CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210745Orig1s000
210745Orig2s000

OTHER REVIEW(S)

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)

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

Date of This Review:	August 12, 2025
Requesting Office or Division:	Division of Rheumatology and Transplant Medicine (DRTM)
Application Type and Number:	NDA 210745
Product Name, Dosage Form, and Strength:	Otezla XR (apremilast) extended-release tablets, 75 mg
Applicant Name:	Amgen Inc.
FDA Received Date:	August 11, 2025
TTT ID #:	2024-11941-2
DMEPA 1 Safety Evaluator:	Sarah K. Vee, PharmD
DMEPA 1 Team Leader:	Damon Birkemeier, PharmD, FISMP

1 PURPOSE OF MEMORANDUM

Amgen Inc. submitted revised container label and carton labeling received on August 11, 2025 for Otezla XR. The Division of Rheumatology and Transplant Medicine (DRTM) requested that we review the revised container label and carton labeling for Otezla XR (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to labeling discussion comments (i.e., delete the storage conditions statement "(b) (4) (b) (4)." and add the storage conditions statement "Store between 20°C and 25°C (68°F and 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature]").[a]

2 CONCLUSION

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

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[a] Integrated Quality Assessment for Otezla XR (NDA 210745). Silver Spring (MD): FDA, CDER, OPQ (US); 2025 MAY 28. Available from: https://darrts.fda.gov/darrts/faces/ViewDocument?documentId=090140af807cc93e.

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/s/

SARAH K VEE
08/12/2025 01:30:00 PM

DAMON A BIRKEMEIER
08/12/2025 01:34:33 PM

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

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

Memorandum

Date: July 15, 2025

To: Strother D. Dixon, Regulatory Project Manager, Division of Dermatology and Dentistry (DDD)

Elizabeth R. Rizza, 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 OTEZLA XR™ (apremilast) extended-release tablets, for oral use

NDA: 210745

Background:
In response to DDD's consult request dated January 10, 2025, OPDP has reviewed the proposed Prescribing Information (PI) for the original NDA submission for OTEZLA XR™ (apremilast).

PI:
OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on June 26, 2025, and our comments are provided below/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
07/15/2025 06:37:36 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:	April 24, 2025
Requesting Office or Division:	Division of Rheumatology and Transplant Medicine (DRTM)
Application Type and Number:	NDA 210745
Product Name, Dosage Form, and Strength:	Otezla XR (apremilast) extended-release tablets, 75 mg
Applicant Name:	Amgen Inc.
FDA Received Date:	April 18, 2025
TTT ID #:	2024-11941-1
DMEPA 1 Safety Evaluator:	Sarah K. Vee, PharmD
DMEPA 1 Team Leader:	Damon Birkemeier, PharmD, FISMP

1 PURPOSE OF MEMORANDUM

Amgen Inc. submitted revised carton labeling (blister/wallet and sleeve labeling) received on April 18, 2025 for Otezla XR. The Division of Rheumatology and Transplant Medicine (DRTM) requested that we review the revised titration pack blister/wallet and sleeve labeling for Otezla XR (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

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

[a] Vee, S. Label and Labeling Review for Otezla XR (NDA 210745). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2025 APR 07. TTT ID: 2024-11941.

APPENDIX A. INFORMATION REQUEST RESPONSE RECEIVED ON APRIL 18, 2025

- Information Request Response Available from \\CDSESUB1\EVSPROD\nda210745\0025\m1\us\111-information-amendment\rtq-08042025.pdf

APPENDIX B. IMAGES OF LABELS AND LABELING RECEIVED ON APRIL 18, 2025

Blister/Wallet Labeling:

(b) (4)

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/s/

SARAH K VEE
04/24/2025 01:31:49 PM

DAMON A BIRKEMEIER
04/24/2025 03:06:57 PM

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: April 24, 2025

TO: Raj Nair, M.D.
Director
Division of Rheumatology and Transplant Medicine (DRTM)
Office of Immunology and Inflammation (OII)
Office of New Drugs (OND)

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

THROUGH: Seongeun Julia Cho, Ph.D.
Director
Division of Generic Drug Study Integrity (DGDSI)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: Review of Clinical Inspection at QPS Bio-Kinetic Clinical Applications, LLC, Springfield, MO

1. Inspection Summary

The Office of Study Integrity and Surveillance (OSIS) arranged clinical inspections of study 20200369 (NDA 210745, OTEZLA XR™ Extended-Release Tablets) conducted at QPS Bio-Kinetic Clinical Applications, LLC, Springfield, MO.

Form FDA 483 was not issued to QPS Bio-Kinetic Clinical Applications, LLC, Springfield, MO, at the inspection close-out. There was one discussion item regarding documentation. Based on the inspection finding, the discussion item has no impact on the reliability of the data and human subject protection for study 20200369 conducted at QPS Bio-Kinetic Clinical Applications, LLC, Springfield, MO.

2. Inspected Study

NDA 210745

Study Number: 20200369
Study Title: An Open-label, Randomized, Crossover Study to Evaluate the Relative bioavailability and the Effect of Food on an Apremilast Extended-release

Formulation in Healthy Subjects

Dates of study conduct: July 19, 2022, to November 29, 2022

Clinical Site: QPS Bio-Kinetic Clinical Applications, LLC
1820 West Mount Vernon Street, Springfield, MO

Principal Investigator: William J. Howitt, M.D.

3. Inspectional Findings

3.1 QPS Bio-Kinetic Clinical Applications, LLC, Springfield, MO

OII investigator Karen M. Montgomery inspected QPS Bio-Kinetic Clinical Applications, LLC, Springfield, MO, from March 10 to 12, 2025.

3.1.1 Previous Inspection

The site was inspected in November 2022 and classified as NAI.

3.1.2 Current Inspection

The current inspection included auditing the following items:
- Case report forms (CRFs)
- Informed consent process
- Protocol deviations
- Institutional Review Board approvals
- Randomization
- Test article accountability, and storage
- Adverse events

3.1.3 Inspection findings

At the conclusion of the inspection, investigator Karen M. Montgomery did not issue Form FDA 483 to the clinical site. One discussion item was communicated with Managements:

Discussion item 1:
The raw data logs for centrifuge times did not indicate what centrifuge was used for processing biological samples for the study.

OSIS Evaluation 1:
The centrifugation conditions (i.e., speed, time, temperature), subject number and sampling time are documented in the raw date log. There is no requirement to document a centrifuge ID. The discussion item has no impact on the reliability of the data and

human subject protection for study 20200369 conducted at this site.

Draft: XC 4/21/2025, 4/23/2025, 4/24/2025
Edit: MO 4/23/2025; JC 4/24/2025

OSIS File: BE 10487

eNSpect Assignment ID: 259029
eNSpect Op ID: 311252

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/s/

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MEI OU
04/24/2025 02:59:10 PM

SEONGEUN CHO
04/24/2025 03:42:56 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)

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

Date of This Review:	April 7, 2025
Requesting Office or Division:	Division of Rheumatology and Transplant Medicine (DRTM)
Application Type and Number:	NDA 210745
Product Name, Dosage Form, and Strength:	Otezla XR (apremilast) extended-release tablets, 75 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant Name:	Amgen Inc.
FDA Received Date:	October 30, 2024
TTT ID #:	2024-11941
DMEPA 1 Safety Evaluator:	Sarah K. Vee, PharmD
DMEPA 1 Team Leader:	Damon Birkemeier, PharmD, FISMP, NREMT

1 INTRODUCTION

As part of the approval process for Otezla XR (apremilast) extended-release tablets, the Division of Rheumatology and Transplant Medicine (DRTM) requested that we review the proposed Otezla XR Prescribing Information, Medication Guide, container label, and carton labeling for areas of vulnerability that may lead to medication errors.

1.1 REGULATORY HISTORY

NDA 210745 was originally submitted on December 14, 2017 by Celgene Corporation, which was subsequently withdrawn by Celgene on August 17, 2018. Amgen acquired the ownership of NDA 210745 on June 21, 2022.

Thus, Amgen Inc. resubmitted the NDA on October 30, 2024.

2 MATERIALS CONSIDERED

This section lists the materials considered for our review.

Table 1. Materials Considered for this Review	
Materials Considered	Appendix Section
Relevant Product Information	A
Labels and Labeling	B

3 CONCLUSION

We evaluated the proposed Otezla XR Prescribing Information and determined that it is acceptable from a medication error perspective.

However, the proposed Otezla XR titration pack blister 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 for Amgen Inc. in Section 5.

4 RECOMMENDATIONS FOR AMGEN INC.

A. General Comments (Titration Pack Blister and Carton Labeling)

1. As currently presented the principal display panel of the blister labeling only states “Otezla XR” even though the titration pack contains “Otezla”, thus is misleading. To be consistent with Section 16 of the prescribing information, the principal display panel should be revised to also include Otezla and list the strengths under the corresponding proprietary name, for example:

Otezla XR (apremilast) extended-release tablets 75 mg

Oteza (apremilast) tablets 10 mg, 20 mg, 30 mg

B. Titration Pack Blister Labeling

1. The graphic  does not convey the important frequency of administration direction to take the Otezla tablets twice daily. We recommend replacing the graphic with "Twice daily" or "Twice daily in morning and evening" to be consistent with the "once daily" direction for Otezla XR for weeks 3 and 4.

2. As currently presented, the format of the expiration date is not defined. 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 forward slash to separate the portions of the expiration date. See *Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers (June 2021).*[a]

A. Titration Pack Carton Labeling

1. The quantity statement "41 tablets" may be improved to increase clarity. We recommend revising the statement to "Contains 41 total tablets" or "Treatment Initiation pack contains 41 total tablets for the first 28 days of treatment".

[a] Guidance for Industry: Product Identifiers Under the Drug Supply Chain Security Act - Questions and Answers. 2021. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/product-identifiers-under-drug-supply-chain-security-act-questions-and-answers.

APPENDICES: MATERIALS CONSIDERED FOR THIS REVIEW

APPENDIX A. RELEVANT PRODUCT INFORMATION

Table 2 presents relevant product information for Otezla XR received on October 30, 2024 from Amgen Inc., and Otezla.

Table 2. Relevant Product Information for Otezla XR and Otezla		
Product Name	Otezla XR	Otezla (NDA 205437)
Initial Approval Date	N/A	March 21, 2014
Active Ingredient	apremilast	
Indication	Psoriatic Arthritis • OTEZLA/OTEZLA XR is indicated for the treatment of adult patients with active psoriatic arthritis. Plaque Psoriasis • OTEZLA/OTEZLA XR is indicated for the treatment of adult patients with plaque psoriasis who are candidates for phototherapy or systemic therapy. • OTEZLA is indicated for the treatment of pediatric patients 6 years of age and older and weighing at least 20 kg with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. • OTEZLA XR is indicated for the treatment of pediatric patients 6 years of age and older and weighing at least 50 kg with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. Oral Ulcers Associated with Behçet's Disease • OTEZLA/OTEZLA XR is indicated for the treatment of adult patients with oral ulcers associated with Behçet's Disease.	
Dosage Form	extended-release tablets	tablets
Strength	75 mg	10 mg, 20 mg, 30 mg
Route of Administration	oral	

<table>
<tr><th colspan="3">Table 2. Relevant Product Information for Otezla XR and Otezla</th></tr>
<tr><td>Product Name</td><td>Otezla XR</td><td>Otezla (NDA 205437)</td></tr>
<tr><td>Dose and Frequency</td><td colspan="2">
<u>Adult Patients with Psoriatic Arthritis, Plaque Psoriasis, or Behçet's Disease</u>
The recommended initial dosage titration from Day 1 to Day 5 is shown in Table 1. Following the 5-day titration with OTEZLA, the recommended maintenance dosage is OTEZLA 30 mg twice daily or OTEZLA XR 75 mg once daily taken orally starting on Day 6. This titration is intended to reduce the gastrointestinal symptoms associated with initial therapy.
Table 1. Dosage Titration Schedule for Adult Patients with Psoriatic Arthritis, Plaque Psoriasis, or Behçet's Disease
<table>
<tr><th colspan="9">OTEZLA Dosage Titration[a]</th><th>OTEZLA/OTEZLA XR Maintenance Dosage</th></tr>
<tr><td>Day 1</td><td colspan="2">Day 2</td><td colspan="2">Day 3</td><td colspan="2">Day 4</td><td colspan="2">Day 5</td><td>Day 6 & thereafter</td></tr>
<tr><td>AM</td><td>AM</td><td>PM</td><td>AM</td><td>PM</td><td>AM</td><td>PM</td><td>AM</td><td>PM</td><td></td></tr>
<tr><td>10 mg</td><td>10 mg</td><td>10 mg</td><td>10 mg</td><td>20 mg</td><td>20 mg</td><td>20 mg</td><td>20 mg</td><td>30 mg</td><td>OTEZLA 30 mg BID
OR
OTEZLA XR 75 mg QD</td></tr>
<tr><td colspan="10">BID = twice daily; QD = once daily
[a] OTEZLA tablets should be used for the initial titration regardless of whether OTEZLA or OTEZLA XR will be used for the maintenance dosage.</td></tr>
</table>
<u>Pediatric Patients 6 Years of Age and Older and Weighing at Least 20 kg with Moderate to Severe Plaque Psoriasis</u>
The recommended dosage for pediatric patients 6 years of age and older and weighing at least 20 kg with moderate to severe plaque psoriasis is based on body weight. Following the appropriate initial titration schedule shown in Table 2, the recommended maintenance dosage is OTEZLA 30 mg twice daily or OTEZLA XR 75 mg once daily taken orally for pediatric patients who weigh at least 50 kg and OTEZLA 20 mg twice daily taken orally for pediatric patients who weigh from 20 kg to less than 50 kg. This titration is intended to reduce the gastrointestinal symptoms associated with initial therapy.
Table 2. Dosage Titration Schedule for Pediatric Patients 6 Years of Age and Older and Weighing at Least 20 kg with Moderate to Severe Plaque Psoriasis
<table>
<tr><th></th><th colspan="8">OTEZLA Dosage Titration[a]</th><th>OTEZLA/OTEZLA XR Maintenance Dosage</th></tr>
<tr><td>Body Weight</td><td>Day 1</td><td colspan="2">Day 2</td><td colspan="2">Day 3</td><td colspan="2">Day 4</td><td colspan="2">Day 5</td><td>Day 6 & thereafter</td></tr>
<tr><td></td><td>AM</td><td>AM</td><td>PM</td><td>AM</td><td>PM</td><td>AM</td><td>PM</td><td>AM</td><td>PM</td><td></td></tr>
</table>
</td></tr>
</table>

Table 2. Relevant Product Information for Otezla XR and Otezla

Product Name	**Otezla XR**	**Otezla** (NDA 205437)

50 kg or more	10 mg	10 mg	10 mg	10 mg	20 mg	20 mg	20 mg	20 mg	30 mg	OTEZLA 30 mg BID **OR** OTEZLA XR 75 mg QD
20 kg to less than 50 kg	10 mg	10 mg	10 mg	10 mg	20 mg	20 mg	20 mg	20 mg	20 mg	OTEZLA 20 mg BID

BID = twice daily; QD = once daily
[a] OTEZLA tablets should be used for the initial titration regardless of whether OTEZLA or OTEZLA XR will be used for the maintenance dosage.

Switching Between OTEZLA and OTEZLA XR

Patients treated with OTEZLA 30 mg twice daily may be switched to OTEZLA XR 75 mg once daily the day following the last dose of OTEZLA 30 mg.

Patients treated with OTEZLA XR 75 mg once daily may be switched to OTEZLA 30 mg twice daily the day following the last dose of OTEZLA XR 75 mg.

Dosage Adjustment in Patients with Severe Renal Impairment

Adult Patients with Psoriatic Arthritis, Plaque Psoriasis, or Behçet's Disease (b) (4)

For initial dosage titration, titrate OTEZLA using only the AM schedule (b) (4) Table 1 (b) (4) and skip the PM doses. The recommended maintenance dosage in this group is 30 mg once daily.

Pediatric Patients 6 Years of Age and Older and Weighing at Least 20 kg with Moderate to Severe Plaque Psoriasis (b) (4)

For initial dose titration, titrate OTEZLA using only the AM schedule (b) (4) Table 2 (b) (4) for the appropriate body weight category and skip the PM doses. The recommended maintenance dosage is OTEZLA 30 mg once daily for pediatric patients who weigh at least 50 kg and OTEZLA 20 mg once daily for pediatric patients who weigh 20 kg to less than 50 kg.

<table>
<tr><th colspan="3">Table 2. Relevant Product Information for Otezla XR and Otezla</th></tr>
<tr><td>Product Name</td><td colspan="2">Otezla XR</td><td>Otezla (NDA 205437)</td></tr>
<tr><td>How Supplied</td><td colspan="2"><table>
<tr><th>Package configuration</th><th>Tablet strength</th></tr>
<tr><td>28-day treatment initiation pack</td><td>41-tablet blister titration pack including tablets for titration and maintenance dosage:
OTEZLA:
4 tablets (10 mg each), 4 tablets (20 mg each), and 19 tablets (30 mg each)
and
OTEZLA XR:
14 tablets (75 mg each)</td></tr>
<tr><td>Bottles of 30</td><td>OTEZLA XR: 30 tablets (75 mg each)</td></tr>
</table></td><td><table>
<tr><th>Package configuration</th><th>Tablet strength</th></tr>
<tr><td colspan="2">Configurations for 30 mg BID Dosage</td></tr>
<tr><td>28-day treatment initiation pack</td><td>55-tablet blister pack including tablets for titration and maintenance dosage: 4 tablets (10 mg each), 4 tablets (20 mg each), and 47 tablets (30 mg each)</td></tr>
<tr><td>60-count bottle</td><td>30 mg</td></tr>
<tr><td colspan="2">Configurations for 20 mg BID Dosage</td></tr>
<tr><td>28-day treatment initiation pack</td><td>55-tablet blister pack including tablets for titration and maintenance dosage: 4 tablets (10 mg each) and 51 tablets (20 mg each)</td></tr>
<tr><td>60-count bottle</td><td>20 mg</td></tr>
</table></td></tr>
<tr><td>Storage</td><td colspan="2">Store OTEZLA XR tablets (b) (4)</td><td>Store OTEZLA tablets below 30°C (86°F).</td></tr>
</table>

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,[b] along with postmarket medication error data, we reviewed the following Otezla XR labels and labeling submitted by Amgen Inc.

- Prescribing Information received on October 30, 2024, available from \\Cdsesub1\evsprod\NDA210745\0017\m1\us\114-labeling\draft\labeling\a-otezla-us-pi-v9-qd-xr-c-2024-xxxx.docx
- Container label(s) received on October 30, 2024
- Carton labeling received on October 30, 2024

B.2 Container Label and Carton Labeling Images

Container Label:

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

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04/07/2025 02:28:33 PM

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: 2/4/2025

TO: Division of Rheumatology and Transplant Medicine (DRTM)
Office of Immunology and Inflammation (OII)

FROM: Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Decline to conduct on-site inspections**

RE: NDA 210745

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

Rationale

QPS-MRA, (6280 Sunset Drive) South Miami: The Office of Inspections and Investigations (OII) conducted an inspection for the clinical site in May 2023. The inspection was conducted under the following submission: BLA non-responsive.

OSIS concluded that the data from the reviewed studies were reliable.

Altasciences Clinical Research, Inc., Laval: OII conducted an inspection for the clinical site in June 2024. The inspection was conducted under the following submission: NDA non-responsive.

OSIS concluded that data from the reviewed studies were reliable.

(b) (4): OSIS conducted an inspection for the analytical site in (b) (4) (b) (4). The inspection was conducted under the following submission: NDA non-responsive.

OSIS concluded that data from the reviewed studies were reliable.

Sites

Facility Type	Facility Name	Facility Address
Clinical	QPS-Miami Research Associates	6280 Sunset Drive, Suite 600, South Miami, FL
Clinical	Altasciences Clinical Research, Inc.	10103, 10203, and 10183 Metcalf Avenue, Overland Park, KS
Analytical	(b) (4)	

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02/04/2025 11:17:18 AM

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

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

Memorandum

Date: August 16, 2018

To: Ngoc-Linh Do, Regulatory Project Manager, (DPARP)

From: Meeta Patel, Pharm.D., Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Kathleen Klemm, Team Leader, OPDP

Subject: OPDP Labeling Comments for Otezla XR (apremilast) extended release tablets, for oral use

NDA: 210745

In response to DPARP's consult request dated January 10, 2018, OPDP has reviewed the proposed product labeling (PI) and carton and container labeling for the original NDA submission for Otezla XR.

PI: OPDP has reviewed the proposed labeling are based on the draft PI received by electronic mail from DPARP on August 9, 2018. We have no comments at this time.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling submitted by the Sponsor to the electronic document room on December 14, 2017, and our comments are provided below.

On the Draft Blister 75 mg Card, there is a titration from Otezla to Otezla XR. However, the dosage statement says, "(b) (4) ." This may be confusing to patients. We recommend changing it to (emphasis added), "(b) (4) ."

Thank you for your consult. If you have any questions, please contact Meeta Patel at (301) 796-4284 or meeta.patel@fda.hhs.gov.

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/s/

MEETA N PATEL
08/16/2018

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: 6/1/2018

TO: Division of Pulmonary, Allergy and Rheumatology Products
Office of Drug Evaluation II

FROM: Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Recommendation to accept data without an on-site inspection**

RE: NDA 210745

The Division of New Drug Bioequivalence Evaluation (DNDBE) within the Office of Study Integrity and Surveillance (OSIS) recommends accepting data without an on-site inspection. The rationale for this decision is noted below.

Rationale

OSIS recently inspected the site listed below. The inspectional outcome from the inspections was classified as No Action Indicated (NAI).

Inspection Site

Facility Type	Facility Name	Facility Address
Analytical	(b) (4)	

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/s/

SHILA S NKAH
06/01/2018

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: May 7, 2018

TO: Billy Dunn, M.D.
Director
Division of Neurology Products
Office of Drug Evaluation I, OND

FROM: Himanshu Gupta, Ph.D.
Division of Generic Drug Bioequivalence Evaluation
Office of Study Integrity and Surveillance
Office of Translational Sciences

THROUGH: Seongeun Cho, Ph.D.
Director
Division of Generic Drug Bioequivalence Evaluation
Office of Study Integrity and Surveillance
Office of Translational Sciences

SUBJECT: Routine inspection of Covance Clinical Research Unit, Daytona Beach, FL.

Inspection Summary

The Office of Study Integrity and Surveillance (OSIS) arranged an inspection of non-responsive) conducted at Covance Clinical Research Unit, Daytona Beach, FL.

No objectionable conditions were observed and Form FDA 483 was not issued at the inspection close-out. The final inspection classification is No Action Indicated (NAI).

After reviewing the inspectional findings, I conclude the data from the audited study are reliable. Thus, the data from Study non-responsive and other studies of similar design are acceptable for further Agency review.

Inspected Study

BLA non-responsive.

Study Number: non-responsive
Study Title:

Dates of conduct: non-responsive

Clinical site: Covance Clinical Research Unit
1900 Mason Avenue, Suite 140
Daytona Beach, FL 32117

ORA investigator Craig A. Garmendia inspected Covance Clinical Research Unit, Daytona Beach, FL from March 5-8, 2018.

The inspection included a thorough examination of study records, including the informed consent process, protocol compliance, institutional review board records, drug accountability and storage, and adverse events.

At the conclusion of the inspection, investigator Craig A. Garmendia did not observe any objectionable conditions and did not issue Form FDA 483 to the clinical site.

Conclusion

After reviewing the EIR and inspectional findings, I conclude the data from the audited study are reliable. Therefore, I recommend accepting the data from non-responsive for further review. In addition, the data from studies of similar design submitted to pending applications (Attachment 1) are acceptable for further Agency review.

Based on the inspectional findings, studies of similar design conducted between the previous inspection (June, 2014) and the end of the current surveillance interval are acceptable for review by the Agency without an inspection.

Himanshu Gupta, Ph.D.
Staff Fellow

Final Classification:

NAI- Covance Clinical Research Unit
Daytona Beach, FL
FEI#: 3004834650

cc:
OTS/OSIS/Kassim/Choe/Mitchell/Fenty-Stewart/Nkah
OTS/OSIS/DNDBE/Bonapace/Dasgupta/Ayala/Biswas/
OTS/OSIS/DGDBE/Cho/Choi/Skelly/Au/Gupta

Draft: HG 04/25/2018, 4/30/2018, 5/7/2018
Edit: SA 04/26/2018; 05/01/2018, 5/3/2018; JC 5/3/2018

ECMS: Cabinets/CDER_OC/OSI/OSIS--Office of Study Integrity and Surveillance/INSPECTIONS/BE Program/CLINICAL SITES/Covance Clinical Research Unit, Daytona Beach, FL/BLA non-responsive

OSIS File #: non-responsive), BE 8011 (NDA 210745)

FACTS: 11809389

Attachment 1
Studies in support of Pending Applications

Application #	Study #	Drug Name(s)	Dates of conduct
BLA non-responsive	non-responsive		
NDA 210745	Study CC-10004-CP-035	apremilast extended release	Sep – Nov 2016

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/s/

HIMANSHU GUPTA
05/07/2018

STANLEY AU
05/07/2018
Acting Team Lead

SEONGEUN CHO
05/07/2018

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: May 3, 2018

TO: Curtis Rosebraugh, M.D., M.P.H.
Director
Office of Drug Evaluation II
Office of New Drugs

FROM: Amanda Lewin, Ph.D.
Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

THROUGH: Arindam Dasgupta, Ph.D.
Deputy Director
Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: Routine inspection of Covance CRU Inc., Madison, WI.

Inspection Summary

The Office of Study Integrity and Surveillance (OSIS) arranged an inspection of study CC-10004-CP-035 (NDA 210745) conducted at Covance CRU Inc., Madison, WI.

No objectionable conditions were observed and Form FDA 483 was not issued at the inspection close-out. The final inspection classification is No Action Indicated (NAI).

After reviewing the inspectional findings, I conclude the data from the audited study is reliable. Thus, I recommend that the data from study CC-10004-CP-035 and other studies of similar design be accepted for further Agency review.

Inspected Study:

NDA 210745

Study Number: CC-10004-CP-035
Study Title: "A Phase 1, Open Label, Randomized, Two Part Study to Evaluate the Pharmacokinetic Exposure of a Once-Daily (QD) Apremilast Formulation Relative to the Twice-Daily (BID) Reference Immediate

Release (IR) Tablet and the Effect of Food on the QD Apremilast Formulation in Healthy Subjects."

Dates of conduct: 9/7/2016 – 11/22/2016

Clinical site: Covance CRU Inc.
3402 Kinsman Blvd
Madison, WI

ORA investigator Corey K Reno (BIMOW) inspected Covance CRU Inc., Madison, WI from April 2-6, 2018.

The inspection included a thorough examination of study records (paper-based), subject records, informed consent process, protocol compliance, institutional review board approvals, sponsor and monitor correspondence, test article accountability and storage, randomization, adverse events, and case report forms.

At the conclusion of the inspection, investigator Reno did not observe any objectionable conditions and did not issue Form FDA 483 to the clinical site.

Conclusion:

After reviewing the inspectional findings, I conclude the data from the audited studies are reliable. Therefore, I recommend that the data from study CC-10004-CP-035 (NDA 210745) be accepted for further review.

Based on the inspectional findings, studies of similar design conducted between the previous inspection (August 2015) and the end of the current surveillance interval should be accepted for review by the Agency without an inspection.

Amanda Lewin, Ph.D.
Pharmacologist

Final Classification:

NAI- Covance CRU Inc.
Madison, WI
FEI#: 1046818

cc:
OTS/OSIS/Kassim/Choe/Mitchell/Fenty-Stewart/Nkah
OTS/OSIS/DNDBE/Bonapace/Dasgupta/Ayala/Biswas/Lewin
OTS/OSIS/DGDBE/Cho/Choi/Skelly/Au

Draft: AL 5/2/2018
Edit: GB 5/02/2018; AD 5/02/2018

ECMS: Cabinets/CDER_OTS/Office of Study integrity and Surveillance/INSPECTIONS/BE Program/Clinical Sites/Covance, Inc., Madison, WI, USA

OSIS File #: BE 8011

FACTS: 11826550

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/s/

AMANDA E LEWIN
05/03/2018

GOPA BISWAS
05/03/2018

ARINDAM DASGUPTA
05/03/2018