CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

213691Orig1s000

OTHER REVIEW(S)

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)

Date of This Memorandum:	May 13, 2020
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	NDA 213691
Product Name and Strength:	Impeklo (clobetasol propionate) lotion, 0.05%
Applicant/Sponsor Name:	Single Ingredient Product
OSE RCM #:	2019-1574-1
DMEPA Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA Team Leader:	Sevan Kolejian, PharmD, MBA

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels and carton labeling received on May 12, 2020 for Impeklo. Division of Dermatology and Dentistry (DDD) requested that we review the revised container labels and carton labeling for Impeklo (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.[a]

2 CONCLUSION

The Applicant implemented all of our recommendations and we have no additional recommendations at this time.

[a] Patel M. Label and Labeling Review for clobetasol propionate (NDA 213691). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 FEB 21. RCM No.: 2019-1574.

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MADHURI R PATEL
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SEVAN H KOLEJIAN
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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 23, 2020
To:	Strother Dixon Regulatory Project Manager **Division of Dermatology and Dentistry (DDD)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Barbara Fuller, RN, MSN, CWOCN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Susan Redwood, MPH, BSN, RN Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Laurie Bounaccorsi, 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 (clobetasol propionate) lotion
Dosage Form and Route:	for topical use
Application Type/Number:	NDA 213691
Applicant:	Mylan Pharmaceuticals Inc.

1 INTRODUCTION

On July 19, 2019, Mylan Pharmaceuticals Inc., submitted for the Agency's review an original 505(b)(2) New Drug Application (NDA) 213691 for TRADENAME (clobetasol propionate) lotion, for topical use. This NDA for Clobetasol Propionate lotion refers to the listed drug, CLOBEX® (clobetasol propionate) lotion, 0.05% NDA 021535, held by Galderma Laboratories L.P, that is listed in the current edition of orange book. The indication for the proposed clobetasol propionate lotion, 0.05% is the same as the listed drug (for relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses only in patients 18 years of age or older). The proposed new drug product has the same composition as the listed drug, differing only in the planned container closure system of the product.

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 Dentristry (DDD) on August 16, 2019, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) and Instructions for Use (IFU) for TRADENAME (clobetasol propionate) lotion, for topical use.

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 (clobetasol propionate) lotion PPI and IFU received on July 19, 2019, revised by the Review Division throughout the review cycle, and received by DMPP on March 12, 2020.
- Draft TRADENAME (clobetasol propionate) lotion Prescribing Information (PI) received on July 19, 2019, revised by the Review Division throughout the review cycle, and received by OPDP on March 12, 2020.
- Approved CLOBEX (clobetasol propionate) Lotion, 0.05%, for topical use NDA 021535 labeling dated November 30, 2012.

3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8th 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 it is 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 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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LASHAWN M GRIFFITHS
03/23/2020 10:25:56 AM

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

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

Memorandum

Date: March 19, 2020

To: Amy Woitach/Clinical Reviewer, M.D.
Division of Dermatology and Dental Products (DDDP)

Strother Dixon, 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 clobetasol propionate lotion

NDA: 213691

In response to DDDP's consult request dated August 16, 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 clobetasol propionate lotion.

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 July 19, 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.

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LAURIE J BUONACCORSI
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LABEL AND LABELING REVIEW
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)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	February 21, 2020
Requesting Office or Division:	Division of Dermatology and Dental Products (DDDP)
Application Type and Number:	NDA 213691
Product Name, Dosage Form, and Strength:	(clobetasol propionate) lotion, 0.05%
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Mylan Pharmaceuticals, Inc.
FDA Received Date:	July 19, 2019
OSE RCM #:	2019-1574
DMEPA Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA Team Leader:	Sevan Kolejian, PharmD, MBA

1 REASON FOR REVIEW

As part of the approval process for (clobetasol propionate) lotion, 0.05%, the Division of Dermatology and Dental Products (DDDP) requested that we review the proposed labels and labeling for areas that may lead to medication errors.

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Table 1. Materials Considered for this Label and Labeling Review	
Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B – N/A
Human Factors Study	C – N/A
ISMP Newsletters*	D – N/A
FDA Adverse Event Reporting System (FAERS)*	E – N/A
Other	F – N/A
Labels and Labeling	G

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

We reviewed the Prescribing Information (PI), Patient Package Insert (PPI), Instructions for Use (IFU), container labels and carton labeling and noted that the label and labeling can be improved to increase the prominence of important information (e.g. established name), to prevent wrong dose errors, and to facilitate product identification. The carton labeling can also be improved to align formatting of product identifiers with the FDA released draft guidance on product identifiers[a]. We note the use of the proposed proprietary name, (b) (4) *** which we found unacceptable due to misbranding[b].

[a] The draft guidance is available from: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621044.pdf

[b] Patel, M. Proprietary Name Review for (b) (4) *** (NDA (b) (4)). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2019 SEP 05. Panorama No. (b) (4).

4 CONCLUSION & RECOMMENDATIONS

We conclude that the proposed label and labeling can be improved to increase the prominence of important information, prevent wrong dose errors, and to facilitate product identification. We provide recommendations below in Section 4.1 for the Division and Section 4.2 for the Applicant to address our concerns.

4.1 RECOMMENDATIONS FOR DIVISION OF DERMATOLOGY AND DENTAL PRODUCTS (DDDP)

A. General Comments

1. The proposed proprietary name, [redacted] (b) (4) ***, used throughout the prescribing information (PI) and Patient Packaging Insert (PPI), and Instructions for Use (IFU) was found unacceptable by DMEPA under NDA 213691 on September 5, 2019 due to misbranding. Remove the proposed proprietary name, [redacted] (b) (4) ***, throughout the PI, PPI, and IFU. Until a new name is found to be conditionally acceptable, the placeholder, "TRADENAME" may be used.

4.2 RECOMMENDATIONS FOR MYLAN PHARMACEUTICALS, INC.

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

A. General Comments (Container labels & Carton Labeling)

1. The proposed proprietary name, [redacted] (b) (4) ***, used throughout the container label and carton labeling, was found unacceptable by DMEPA under NDA 213691 on September 5, 2019 due to misbranding. Remove the proposed proprietary name, [redacted] (b) (4) ***, throughout the container label and carton labeling. Until a new name is found to be conditionally acceptable, the placeholder, "TRADENAME" may be used. Once a proprietary name is found conditionally acceptable, the placeholder "Tradename" must be replaced with the proprietary name on the container label and carton labeling and the revised label and labeling must be submitted to the Agency for review.
2. The established name lacks prominence commensurate with the proprietary name. Increase the prominence of the established name taking into account all pertinent factors, including typography, layout, contrast, and other printing features in accordance with 21 CFR 201.10(g)(2). Additionally, the established name is not at least half the size of the proprietary name. Revise the established name to be in accordance with 21 CFR 201.10(g)(2).
3. To ensure consistency with the Prescribing Information, revise the statement, [redacted] (b) (4) to read "Recommended Dosage". If space is limited, the statement may read "Recommended Dosage: See prescribing information."
4. As currently presented, the format for the expiration date is not defined. To minimize confusion and reduce the risk for deteriorated drug medication errors,

identify the format you intend to use. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or a space be used to separate the portions of the expiration date.

B. Carton Labeling

1. In September 2018, FDA released draft guidance on product identifiers required under the Drug Supply Chain Security Act.[c] The Act requires manufacturers and repackagers, respectively, to affix or imprint a product identifier to each package and homogenous case of a product intended to be introduced in a transaction in(to) commerce beginning November 27, 2017, and November 27, 2018, respectively. The human-readable product identifier contains the NDC, serial number, lot, and expiration date. The DSCSA guidance on product identifiers recommends the format below for the human-readable portion of the product identifier. The guidance also recommends that the human-readable portion be located near the 2D data matrix barcode.

   NDC: [insert product's NDC]
   SERIAL: [insert product's serial number]
   LOT: [insert product's lot number]
   EXP: [insert product's expiration date]

   We recommend that you review the draft guidance for the recommended format.

[c] The draft guidance is available from: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621044.pdf

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for clobetasol propionate received on July 19, 2019 from Mylan Pharmaceuticals, Inc., and the listed drug (LD).

Table 2. Relevant Product Information for clobetasol propionate and the Listed Drug		
Product Name	clobetasol propionate	Clobex[d] (NDA 021535)
Initial Approval Date	N/A	July 24, 2003
Active Ingredient	clobetasol propionate	clobetasol propionate
Indication	relief of the inflammatory and pruritic manifestations of corticosteroid responsive dermatoses only in patients 18 years of age or older	relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses only in patients 18 years of age or older
Route of Administration	topical	topical
Dosage Form	lotion	lotion
Strength	0.05%	0.05%
Dose and Frequency	apply to the affected skin areas twice daily and rubbed in gently and completely. The total dosage should not exceed 50 g per week. Do not use more than (b) (4) pump actuations per application or (b) (4) pump actuations per day.	apply to the affected skin areas twice daily and rubbed in gently and completely. The total dosage should not exceed 50 g (50 mL or 1.75 fl. oz.) per week.
How Supplied	68 g metered dose pump - White bottle with a metered-dose pump having an integral pump locking feature. Each pump actuation delivers 0.15 mg of clobetasol propionate, USP in 0.30 g of lotion. The metered-dose pump is capable of dispensing (b) (4) actuations to deliver (b) (4) g of lotion.	2 fl oz (59 mL) and 4 fl oz (118 mL) bottles

[d] Clobex (clobetasol propionate) lotion [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2020 FEB 05. Available from: https://www.accessdata.fda.gov/spl/data/b20424b0-0e9d-420a-b1f6-88abac9a4fa2/b20424b0-0e9d-420a-b1f6-88abac9a4fa2.xml.

Storage	Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Protect from freezing.	Store at USP controlled room temperature 68° to 77°F (20°-25°C), with excursions permitted between 59° and 86°F (15° - 30°C). Protect from freezing.
Container Closure	white bottle with a metered-dose pump having an integral pump locking feature	high density polyethylene bottles

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APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[e] along with postmarket medication error data, we reviewed the following clobetasol propionate labels and labeling submitted by Mylan Pharmaceuticals, Inc..

- Container label received on July 19, 2019
- Carton labeling received on July 19, 2019
- Instructions for Use (Image not shown) received on July 19, 2019, available from \\cdsesub1\evsprod\nda213691\0001\m1\us\114-labeling\draft\labeling\draft-labeling-text.pdf
- Patient Package Insert (Image not shown) received on July 19, 2019, available from \\cdsesub1\evsprod\nda213691\0001\m1\us\114-labeling\draft\labeling\draft-labeling-text.pdf
- Prescribing Information (Image not shown) received on July 19, 2019, available from \\cdsesub1\evsprod\nda213691\0001\m1\us\114-labeling\draft\labeling\draft-labeling-text.pdf

G.2 Label and Labeling Images

[e] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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