, 15% approved under NDA 21470 on December 24, 2002 for the topical treatment of inflammatory papules and pustules of mild to moderate rosacea. Finacea (azelaic acid) Gel, 15% is currently marketed by the applicant of this NDA application.

Executive Summary Section

Azelaic acid is a white, odorless (b) (4). It is poorly soluble in water at 20°C (0.24%) but freely soluble in boiling water and in ethanol. This drug substance is commercially produced by the (b) (4). The full description of manufacturing process, process controls, in-process testing, packaging, and release and stability testing for the azelaic acid manufactured by Bayer Pharma AG as the active ingredient for Finacea (azelaic acid) Foam, 15% is provided in DMF 9289 and DMF (b) (4). Both DMFs have been reviewed and found to be adequate to support this NDA application.

The drug substance release specification for azelaic acid includes testing and acceptance criteria for appearance, identity, melting range, clarity of solution, color of solution, assay, related substances, (b) (4) heavy metals, water content, residual solvents (b) (4) particle size, and polymorphism. The proposed API specification is satisfactory.

In summary, azelaic acid manufactured by Bayer Pharma AG is considered adequate for use as the active ingredient in the drug product, Finacea (azelaic acid) Foam, 15%.

(2) Drug Product

Finacea (azelaic acid) Foam, 15%, for topical administration is a new hydrophilic foam formulation containing 15% w/w (b) (4) azelaic acid in an oil-in-water emulsion that is filled in an aluminum can with spray valve and cap and pressurized using a propellant for foam delivery. This drug product is intended for the treatment of inflammatory papules and pustules of mild to moderate rosacea.

This drug product is a pressurized oil-in-water emulsion that appears as a white to off-white foam upon actuation. The collapsed foam also appears as a white to off-white soft mass. The emulsion contains 15% w/w azelaic acid as the active ingredient and benzoic acid, USP/NF (b) (4) cetostearyl alcohol, USP/NF (b) (4), Dimethyl isosorbide (b) (4), medium-chain triglycerides, USP/NF (b) (4), methylcellulose, USP/NF (b) (4), mono- and di-glycerides, USP/NF (b) (4), (b) (4) polyoxyl 40 stearate, USP/NF (b) (4), polysorbate 80, USP/NF (b) (4), propylene glycol, USP/NF (b) (4), (b) (4), xanthan gum, USP/NF (b) (4), sodium hydroxide, USP/NF (b) (4), and purified water, USP/NF (b) (4) as the excipients. (b) (4)

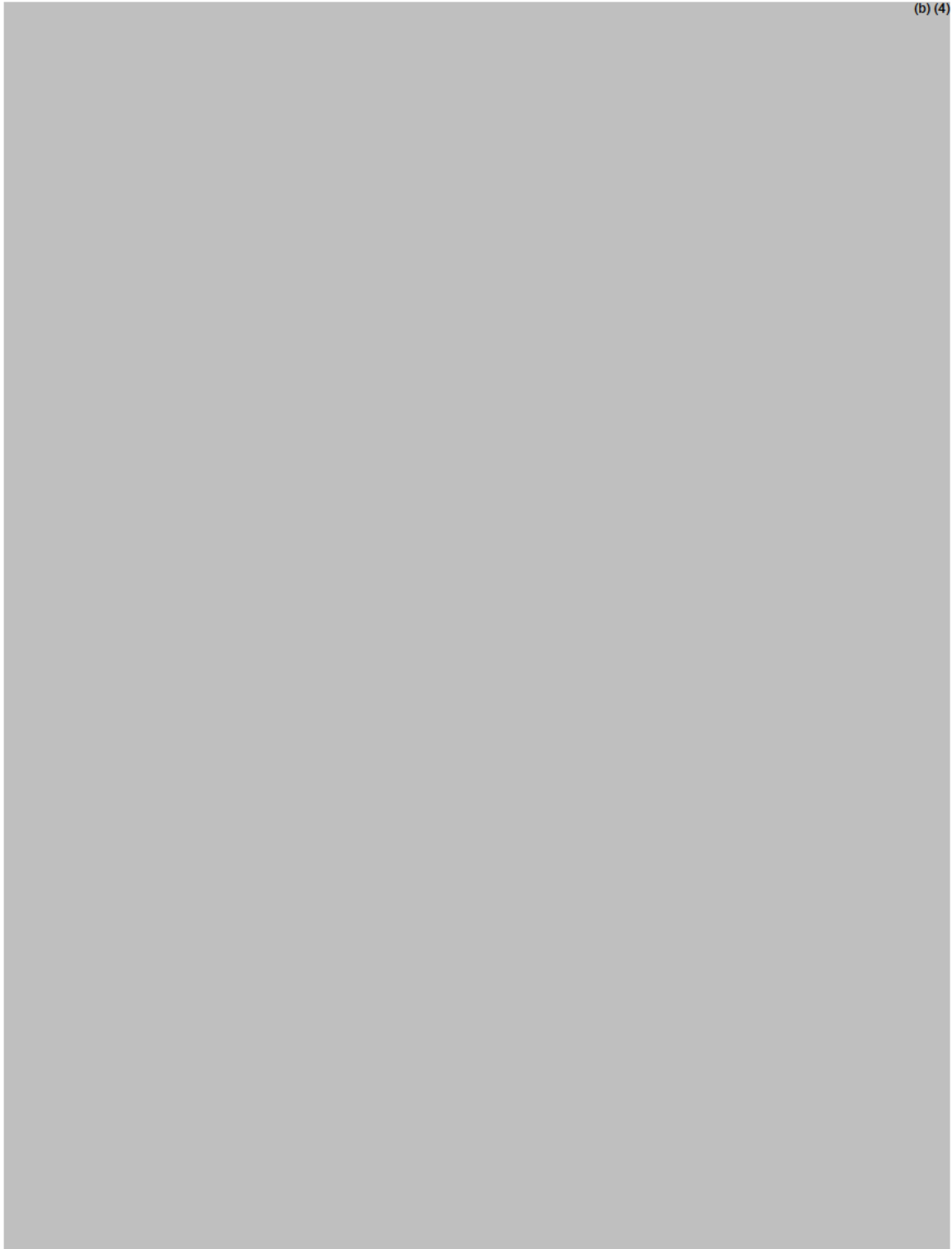
(b) (4) The excipients used in the manufacture of Finacea (azelaic acid) Foam, 15% are all compendial with the exception of dimethyl isosorbide. However, dimethyl isosorbide is tested and



Executive Summary Section

accepted according to compendial requirements. Therefore, the proposed drug product formulation/composition is satisfactory.

(b) (4)



Executive Summary Section

This application includes 36-month long-term and intermediate stability results from one batch and 24-month long-term and intermediate stability results from two additional batches of drug product manufactured at intended commercial scales and packaged in both 30g spray can for physician sample and 50g spray can planned for marketing. This application also includes currently available stability results from the on-going stability studies of 4 additional batches drug product manufactured at (b) (4). All long-term, intermediate, and accelerated stability results to-date meet the drug product stability specification. Based on long-term and intermediate stability results showing no significant trends or changes in the drug product quality attributes, the applicant has proposed an expiration dating period of (b) (4) months for the drug product. The proposed (b) (4) month expiration dating period for the drug product is adequately supported by stability data and therefore, is granted. The applicant has also expressed that the results from the intermediate stability studies demonstrate that the drug product will maintain its proposed shelf-life even when stored in (b) (4) but has not requested any flexibility in the labeling of the drug product storage condition. The proposed storage condition prescribed in the package insert and carton label is "store at 25°C (77°F); excursions permitted between 15-30°C (59-86°F)". This drug product is to be commercialized as pressurized canister and for safety precaution, the applicant has included the statement "Do not store above 120 °F (49 °C)" in the package insert and on the carton label. The proposed storage conditions and cautions provided in the package insert and on the carton label are appropriate.

The applicant has committed to continue and complete the stability testing of all seven commercial scales batches of the drug product for 36 months under the long-term and intermediate conditions and for 6 months under accelerated conditions.

In conclusion, the applicant of this NDA has provided sufficient information to assure the identity, strength, purity, and quality of the drug product.

B. Description of How the Drug Product is Intended to be Used

Finacea (azelaic acid) Foam, 15% is an oil-in-water emulsion that is filled into an aluminum can with spray valve and cap and is pressurized with propellant to allow for foam delivery. This drug product is intended for topical administration to affected skin for the treatment of inflammatory papules and pustules of mild to moderate rosacea.

C. Basis for Approvability or Not-Approval Recommendation

21 CFR 314.125 (b)(13)

- The final recommendation from the Office of Compliance is still "Pending".



Executive Summary Section

21 CFR 314.125 (b)(6)

- Label/labeling issues have not been resolved.

(see the **List of Deficiencies** on p.68)

III. Administrative

A. Reviewer's Signature:

Hamid
Shafiei -S

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ou=FDA, ou=People, cn=Hamid Shafiei -
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Hamid Shafiei, Ph.D.

B. Endorsement Block:

Moojhong Rhee -S

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ou=People, cn=Moojhong Rhee -S,
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Date: 2015.05.29 11:23:40 -04'00'

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

CMC Assessment Section

CMC Assessment**I. Review Of Common Technical Document-Quality (Ctd-Q) Module 3.2:
Body Of Data****S DRUG SUBSTANCE**

The information on the drug substance, unless otherwise stated, is cross referenced to DMF 9289 and DMF (b) (4). DMF 9289 was reviewed last by CMC Reviewer Lorenzo A. Rocca on 12/08/2006 and was found to be adequate. All annual reports and quality amendments submitted after 12/08/2006 has been reviewed by Dr. Joel Hathaway on 01/30/2015 and found to be still adequate. DMF (b) (4) (this DMF provides information regarding the (b) (4) was submitted on 06/24/2014. DMF (b) (4) has also been reviewed by Dr. Joel Hathaway on 02/02/2015 and found to be adequate.

S.1 General Information***S.1.1 Nomenclature***

Azelaic acid: 1,7-Heptanedicarboxylic acid

S.1.2 Structure

Azelaic Acid

Empirical Formula: $C_9H_{16}O_4$

Molecular Mass: 188.22

CAS Number: 123-99-9

S 1.3 General Properties

This drug substance is a white (b) (4) with UV absorption maximum (b) (4)

CMC Assessment Section

II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1

A. Labeling & Package Insert

1. Package Insert

(a) "Highlights" Section

Item	Comments on Information Provided in NDA
Drug name (201.57(a)(2))	
Proprietary name and established name	Finacea (azelaic acid) Unsatisfactory
Dosage form, route of administration	Foam, 15% for topical use Satisfactory
Controlled drug substance symbol (if applicable)	N/A
Dosage Forms and Strengths (201.57(a)(8))	
	Foam, 15% Satisfactory
Whether the drug product is scored	N/A

- The product name appears as (b) (4)
The product name should be revised to Finacea (azelaic acid) Foam, 15%.

(b) "Full Prescribing Information" Section

3: Dosage Forms and Strengths

Each gram of Finacea (b) (4) (azelaic acid) Foam, (b) (4) contains 0.15 g of azelaic acid (15% w/w) in a white to off-white foam.

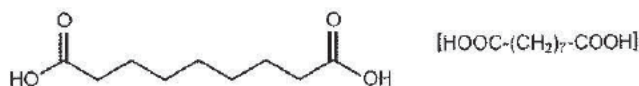
Item	Comments on Information Provided in NDA
Available dosage forms	Foam Satisfactory*
Active moiety expression of strength with equivalence statement (if applicable)	Azelaic acid 15% w/w Satisfactory
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting, when applicable.	A white to off-white foam Satisfactory

- The product name appears as (b) (4)
The product name should be revised to Finacea (azelaic acid) Foam, 15%.

CMC Assessment Section

#11: Description

Finacea Foam (azelaic acid) Foam, (b) (4) contains 15% (w/w) azelaic acid, a naturally-occurring saturated dicarboxylic acid suspended in an oil-in-water (O/W) emulsion vehicle. The hydrophilic emulsion is filled into aluminum containers, crimped with a continuous spray valve, and pressurized with a (b) (4) propellants consisting of propane, butane, and isobutane. Chemically, azelaic acid is 1,7-heptanedicarboxylic acid. The structural formula of azelaic acid is:



Azelaic acid has a molecular formula of $\text{C}_9\text{H}_{16}\text{O}_4$ and a molecular weight of 188.22. Each gram of Finacea Foam contains 0.15 g of azelaic acid. Finacea Foam also contains benzoic acid, cetostearyl alcohol, dimethyl isosorbide, medium-chain triglycerides, methylcellulose, mono- and di-glycerides, polyoxyl 40 stearate, polysorbate 80, propylene glycol, purified water, sodium hydroxide, and xanthan gum as inactive ingredients.

Item	Comments on Information Provided in NDA
Proprietary name and established name	Finacea (b) (4) (azelaic acid) Foam Unsatisfactory
Dosage form and route of administration	Foam, Route of administration is not specified. Unsatisfactory
Active moiety expression of strength with equivalence statement (if applicable)	Finacea (b) (4) (azelaic acid) Foam, (b) (4) contains 15% (w/w) azelaic acid Satisfactory*
Inactive ingredient information (quantitative, if injectables 21CFR201.100(b)(5)(iii)), listed by USP/NF names (if any) in alphabetical order (USP <1091>)	All inactive ingredients are listed. Satisfactory
Statement of being sterile (if applicable)	N/A
Pharmacological/ therapeutic class	Not Specified Unsatisfactory
Chemical name, structural formula, molecular weight	Chemical name: Azelaic acid: 1,7-heptanedicarboxylic acid Molecular formula: $\text{C}_9\text{H}_{16}\text{O}_4$ Molecular weight: 188.22 Molecular structure:  Satisfactory
If radioactive, statement of important nuclear characteristics.	N/A
Other important chemical or physical properties (such as pKa or pH)	None Satisfactory

CMC Assessment Section

- The product name appears as (b) (4)
The product name should be revised to Finacea (azelaic acid) Foam, 15%.
- Specify the Route of administration.
- Specify pharmacological/ therapeutic class.

#16: How Supplied/Storage and Handling

16.1 How Supplied

Finacea (b) (4) (azelaic acid) Foam, 15% is a white to off-white emulsion supplied in a pressurized 50 g (NDC 50419-825-05) aluminum can.

16.2 Storage and Handling

Store at 25°C (77°F); excursions permitted between 15-30°C (59-86°F) [See USP Controlled Room Temperature].

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 store at temperatures above 120°F (49°C).

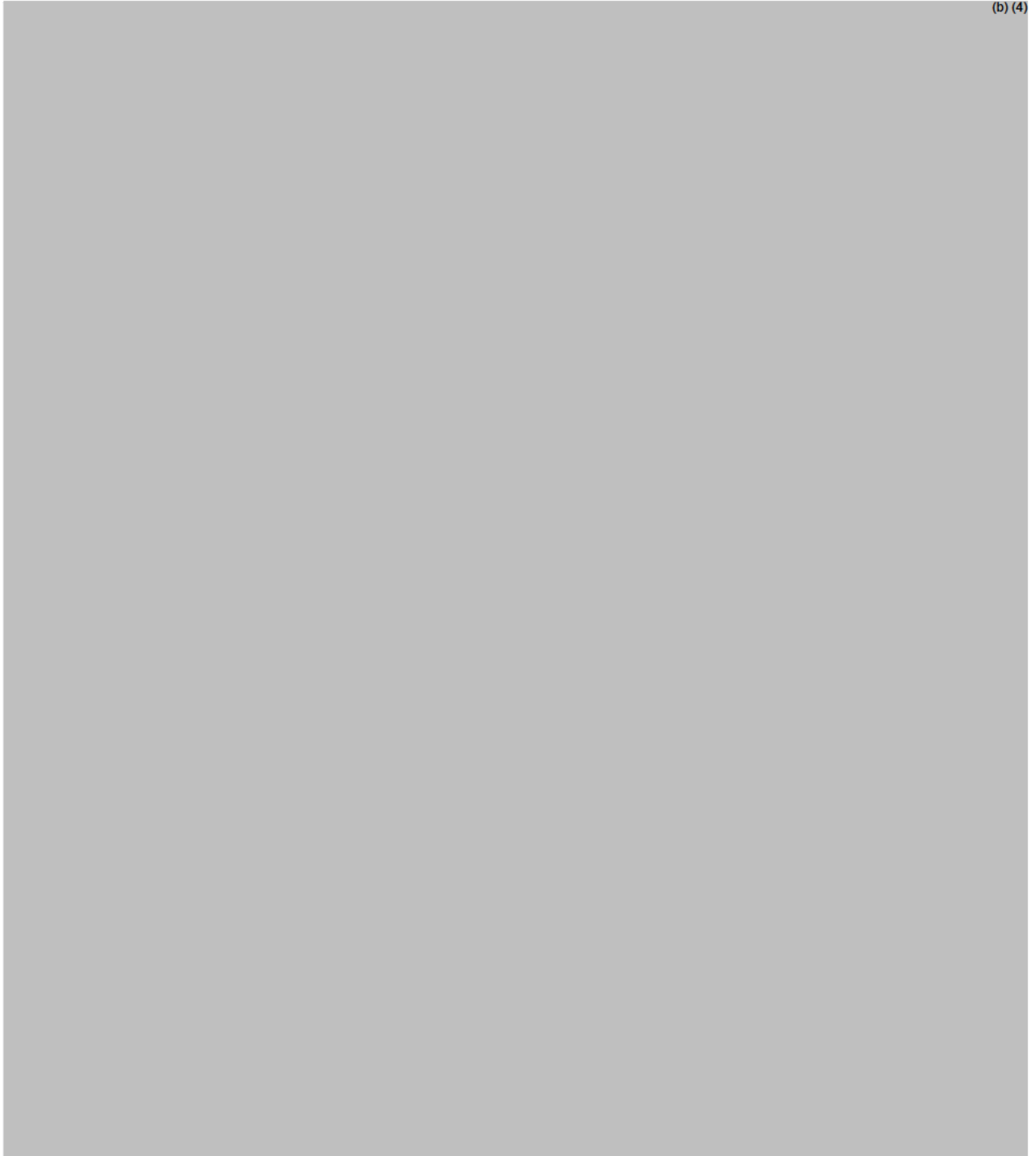
Keep out of reach of children.

Shake well before use.

Item	Information Provided in NDA
Strength of dosage form	Foam, 15% Unsatisfactory
Available units (e.g., bottles of 100 tablets)	50g aluminum can Satisfactory
Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number	a white to off-white emulsion supplied in a pressurized 50 g (NDC 50419-825-05) aluminum can Satisfactory
Special handling (e.g., protect from light)	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 store at temperatures above 120°F (49°C). Keep out of reach of children. Shake well before use. Satisfactory
Storage conditions	Store at 25°C (77°F); excursions permitted between 15-30°C (59-86°F) Satisfactory
Manufacturer/distributor name (21 CFR 201.1(h)(5))	Provided at the end of the package insert. Satisfactory

CMC Assessment Section

- The product name appears as [REDACTED] (b) (4)
The product name should be revised to Finacea (azelaic acid) Foam, 15%.

2. Immediate container labels

CMC Assessment Section

B. Environmental Assessment Or Claim Of Categorical Exclusion

The applicant has requested categorical exclusion from providing environmental assessment for Finacea (azelaic acid) Foam, 15% according to 21 CFR 25.31 (b). The applicant has estimated that the amount of active moiety produced in the fifth year after launch of the of drug product, Finacea Foam to be (b) (4). Based on the estimated amount of active moiety, the expected introduction concentration (EIC) in the aquatic environment is calculated to be (b) (4) which is below 1.0ppb. Therefore, the categorical exclusion from the environmental assessment is granted.

III. List Of Deficiencies to be Communicated

The following labels/labeling issues should be resolved:

1) Package insert:**“Highlights” Section:**

- The product name appears as (b) (4). The product name should be revised to Finacea (azelaic acid) Foam, 15%.

“Dosage Forms and Strengths” Section:

- The product name appears as (b) (4). The product name should be revised to Finacea (azelaic acid) Foam, 15%.

“Description” Section:

- The product name appears as (b) (4). The product name should be revised to Finacea (azelaic acid) Foam, 15%.
- Specify the Route of administration.
- Specify pharmacological/ therapeutic class.

“How Supplied/Storage and Handling” Section:

- The product name appears as (b) (4). The product name should be revised to Finacea (azelaic acid) Foam, 15%.

2) Immediate container label:

CMC Assessment Section

**IV. Attachments**

EES Reports

Initial Manufacturing (CGMP/Facilities) Assessment (IMA) and Filing Review for Pre- Marketing Applications (Original)

- I. Review Cover Sheet
- II. Application Detail
- III. Filing Checklist
- IV. Manufacturing Summary
- V. Overall Conclusions and Recommendations

I. Review Cover Sheet

1. OMPQ Reviewer: Christina Capacci-Daniel, PhD
2. NDA/BLA Number: NDA 207071
Submission Date: September 30, 2014
21st C. Review Goal Date: May 30, 2015
PDUFA Goal Date: July 30, 2015

3. PRODUCT PROPERTIES:

Trade or Proprietary Name:	Finacea Foam
Established or Non-Proprietary Name (USAN) and strength:	Azelaic Acid
Dosage Form:	Topical Foam, 15%

4. SUBMISSION PROPERTIES:

Review Priority :	Standard
Applicant Name:	Bayer HealthCare Pharmaceuticals Inc.
Responsible Organization (OND Division):	DDDP

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For Pre-Marking Applications

II. Application Detail

1. INDICATION: Topical treatment of (b) (4) rosacea
2. ROUTE OF ADMINISTRATION: Topical
3. STRENGTH/POTENCY: Foam, 15%
4. Rx/OTC DISPENSED: ☒Rx ☐OTC
5. ELECTRONIC SUBMISSION (yes/no)? YES
6. PRIORITY CONSIDERATIONS:

	Parameter	Yes	No	Unk	Comment
1.	NME / PDUFA V		☒		
2.	Breakthrough Therapy Designation		☒		
3.	Orphan Drug Designation		☒		
4.	Unapproved New Drug		☒		
5.	Medically Necessary Determination		☒		
6.	Potential Shortage Issues [either alleviating or non-approval may cause a shortage]		☒		
7.	Rolling Submission		☒		
8.	Drug/device combination product with consult		☒		
9.	Complex manufacturing		☒		
10.	Other (e.g., expedited for an unlisted reason)		☒		

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III. FILING CHECKLIST

The following parameters are necessary in order to initiate a full review (i.e., the application is complete enough to start review but may have deficiencies). On **initial** review of the NDA application:

A. COMPLETENESS OF FACILITY INFORMATION				
	Parameter	Yes	No	Comment
11.	Is all site information complete (e.g., contact information, responsibilities, address)?	☒		356h
12.	Do all sites indicate they are ready to be inspected (on 356h)?	☒		
13.	Is a single comprehensive list of all involved facilities available in one location in the application?	☒		356h
14.	For testing labs, is complete information provided regarding which specific test is performed at each facility and what stage of manufacturing?	☒		Assays at testing facilities have been identified (polymorphism, particle size determination, DP pressure and leakage rate)
15.	Additional notes (non-filing issue) 1. Are all sites registered or have FEI #?	☒		
	2. Do comments in EES indicate a request to participate on inspection(s)?	☒		All facilities have been initially processed by OPF in Inspection Management. OMPQ would like to participate in the DP inspection.
	3. Is this first application by the applicant?		☒	

*If any information regarding the facilities is missing/omitted, communicate to OPS/ONDQA regarding missing information and copy EESQuestions. Notify OMPQ management if problems are not resolved within 3 days and it can be a *potential* filing issue.

OMPQ Initial Manufacturing (CGMP/Facilities) Assessment and Filing Review
For Pre-Marking Applications

B. DRUG SUBSTANCE (DS) / DRUG PRODUCT (DP)				
	Parameter	Yes	No	Comment
16.	Have any Comparability Protocols been requested?		☒	

IMA CONCLUSION				
	Parameter	Yes	No	Comment
17.	Does this application fit one of the EES Product Specific Categories?	☒		First FDA Evaluation: • (b) (4) •
18.	Have EERs been cross referenced against the 356h and product specific profile for accuracy and completion? Have all EERs been updated with final PAI recommendation?		☒	All facilities have been processed through the OPF D/R stage of IMS.
19.	From a CGMP/facilities perspective, is the application fileable? If the NDA is not fileable from a product quality perspective, state the reasons and provide filing comments to be sent to the Applicant.	☒		

IV. Manufacturing Summary: Critical Issues and Complexities

Does the submission contain any of the following elements?			
Nanotechnology ☐	RTRT Proposal ☐	PAT ☐	Drug/Device Combo ☐
PET ☐	Design Space ☐	Continuous Mfg ☐	Naturally derived API ☐
Other (explain):		☒ Not Applicable	

Manufacturing Highlights

1. Drug Substance

	Parameter	Yes	No	Comment
	Is manufacturing process considered complex (e.g., unusual unit operations, innovative manufacturing technology, unusual control strategy)?		☒	DMF 9289 (API) & DMF (b) (4)

(b) (4)

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OMPQ Initial Manufacturing (CGMP/Facilities) Assessment and Filing Review
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(b) (4)

3. Facility-Related Risks (e.g., expected in-process testing not being performed, questionable development, unexplained stability failures, data integrity issues, etc.). Describe any potential 21CFR 211 compliance issues.

- There are no outstanding facility related risks.

4. Drug Product Facility Inspectional History that could impact the manufacturing of this product

- The Drug Product Facility has never been inspected by the FDA.

Additional information not covered above

- N/A

OMPQ Initial Manufacturing (CGMP/Facilities) Assessment and Filing Review
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Manufacturing Facilities Chart (created 11/4/2014):

Establishment Name	FEI Num	District Short	Country Code	Responsibilities	Profile Code	Inspection History, Dates, Classifications	Most Recent Milestone	Comment
Bayer Pharma AG	3003229486	EEU	DEU	API Testing (polymorphism)	(b) (4)	12/6/2012 NAI (b) (4)	(b) (4) Acceptable Based on Profile	Acceptable based on inspectional history
Bayer Pharma AG	3002808063	EEU	DEU	API (b) (4) (b) (4) particle size determination		3/27/2014 NAI (b) (4)	(b) (4) Acceptable Based on Profile	Acceptable based on inspectional history
Bayer Pharma AG	3002808084	EEU	DEU	API manufacturing, release testing		5/24/2013 VAI (b) (4)	(b) (4) Acceptable Based on Profile	Acceptable based on inspectional history

(b) (4)

OMPQ Initial Manufacturing (CGMP/Facilities) Assessment and Filing Review
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V. Overall Conclusions and Recommendations

Is the application fileable? (yes/no, Yes to questions 11-12) YES
Based on Section IV, is a KTM warranted for any PAI? (yes/no). If yes, please identify the sites in the above chart. • A KTM and/or Pre-Inspection Briefing will be done for (b) (4) operations, process parameters, stability data, and the process validations studies.
Are there comments/issues to be included in the 74 day letter, including appropriate identification of facilities? (yes/no) NO
Comments for 74 Day Letter
1.
2.
3.

REVIEW AND APPROVAL (DARRTS)

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

/s/

CHRISTINA A CAPACCI-DANIEL
11/24/2014

MAHESH R RAMANADHAM
11/24/2014