CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761364Orig1s000

OTHER REVIEW(S)

M E M O R A N D U M

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

DATE: October 7, 2024

TO: Jill Lindstrom, MD
Director
Division of Dermatology and Dentistry
Office of New Drugs

FROM: Kara A. Scheibner, Ph.D.
Pharmacologist
Division of Generic Drug Study Integrity (DGDSI)
Office of Study Integrity and Surveillance (OSIS)

THROUGH: Kimberly A. Benson, Ph.D.
Deputy Director
DGDSI/OSIS

SUBJECT: Review of Analytical Inspection of (b) (4) (b) (4)

1. Inspection Summary

The Office of Study Integrity and Surveillance (OSIS) conducted an analytical inspection of study DMB-3115-1 (BLA 761364) conducted (b) (4) (b) (4).

Form FDA 483 was issued at the inspection close-out. However, after reviewing the inspectional findings, exhibits provided in the EIR, and the firm's response to Form FDA 483, there are no concerns regarding the reliability of the data for inspected study DMB-3115-1.

2. Inspected Studies:

BLA 761364

Study Number: DMB-3115-1
Study Title: "Comparative pharmacokinetic study of ustekinumab biosimilar (DMB-3115 Formulation A), EU-Stelara, and US-Stelara in healthy adult subjects"

Dates of study conduct: 06/11/2020 – 04/21/2021

3. Inspectional Findings

OSIS reviewer Kara A. Scheibner, Ph.D. inspected [redacted]

3.1 Previous Inspection

This was the first OSIS inspection of [redacted] under the BA/BE program.

3.2 Current Inspection

The current inspection included auditing the following items:

- [redacted] facilities and operations
- Standard Operating Procedures (SOPs)
- Source method validation and study data for pharmacokinetic (PK), anti-drug antibody (ADA), and neutralizing antibody (NAb) assays including:
  - Method sheet/sample preparation
  - Plate maps
  - Plate elctrochemiluminescent (ECL) data from the MSD reader
  - Assay summary/run acceptance
  - File notes
  - Deviations
- Sample receipt, reconciliation, storage, and movement documents
- Communications
- Instrument records

3.3 Inspection findings

At the conclusion of the inspection, I observed objectionable conditions and issued Form FDA 483 to [redacted]. The Form FDA 483 observations (**Attachment 1**), the firm's response dated 09/26/2024 (**Attachment 2**, **Appendices 1-8**), and my evaluation are presented below.

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/s/

KARA A SCHEIBNER
10/07/2024 11:22:28 AM

KIMBERLY A BENSON
10/07/2024 11:32:25 AM

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

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

Memorandum

Date: September 27, 2024

To: Susan Rhee, Regulatory Project Manager, Division of Dermatology and Dentistry (DDD)

Sangeeta Jain, Clinical Reviewer, DDD

Matthew White, Associate Director for Labeling, DDD

From: Montherson L. Saint Juste, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: James Dvorsky, Team Leader, OPDP

Subject: OPDP Labeling Comments for IMULDOSA (ustekinumab- srlf) injection, for subcutaneous or intravenous use

BLA: 761364

Background:
In response to DDD's consult request dated February 2, 2024, OPDP has reviewed the proposed Prescribing Information (PI), Medication Guide/Instructions for Use (IFU), and carton and container labeling for the original BLA submission for IMULDOSA (ustekinumab-srlf).

PI/Medication Guide/IFU:
OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on September 23, 2024, and our comments are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review was completed for the proposed Medication Guide/IFU, and comments were sent under separate cover on September 23, 2024.

Carton and Container Labeling:
OPDP's review of the proposed carton and container labeling is based on the draft labeling accessed from SharePoint on September 27, 2024, and we do not have any comments at this time.

Thank you for your consult. If you have any questions, please contact Montherson L. Saint Juste at 301-796-1200 or Montherson.SaintJuste@fda.hhs.gov.

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/s/

MONTHERSON L SAINT JUSTE
09/30/2024 03:41:27 PM

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

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

Memorandum

Date: September 27, 2024

To: Susan Rhee, Regulatory Project Manager, Division of Dermatology and Dentistry (DDD)

Sangeeta Jain, Clinical Reviewer, DDD

Matthew White, Associate Director for Labeling, DDD

From: Montherson L. Saint Juste, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: James Dvorsky, Team Leader, OPDP

Subject: OPDP Labeling Comments for IMULDOSA (ustekinumab- srlf) injection, for subcutaneous or intravenous use

BLA: 761364

Background:
In response to DDD's consult request dated February 2, 2024, OPDP has reviewed the proposed Prescribing Information (PI), Medication Guide/Instructions for Use (IFU), and carton and container labeling for the original BLA submission for IMULDOSA (ustekinumab-srlf).

PI/Medication Guide/IFU:
OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on September 23, 2024, and our comments are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review was completed for the proposed Medication Guide/IFU, and comments were sent under separate cover on September 23, 2024.

Carton and Container Labeling:
OPDP's review of the proposed carton and container labeling is based on the draft labeling accessed from SharePoint on September 27, 2024, and we do not have any comments at this time.

Thank you for your consult. If you have any questions, please contact Montherson L. Saint Juste at 301-796-1200 or Montherson.SaintJuste@fda.hhs.gov.

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MONTHERSON L SAINT JUSTE
09/27/2024 07:28:45 PM

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

PATIENT LABELING REVIEW

Date:	September 23, 2024
To:	Sascha Randolph, RDH, BSDH, PHDHP 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)**
From:	Maria Nguyen, MSHS, BSN, RN Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Montherson Saint Juste, PharmD, MS Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Medication Guide (MG) and Instructions for Use (IFU)
Drug Name (established name):	IMULDOSA (ustekinumab-srlf)[1]
Dosage Form and Route:	injection, for subcutaneous or intravenous use
Application Type/Number:	BLA 761364
Applicant:	Accord BioPharma, Inc.

[1]IMULDOSA has been developed as a proposed biosimilar to US-licensed STELARA (ustekinumab). The proposed proprietary name, IMULDOSA, was found conditionally acceptable on December 21, 2023. The nonproprietary name, ustekinumab-srlf, was found conditionally acceptable on July 25, 2024.

1 INTRODUCTION

On October 9, 2023, Accord BioPharma, Inc., submitted for the Agency's review Biological License Application (BLA) 761364 for IMULDOSA (ustekinumab-srlf) injection, a proposed biosimilar to US-licensed STELARA (ustekinumab) injection (BLA 125261 and BLA 761044) for treatment of the following:

- patients 6 years or older (b) (4) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy
- patients 6 years or older (b) (4) with active psoriatic arthritis
- adults with moderately to severely active Crohn's Disease
- adults with moderately to severely active ulcerative colitis

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Dermatology and Dentistry (DDD) on February 12, 2024, for DMPP and OPDP to review the Applicant's proposed Medication Guide (MG) and Instructions for Use (IFU) for IMULDOSA (ustekinumab-srlf) injection, for subcutaneous or intravenous 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 IMULDOSA (ustekinumab-srlf) MG and IFU received on October 9, 2023, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on September 17, 2024.
- Draft IMULDOSA (ustekinumab-srlf) Prescribing Information (PI) received on October 9, 2023, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on September 17, 2024.
- Approved US-licensed STELARA (ustekinumab) labeling dated March 18, 2024, and IFU dated April 6, 2020.

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%.

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 MG and IFU document using the Arial font, size 10.

In our collaborative review of the MG and IFU we:

- simplified wording and clarified concepts where possible
- ensured that the MG and IFU are consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information
- ensured that the MG and IFU are free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the MG meets the Regulations as specified in 21 CFR 208.20
- ensured that the MG meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)
- ensured that the IFU meets the criteria as specified in both the FDA Guidance for Useful Written Consumer Medication Information (published July 2006) and Instructions for Use-Patient Labeling for Human Prescription Drug and Biological Products (published July 2022).
- ensured that the MG and IFU are consistent with the approved labeling for the US-licensed STELARA (ustekinumab) injection where applicable.

4 CONCLUSIONS

The MG 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 MG 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 MG and IFU.

Please let us know if you have any questions.

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/s/

MARIA T NGUYEN
09/23/2024 11:42:01 AM
DMPP-OPDP review of ustekinumab-srlf (IMULDOSA) BLA 761364 MG and IFU

MONTHERSON L SAINT JUSTE
09/23/2024 11:46:20 AM

LASHAWN M GRIFFITHS
09/23/2024 12:03:17 PM

MEMORANDUM
REVIEW OF REVISED LABELS

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
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:	September 4, 2024
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761364
Product Name, Dosage Form, and Strength:	Imuldosa (ustekinumab-srlf) injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe; 130 mg/26 mL (5 mg/mL) single-dose vial
Applicant Name:	Accord BioPharma Inc.
FDA Received Date:	September 3, 2024
TTT ID #:	2023-6803-4
DMEPA 1 Safety Evaluator:	Amy J. Bao, PharmD, MPH
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

1 PURPOSE OF MEMORANDUM

Accord BioPharma Inc. submitted revised container labels received on September 3, 2024 for Imuldosa. The Division of Dermatology and Dentistry (DDD) requested that we review the revised container labels for Imuldosa (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

Accord BioPharma Inc. implemented all of our recommendations and we have no additional recommendations at this time.

1 Page(s) of Draft Labeling has been Withheld in Full as b4 (CCI/ TS) immediately following this page

[a] Bao, A. Label and Labeling Review for Imuldosa (BLA 761364). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 Aug 28. TTT ID: 2023-6803-3.

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/s/

AMY J BAO
09/04/2024 03:31:00 PM

YEVGENIYA M KOGAN
09/06/2024 10:33:13 AM

MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	August 28, 2024
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761364
Product Name, Dosage Form, and Strength:	Imuldosa (ustekinumab-srlf) injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe; 130 mg/26 mL (5 mg/mL) single-dose vial
Applicant Name:	Accord BioPharma Inc.
FDA Received Date:	August 20, 2024
TTT ID #:	2023-6803-3
DMEPA 1 Safety Evaluator:	Amy J. Bao, PharmD, MPH
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

1 PURPOSE OF MEMORANDUM

Accord BioPharma Inc. submitted revised container labels and carton labeling received on August 20, 2024 for Imuldosa. The Division of Dermatology and Dentistry (DDD) requested that we review the revised container labels and carton labeling for Imuldosa (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 to replace the "-xxxx" suffix placeholder with the conditionally acceptable nonproprietary name suffix when it is determined.[a]

2 CONCLUSION

The container labels are unacceptable from a medication error perspective. The prefilled syringe container labels are missing the linear barcode.

3 RECOMMENDATIONS FOR ACCORD BIOPHARMA INC.

A. Container Labels

1. The linear barcode is missing on the prefilled syringe container labels. The linear barcode is often used as an additional verification during the medication use process; therefore, it is an important safety feature that should be part of the label and is a requirement per 21 CFR 201.25(c)(2). Add the product's linear barcode to the prefilled syringe and vial container labels in accordance with 21CFR 201.25(c)(2). The bar code should be placed in a conspicuous location where it will not be difficult to read because of distorted text, and in an area where it will not be damaged because it appears at the point of label separation (e.g., perforation). Additionally, ensure the barcode is oriented on the container label such that it is not distorted or obstructed by the container curvature (i.e., oriented in a vertical position) in order to improve scannability.

5 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

[a] Bao, A. Label and Labeling Review for Imuldosa (BLA 761364). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 Mar 27. TTT ID: 2023-6803.

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/s/

AMY J BAO
08/28/2024 11:35:49 AM

YEVGENIYA M KOGAN
08/29/2024 07:05:47 AM

M E M O R A N D U M

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

DATE: 8/20/2024

TO: Division of Dermatology and Dentistry (DDD)
Office of Immunology and Inflammation (OII)

FROM: Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Decline to conduct an on-site inspection**

RE: BLA 761364

The Office of Study Integrity and Surveillance (OSIS) determined that an inspection is not needed for the site listed below. The rationale for this decision is noted below.

Rationale

The Office of Regulatory Affairs (ORA) conducted an inspection for the site in May 2024. The inspection was conducted under the following submission: NON-RESPONSIVE.

OSIS concluded that data from the reviewed study were reliable.

Site

Facility Type	Facility Name	Facility Address
Clinical	PAREXEL International GmbH	Early Phase Clinical Unit – Berlin, Campus DRK Klinikum Berlin Westend, House 31, Spandauer Damm 130, Berlin, Brandenburg, Germany

James J. Lumalcuri -S

Digitally signed by James J. Lumalcuri -S
Date: 2024.08.20 12:52:02 -04'00'

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/s/

JAMES J LUMALCURI
08/20/2024 01:23:33 PM

MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	May 7, 2024
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761364
Product Name, Dosage Form, and Strength:	Imuldosa (ustekinumab-xxxx)[a] injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe; 130 mg/26 mL (5 mg/mL) single-dose vial
Applicant Name:	Accord BioPharma Inc.
FDA Received Date:	May 1, 2024
TTT ID #:	2023-6803-2
DMEPA 1 Safety Evaluator:	Amy J. Bao, PharmD, MPH
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

[a] The non-proprietary name suffix for this product has not yet been determined; therefore, the placeholder established name-xxxx is used throughout this review to refer to the non-proprietary name and suffix for this product.

1 PURPOSE OF MEMORANDUM

Accord BioPharma Inc. submitted revised container labels and carton labeling received on May 1, 2024 for Imuldosa. The Division of Dermatology and Dentistry (DDD) requested that we review the revised container labels and carton labeling for Imuldosa (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.[b]

2 CONCLUSION

Accord BioPharma Inc. implemented all of our recommendations and we have no additional recommendations at this time.

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[b] Bao, A. Label and Labeling Review for Imuldosa (BLA 761364). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 APR 24. TTT ID: 2023-6803-1.

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/s/

AMY J BAO
05/07/2024 03:34:23 PM

YEVGENIYA M KOGAN
05/08/2024 08:51:46 AM

MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	April 24, 2024
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761364
Product Name, Dosage Form, and Strength:	Imuldosa (ustekinumab-xxxx)[a] injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe; 130 mg/26 mL (5 mg/mL) single-dose vial
Applicant Name:	Accord BioPharma Inc.
FDA Received Date:	April 18, 2024
TTT ID #:	2023-6803-1
DMEPA 1 Safety Evaluator:	Amy J. Bao, PharmD, MPH
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

[a] The non-proprietary name suffix for this product has not yet been determined; therefore, the placeholder established name-xxxx is used throughout this review to refer to the non-proprietary name and suffix for this product.

1 PURPOSE OF MEMORANDUM

Accord BioPharma Inc. submitted revised container labels and carton labeling received on April 18, 2024 for Imuldosa. The Division of Dermatology and Dentistry (DDD) requested that we review the revised container labels and carton labeling for Imuldosa (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.[b] We note that the previous label and labeling review included a recommendation to add an additional space for end-users to write the calculated beyond-use date – this recommendation was ultimately retracted and not sent to the Applicant in order to maintain consistency with the Reference Product and other biosimilars under review.

2 CONCLUSION

Accord BioPharma Inc. implemented our recommendations; however, we find that there are still medication error concerns in regard to the nonproprietary name suffix and product identifiers.

3 RECOMMENDATIONS FOR ACCORD BIOPHARMA INC.

A. General Comments (Container Labels & Carton Labeling)

1. The nonproprietary name suffix "srIf" has not been determined to be conditionally acceptable by the Agency. Please revert the changes back and use the "xxxx" placeholder until a conditionally acceptable nonproprietary name suffix is determined. You will receive a Nonproprietary Name Suffix Advice Letter with the determination once we complete our review of the proposed suffixes. Once determined, we request that you ensure the "xxxx" placeholder is replaced with the conditionally acceptable nonproprietary name suffix.
2. We note that the statements "Single-dose prefilled syringe" and "Discard unused portion", which appear on the prefilled syringe container labels and carton labeling, are separated using a hyphen. We recommend deleting the hyphen when these statements appear on individual lines (on the container labels), and replacing the hyphen with a period when these statements appear on the same line (on carton labeling).

B. Carton Labeling

1. A placeholder for the 2D data matrix barcode is missing, please add a placeholder for the 2D data matrix barcode to the prefilled syringe carton labeling. We recommend positioning the 2D data matrix barcode near the human-readable portion of the product identifier See *Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers (June 2021).*

[b] Bao, A. Label and Labeling Review for Imuldosa (BLA 761364). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 MAR 27. TTT ID: 2023-6803.

2. We note that (b) (4) has been included as a placeholder on the prefilled syringe carton labeling. Please confirm what this abbreviation stands for and that it is accurate, as we note it is different from "GTIN", which is used on the vial carton labeling.
3. We recommend revising the serial number placeholder abbreviation on the prefilled syringe carton labeling from "SN" to "S/N" to align with the vial carton labeling and FDA-recommended abbreviations. See *Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers (June 2021).*

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/s/

AMY J BAO
04/24/2024 09:47:54 AM

YEVGENIYA M KOGAN
04/24/2024 05:17:05 PM

LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	March 27, 2024
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761364
Product Name, Dosage Form, and Strength:	Imuldosa (ustekinumab-xxxx)[a] injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe; 130 mg/26 mL (5 mg/mL) single-dose vial
Product Type:	Combination Product (Biologic-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Accord BioPharma Inc. (Accord)
FDA Received Date:	October 10, 2023
TTT ID #:	2023-6803
DMEPA 1 Safety Evaluator:	Amy J. Bao, PharmD, MPH
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

[a] Since the nonproprietary name for this BLA has not yet been determined, the nonproprietary name placeholder, "ustekinumab-xxxx", is used throughout this review.

1 REASON FOR REVIEW

As part of the approval process for Imuldosa (ustekinumab-xxxx) injection, the Division of Dermatology and Dentistry (DDD) requested that we review the proposed Imuldosa prescribing information (PI), medication guide (MG), instructions for use (IFU), container labels, and carton labeling for areas of vulnerability that may lead to medication errors.

1.1 BACKGROUND

BLA 761364 is a 351(k) BLA and the reference product is Stelara, BLA 125261/BLA 761044.

2 MATERIALS 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	N/A
ISMP Newsletters*	N/A
FDA Adverse Event Reporting System (FAERS)*	N/A
Other	N/A
Labels and Labeling	B

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 CONCLUSION AND RECOMMENDATIONS

The proposed prescribing information (PI), medication guide (MG), instructions for use (IFU), container labels, and carton labeling may be improved to promote the safe use of this product from a medication error perspective. We provide the identified medication error issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication error in Section 4 for the Division and in Section 5 for Accord BioPharma Inc.

4 RECOMMEDATIONS FOR DIVISION OF DERMATOLOGY AND DENTISTRY (DDD)

Table 2. Identified Issues and Recommendations for Division of Dermatology and Dentistry (DDD)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Prescribing Information – General Issues			
1.	The nonproprietary name suffix is denoted by the placeholder "-xxxx".	An undefined nonproprietary name suffix placeholder may lead to identification medication errors.	Replace "-xxxx" with the conditionally acceptable nonproprietary name suffix when it is determined.
Highlights of Prescribing Information			
1.	There is one instance where the nonproprietary name is referenced without a suffix.	The nonproprietary name for biosimilars must include a suffix.	Revise (b) (4) to "IMULDOSA (ustekinumab-xxxx)" and replace "-xxxx" with the conditionally acceptable nonproprietary name suffix when it is determined.
Full Prescribing Information – Section 2 Dosage and Administration			
1.	There is no statement about how Imuldosa is not approved for treatment of Ps and PsA in pediatric patients under 60 kg BW.	Lack of clarification may confuse users who are familiar with dosage forms available for the Reference Product.	We recommend adding the statement "There is no dosage form for IMULDOSA that allows weight-based dosing for pediatric patients below 60 kg." below Table 1 and Table 2.

5 RECOMMENDATIONS FOR ACCORD BIOPHARMA INC.

Table 3. Identified Issues and Recommendations for Accord BioPharma Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Labels and Carton Labeling			
1.	The nonproprietary name suffix is denoted by the placeholder "-xxxx".	An undefined nonproprietary name suffix placeholder may lead to identification medication errors.	Replace "-xxxx" with the conditionally acceptable nonproprietary name suffix when it is determined.

Table 3. Identified Issues and Recommendations for Accord BioPharma Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
2.	The 90 mg/mL strength is not clearly differentiated due to the overlap with the font color used for the proprietary name.	Lack of adequate differentiation may contribute to wrong strength errors. Color differentiation is most effective when the color used has no association with a particular feature and there is no pattern in the application of the color scheme.	We recommend revising the color scheme of the 90 mg/mL strength ((b) (4) box surrounding the strength) or proprietary name, such that the strength and the proprietary name appear in their own unique colors that do not overlap.
3.	The route of administration statements on the prefilled syringe labels and labeling contain the word (b) (4).	We reserve the use of the word (b) (4) when there is a safety concern or data that supports the product must be given by a specific route.	We recommend revising the route of administration statements on the prefilled syringe labels and labeling from (b) (4) to "For subcutaneous use".
4.	The net quantity statement does not appear on the principal display panel of the container labels and carton labeling where the information is needed for clarity.	Failure to include the net quantity statement on the principal display panel may result in confusion regarding the contents of the container and carton.	We recommend including a net quantity statement on the principal display panels of the: • Prefilled syringe blister labeling (i.e., "Contains one 45 mg/0.5 mL syringe" and "Contains one 90 mg/mL syringe") • Vial carton labeling (i.e., "Contains one vial"). Ensure the statements are located away from and less prominent than the product strength. *See Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (May 2022).*
5.	The expiration date placeholder is currently	If there are no space limitations, FDA	We recommend revising the expiration date format to

Table 3. Identified Issues and Recommendations for Accord BioPharma Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	displayed as a YYYY-MM format.	recommends that the expiration date on the container labels and carton labeling include a 4-digit year, month, and day in YYYY-MM-DD format (e.g., 2021-01-01) if using only numerical characters or in YYYY-MMM-DD format (e.g., 2021-JAN-01) if using alphabetical characters to represent the month.	either a YYYY-MM-DD or YYYY-MMM-DD format to minimize confusion.
Container Labels			
1.	The 130 mg/26 mL vial container label is missing the "Rx only" statement.	The "Rx only" statement is required on the drug label in accordance with Section 503(b)(4)(A) of the Federal Food, Drug, and Cosmetic Act.	Add the "Rx only" statement to the 130 mg/26 mL vial container label. Ensure the "Rx only" statement is not more prominent than critical information presented on the label (e.g., proprietary name, established name, strength, dosage form and route of administration).
2.	The 130 mg/26 mL vial container label is missing the package type term statement and discard statement ("Single-Dose vial" and "Discard unused portion").	Consistent use of the correct package type term will promote proper use of the drug product. The lack of this information may lead to wrong technique medication errors during preparation or administration of the product. See Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical	Add the package type term statement and discard statement ("Single-Dose vial" and "Discard unused portion") to the 130 mg/26 mL vial container label.

Table 3. Identified Issues and Recommendations for Accord BioPharma Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
		Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018). The presence of these statements on the carton labeling does not guarantee that the information will be available during time of use, as the carton may be separated from the immediate container before use.	
3.	The 130 mg/26 mL vial container label is missing the storage conditions statement ("Store in a refrigerator at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not shake. Do not freeze. Keep out of reach of children.").	The statement of storage conditions is required per USP Chapter <7> Labeling. The presence of this statement on the carton labeling does not guarantee that the information will be available during time of use, as the carton may be separated from the immediate container before use.	Add the storage conditions statement ("Store in a refrigerator at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not shake. Do not freeze. Keep out of reach of children.") to the 130 mg/26 mL vial container label.
4.	The 130 mg/26 mL vial container label is missing the dosage statement ("Recommended Dosage: see Prescribing Information").	Statement of the recommended dosage is required per 21 CFR 201.55. The presence of this statement on the carton labeling does not guarantee that the information will be available during time of use, as the carton may be separated from the	Add the dosage statement ("Recommended Dosage: see Prescribing Information") to the 130 mg/26 mL vial container label.

Table 3. Identified Issues and Recommendations for Accord BioPharma Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
		immediate container before use.	
5.	The linear barcode is missing on the prefilled syringe and vial container labels.	The linear barcode is often used as an additional verification during the medication use process; therefore, it is an important safety feature that should be part of the label and is a requirement per 21 CFR 201.25(c)(2).	Add the product's linear barcode to the prefilled syringe and vial container labels in accordance with 21CFR 201.25(c)(2). The bar code should be placed in a conspicuous location where it will not be difficult to read because of distorted text, and in an area where it will not be damaged because it appears at the point of label separation (e.g., perforation). Additionally, ensure the barcode is oriented on the container label such that it is not distorted or obstructed by the container curvature (i.e., oriented in a vertical position) in order to improve scannability.
Carton Labeling			
1.	The prefilled syringe carton labeling only has a space for end-users to write the date removed from the refrigerator.	Inclusion of a space to write the calculated beyond-use date (30 days after removal from refrigerator) may be more helpful in reminding patients when to discard the product.	Consider adding an additional space for end-users to write the calculated beyond-use date on the prefilled syringe carton labeling. For example: "Discard if not used within 30 days at room temperature. Discard after __/__/__."
2.	The terminology within the statement of dosage statement (i.e., (b) (4)) is inconsistent with the terminology in	To ensure consistency of terminology.	Consider revising the recommended dosage statements to read, "Dosage: see Prescribing Information" or "Recommended Dosage: see Prescribing Information".

Table 3. Identified Issues and Recommendations for Accord BioPharma Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	the Prescribing Information.		
3.	The product identifier is missing on the prefilled syringe carton labeling.	In June 2021, FDA finalized the Guidance for Industry on product identifiers required under the Drug Supply Chain Security Act (DSCSA). The Act requires manufacturers and re-packagers 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. The product identifier includes the NDC, serial number, lot number, and expiration date in both a human-readable form and machine-readable (2D data matrix barcode) format.	We request you add a product identifier placeholder to the prefilled syringe carton labeling.
4.	The placeholder for the lot number is missing on the prefilled syringe carton labeling.	Lot number statement is required on the carton labeling when there is sufficient space per 21 CFR 201.10(i)(1).	Add the placeholder for the lot number in accordance to 21 CFR 201.10(i)(1).
5.	The placeholder for the expiration date is missing on the prefilled syringe carton labeling.	The label of an official drug product shall bear an expiration date per USP General Chapter <7>.	Add the placeholder for the expiration date in accordance with USP General Chapter <7>. We recommend you ensure that there are no other numbers located in close proximity to the expiration date. To minimize confusion and reduce the risk for deteriorated drug medication errors, we recommend

Table 3. Identified Issues and Recommendations for Accord BioPharma Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			identifying the expiration date 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. FDA recommends that a hyphen or forward slash are used to separate the portions of the expiration date.

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table presents relevant product information for Imuldosa that Accord BioPharma Inc. submitted on October 10, 2023, and Stelara.

Table 4. Relevant Product Information for Reference Product and Imuldosa		
Product Name	Stelara[b]	Imuldosa
Initial Approval Date	September 25, 2009	N/A
Active Ingredient	ustekinumab	ustekinumab-xxxx
Indication	Treatment of: Adult patients with: • moderate to severe plaque psoriasis (Ps) who are candidates for phototherapy or systemic therapy • active psoriatic arthritis (PsA) • moderately to severely active Crohn's disease (CD) • moderately to severely active ulcerative colitis Pediatric patients 6 years and older with: • moderate to severe plaque psoriasis, who are candidates for phototherapy or systemic therapy • active psoriatic arthritis (PsA)	
Route of Administration	Subcutaneous, intravenous	
Dosage Form	Subcutaneous injection (prefilled syringe and single-dose vial) Intravenous infusion (single-dose vial)	Subcutaneous injection (prefilled syringe) Intravenous infusion (single-dose vial)
Strength	45 mg/0.5 mL, 90 mg/mL, 130 mg/26 mL	

[b] Stelara [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. March 2023. [cited 2023 Nov 27]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125261s158lbl.pdf

<table>
<tr><th colspan="3">Table 4. Relevant Product Information for Reference Product and Imuldosa</th></tr>
<tr><td>Product Name</td><td>Stelara[b]</td><td>Imuldosa</td></tr>
<tr><td>Dose and Frequency</td><td>
<u>Psoriasis Adult Subcutaneous Recommended Dosage:</u>
<table>
<tr><th>Weight Range (kg)</th><th>Dosage Regimen</th></tr>
<tr><td>less than or equal to 100 kg</td><td>45 mg administered subcutaneously initially and 4 weeks later, followed by 45 mg administered subcutaneously every 12 weeks</td></tr>
<tr><td>greater than 100 kg</td><td>90 mg administered subcutaneously initially and 4 weeks later, followed by 90 mg administered subcutaneously every 12 weeks</td></tr>
</table>
<u>Psoriasis Pediatric Patients (6 to 17 years old) Subcutaneous Recommended Dosage</u>: Weight-based dosing is recommended at the initial dose, 4 weeks later, then every 12 weeks thereafter.
<table>
<tr><th>Weight Range (kg)</th><th>Dose</th></tr>
<tr><td>Less than 60 kg</td><td>0.75 mg/kg</td></tr>
<tr><td>60 kg to 100 kg</td><td>45 mg</td></tr>
<tr><td>Greater than 100 kg</td><td>90 mg</td></tr>
</table>
<u>Psoriatic Arthritis Adult Subcutaneous Recommended Dosage</u>:

The recommended dosage is 45 mg administered subcutaneously initially and 4 weeks later, followed by 45 mg administered subcutaneously every 12 weeks.
For patients with co-existent moderate-to-

</td><td>
<u>Psoriasis Adult Subcutaneous Recommended Dosage:</u>
<table>
<tr><th>Weight Range (kg)</th><th>Dosage Regimen</th></tr>
<tr><td>less than or equal to 100 kg</td><td>45 mg administered subcutaneously initially and 4 weeks later, followed by 45 mg administered subcutaneously every 12 weeks</td></tr>
<tr><td>greater than 100 kg</td><td>90 mg administered subcutaneously initially and 4 weeks later, followed by 90 mg administered subcutaneously every 12 weeks</td></tr>
</table>
<u>Psoriasis Pediatric Patients (6 to 17 years old) Subcutaneous Recommended Dosage</u>: Weight-based dosing is recommended at the initial dose, 4 weeks later, then every 12 weeks thereafter.
<table>
<tr><th>Weight Range (kg)</th><th>Dose</th></tr>
<tr><td>Less than 60 kg</td><td>-</td></tr>
<tr><td>60 kg to 100 kg</td><td>45 mg</td></tr>
<tr><td>Greater than 100 kg</td><td>90 mg</td></tr>
</table>
<u>Psoriatic Arthritis Adult Subcutaneous Recommended Dosage</u>:

The recommended dosage is 45 mg administered subcutaneously initially and 4 weeks later, followed by 45 mg administered subcutaneously every 12 weeks.
For patients with co-existent moderate-to-

</td></tr>
</table>

Table 4. Relevant Product Information for Reference Product and Imuldosa

Product Name	Stelara[b]	Imuldosa
APPEARS THIS WAY ON ORIGINAL	severe plaque psoriasis weighing greater than 100 kg, the recommended dosage is 90 mg administered subcutaneously initially and 4 weeks later, followed by 90 mg administered subcutaneously every 12 weeks. Psoriatic Arthritis Pediatric (6 to 17 years old) Subcutaneous Recommended Dosage: Weight-based dosing is recommended at the initial dose, 4 weeks later, then every 12 weeks thereafter. Weight Range (kg) / Dose Less than 60 kg / 0.75 mg/kg 60 kg to 100 kg / 45 mg Greater than 100 kg with co-existent moderate-to-severe plaque psoriasis / 90 mg Crohn's Disease and Ulcerative Colitis Initial Adult Intravenous Recommended Dosage: As single intravenous infusion using weight-based dosing. Weight Range (kg) / Recommended Dosage Up to 55 kg / 260 mg (2 vials) Greater than 55 kg to 85 kg / 390 mg (3 vials) Greater than 85 kg / 520 mg (4 vials) Crohn's Disease and Ulcerative Colitis Maintenance Adult Subcutaneous Recommended	severe plaque psoriasis weighing greater than 100 kg, the recommended dosage is 90 mg administered subcutaneously initially and 4 weeks later, followed by 90 mg administered subcutaneously every 12 weeks. Psoriatic Arthritis Pediatric (6 to 17 years old) Subcutaneous Recommended Dosage: Weight-based dosing is recommended at the initial dose, 4 weeks later, then every 12 weeks thereafter. Crohn's Disease and Ulcerative Colitis Initial Adult Intravenous Recommended Dosage: As single intravenous infusion using weight-based dosing. Weight Range (kg) / Recommended Dosage Up to 55 kg / 260 mg (2 vials) Greater than 55 kg to 85 kg / 390 mg (3 vials) Greater than 85 kg / 520 mg (4 vials) Crohn's Disease and Ulcerative Colitis Maintenance Adult Subcutaneous Recommended

<table>
<tr><th colspan="3">Table 4. Relevant Product Information for Reference Product and Imuldosa</th></tr>
<tr><td>Product Name</td><td>Stelara[b]</td><td>Imuldosa</td></tr>
<tr><td></td><td><u>Dosage</u>:
A subcutaneous 90 mg dose 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.</td><td><u>Dosage</u>:
A subcutaneous 90 mg dose 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.</td></tr>
<tr><td>How Supplied

APPEARS THIS WAY ON ORIGINAL</td><td>STELARA® (ustekinumab) injection is a sterile, preservative-free, colorless to light yellow solution and may contain a few small translucent or white particles. It is supplied as individually packaged, single-dose prefilled syringes or single-dose vials.
For subcutaneous use:
Prefilled syringes (45 mg/0.5 mL and 90 mg/mL)
Single-dose vial (45 mg/0.5 mL)
For intravenous infusion:
Single-dose vial (130 mg/26 mL)
Each prefilled syringe is equipped with a 27 gauge fixed ½ inch needle, a needle safety guard, and a needle cover that contains dry natural rubber</td><td>IMULDOSA (ustekinumab-xxxx) injection is a sterile, preservative-free, colorless to slightly yellow and clear to slightly opalescent solution. It is supplied as individually packaged, single-dose prefilled syringes or single-dose vials.
For subcutaneous use:
Prefilled syringes (45 mg/0.5 mL and 90 mg/mL)
<table><tr><th>Weight Range (kg)</th><th>Dose</th></tr><tr><td>Less than 60 kg</td><td rowspan="2">45 mg</td></tr><tr><td>60 kg to 100 kg</td></tr><tr><td>Greater than 100 kg with co-existent moderate-to-severe plaque psoriasis</td><td>90 mg</td></tr></table>For intravenous infusion:
Single-dose vial (130 mg/26 mL)
Each prefilled syringe is equipped with a 29 gauge fixed ½ inch needle, a needle safety guard, and a needle cover that does not contain latex.</td></tr>
</table>

Table 4. Relevant Product Information for Reference Product and Imuldosa		
Product Name	Stelara[b]	Imuldosa
Storage	Vials and prefilled syringes must be refrigerated at 2°C to 8°C (36°F to 46°F). Store vials upright. Keep the product in the original carton to protect from light until the time of use. Do not freeze. Do not shake. If needed, individual prefilled syringes may be stored at room temperature up to 30°C (86°F) for a maximum single period of up to 30 days in the original carton to protect from light. Record the date when the prefilled syringe is first removed from the refrigerator on the carton in the space provided. Once a syringe has been stored at room temperature, it should not be returned to the refrigerator. Discard the syringe if not used within 30 days at room temperature storage. Do not use after the expiration date on the carton or on the prefilled syringe.	
Container Closure	Single-dose prefilled syringes, single-dose vials	Single-dose prefilled syringes, single-dose vial

APPENDIX B. LABELS AND LABELING

B.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[c] along with postmarket medication error experiences with similar products, we reviewed the following Imuldosa labels and labeling submitted by Accord BioPharma Inc.

- Container labels received on October 10, 2023
- Carton labeling received on October 10, 2023
- Instructions for Use received on October 10, 2023, available from \\CDSESUB1\EVSPROD\bla761364\0002\m1\us\11431-annot-ifu-comparison-listed-drug-in-word.docx
- Medication Guide received on October 10, 2023, available from \\CDSESUB1\EVSPROD\bla761364\0002\m1\us\11431-annot-labeling-comparison-listed-drug-in-word.docx
- Prescribing Information received on October 10, 2023, available from \\CDSESUB1\EVSPROD\bla761364\0002\m1\us\11431-annot-labeling-comparison-listed-drug-in-word.docx

B.2 Label and Labeling Images

Container labels

(b) (4)

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

5 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

AMY J BAO
03/27/2024 02:55:55 PM

YEVGENIYA M KOGAN
03/28/2024 07:04:50 AM