

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

761349Orig1s000

OTHER REVIEW(S)

**Division of Dermatology and Dentistry
Associate Director for Labeling Review of
the Prescribing Information**

Product Title	COSENTYX® (secukinumab) injection, for subcutaneous or intravenous use
Applicant	Novartis Pharmaceuticals Corporation
Application/Supplement Number	BLA
Type of Application/Submission ¹	New BLA
Is Proposed Labeling in “Old” Format? (Y/N)	N
Is Labeling Being Converted to PLR? (Y/N)	N
Is Labeling Being Converted to PLLR? (Y/N)	N
Proposed Indication/change	New formulation of Cosentyx (secukinumab): 125 mg/ ^{(b) (4)} solution for administration via IV infusion
Approved Indication(s)	The treatment of: <ul style="list-style-type: none"> • moderate to severe plaque psoriasis in patients 6 years and older who are candidates for systemic therapy or phototherapy • active psoriatic arthritis (PsA) in patients 2 years of age and older • adults with active ankylosing spondylitis (AS) • adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation • active enthesitis-related arthritis (ERA) in patients 4 years of age and older
Date FDA Received Application	December 7, 2022
Review Classification (Priority/Standard)	Standard
Action Goal Date	October 7, 2023
Review Date	October 5, 2023
Reviewer	Matthew White

INTRODUCTION

Novartis submitted BLA 761349, proposing a new formulation of Cosentyx (secukinumab) (125 mg ^{(b) (4)} solution for administration via IV infusion) a human interleukin-17A antagonist for the treatment of psoriatic arthritis (PsA), ankylosing spondylitis (AS), and non-radiographic axial spondylarthritis (nr-axSpA) in adults. Cosentyx (secukinumab) injection for subcutaneous administration is currently approved under BLA 125504 for the treatment of:

- moderate to severe plaque psoriasis in patients 6 years and older who are candidates for systemic therapy or phototherapy
- active psoriatic arthritis (PsA) in patients 2 years of age and older
- adults with active ankylosing spondylitis (AS)
- adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation
- active enthesitis-related arthritis (ERA) in patients 4 years of age and older

The following dosage forms and strengths of Cosentyx for subcutaneous administration are currently approved:

- Injection: 300 mg/2 mL solution in a single-dose UnoReady® pen and in a single-dose prefilled syringe
- Injection: 150 mg/mL solution in a single-dose Sensoready® pen and in a single-dose prefilled syringe.
- Injection: 75 mg/0.5 mL solution in a single-dose prefilled syringe (for pediatric patients)

REVIEW

The proposed indications for Cosentyx for intravenous (IV) infusion (the treatment of psoriatic arthritis (PsA), ankylosing spondylitis (AS), and non-radiographic axial spondylarthritis [nr-axSpA] in adults) are managed by the Division of Rheumatology and Transplant Medicine (DRTM). However, Novartis proposes to use the same label for Cosentyx for IV infusion and for subcutaneous injection and labeling sections managed by the Division of Dermatology and Dentistry (DDD) are impacted by the proposed changes implemented for the IV infusion formulation.

This review describes the updates implemented to the DDD managed sections of the PI to help ensure that it

- Is consistent with labeling guidance recommendations and with CDER labeling policies, as appropriate,
- Conveys the essential scientific information needed for safe and effective use of the drug,
- Is clinically meaningful and scientifically accurate,
- Is a useful communication tool for health care practitioners, and
- Is consistent with other PI with the same active moiety, drug class, or similar indication, as appropriate

The following groups provided input concerning the updates to the DDD managed sections of the PI:

- Tatiana Oussova, MD, MPH (Deputy Director for Safety), Maryjoy Mejia, MD, Amy Weitach, DO, MS (Clinical)

The differences between the label approved under BLA 125504 S-067 (approved July 24, 2023) and the agreed upon label for BLA 761349 are shown in the following review of the PI.

HIGHLIGHTS OF PRESCRIBING INFORMATION

-

(b) (4)

Comment: The addition of the intravenous route of administration (ROA) on the same line as the subcutaneous route of administration is consistent with the recommendation outlined on page 11 of the guidance for industry Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products- Content and Format. DDD concurs with the change.

- **Dosage and Administration**

(b) (4)

Comment: DDD concurs with the addition of the ROA to the recommended dosage subheadings for PsO. This is consistent with the changes made to the recommended dosage subheadings for PsA, AS, and nr-axSpA.

- **Dosage Forms and Strengths**

(b) (4)

Comment: DDD concurs with the addition of the “Subcutaneous Injection” subheading. An “Intravenous Infusion” subheading was also added. This is consistent with the format of other biologics with subcutaneous injection and IV infusion formulations (i.e., Stelara (ustekinumab) injection).

FULL PRESCRIBING INFORMATION

- **Dosage and Administration – Subsection 2.2 Important Administration Instructions**

(b) (4)

Comment: DDD concurs with moving the important administration instructions subsection up to 2.2 from 2.7. The “Testing and Procedures Prior to Treatment Initiation” is the first subsection. It is followed by the “Important Administration Instructions” subsection (includes important information to convey prior to administering Cosentyx) and then by the “Recommended Dosage” subsections. This is consistent with the concept outlined in the Labeling Review Tool that when certain dosage- or administration-related information is particularly critical to the safe and effective use of the drug (e.g., lack of knowledge of this information or nonadherence to a recommendation could have serious consequences for patients), this information should appear as the first information presented within the dosage and administration section. DDD also concurs with the addition of the ROA the administration instructions. This helps differentiate instructions for subcutaneous injection verses intravenous infusion.

- **Dosage and Administration – Subsection 2.3 Recommended Dosage in Plaque Psoriasis**

(b) (4)

Comment: DDD concurs with the addition of the ROA to the recommended dosage subheading. This is consistent with the format of other biologics with subcutaneous injection and IV infusion formulations (i.e., Stelara (ustekinumab) injection).

- **Dosage and Administration – Preparation for Use of COSENTYX UnoReady Pen, Sensoready Pen and Prefilled Syringes**

(b) (4)

Comment: DDD concurs with the addition of the ROA to the subsection with information for preparing the Cosentyx UnoReady Pen, Sensoready Pen, and Prefilled Syringes. These dosage forms are only for subcutaneous injection. The

ROA is also conveyed in the subsection added containing the information for the preparation and administration of Cosentyx for intravenous use.

- **Dosage Forms and Strengths**

(b) (4)

Comment: DDD concurs with the addition of the “Subcutaneous Injection” subheading. An “Intravenous Infusion” subheading was also added. This is consistent with the format of other biologics with subcutaneous injection and IV infusion formulations (i.e., Stelara (ustekinumab) injection).

- **Adverse Reactions – Subsection 6.1 Clinical Trials Experience**

(b) (4)

DDD concurs with the addition of the “Adverse Reactions in Clinical Trials of Subcutaneous COSENTYX” subheading. An “Adverse Reactions of Intravenous COSENTYX” subheading was also added.

- **Use in Specific Populations – Subsection 8.4 Pediatric Use**

(b) (4)

Comment: DDD concurs with the addition of the “Subcutaneous Injection” subheading. An “Intravenous Infusion” subheading was also added.

- **Description**

(b) (4)

Comment: DDD concurs with the addition of “for Subcutaneous Use” to the Cosentyx injection subheading. A “Cosentyx Injection for Intravenous Use” subheading was also added.

- **Clinical Pharmacology – Subsection 12.3 Pharmacokinetics**

(b) (4)

Comment: DDD concurs with the addition of information concerning the ROA to the Pharmacokinetics subsection. This differentiates information delineated from subcutaneous Cosentyx versus intravenous Cosentyx.

- **Clinical Studies**

(b) (4)

Comment: DDD concurs with the addition of information concerning the ROA to the Clinical Studies section. This differentiates information delineated from subcutaneous Cosentyx versus intravenous Cosentyx. This is also consistent with the recommendation of the Labeling Review Tool to include the route(s) of administration in the study design description.

- **How Supplied Storage and Handling – Subsection 16.1 How Supplied**

(b) (4)

Comment: DDD concurs with the addition of the “Cosentyx injection for subcutaneous use” subheading. A “Cosentyx injection for intravenous use” subheading was also added. This is consistent with the format of other biologics with subcutaneous injection and IV infusion formulations (i.e., Stelara (ustekinumab) injection).

- **How Supplied Storage and Handling – Subsection 16.2 Storage and Handling**

(b) (4)

Comment: DDD concurs with the addition of the dosage forms to the instructions to refrigerate Cosentyx for clarity.

- **Patient Information**

(b) (4)

Comment: DDD concurs with the addition of the ROA to the instructions for Injection Technique. This is consistent with changes made to Dosage and Administration subsections 2.2 and 2.9.

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/s/

MATTHEW E WHITE
10/05/2023 07:26:43 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 14, 2023

To: Saharat Patanavanich, PharmD, BCACP
Regulatory Project Manager
Division of Rheumatology and Transplant Medicine (DRTM)

Through: LaShawn Griffiths, MSHS-PH, BSN, RN
Associate Director for Patient Labeling
Division of Medical Policy Programs (DMPP)

Marcia Williams, PhD
Team Leader, Patient Labeling
Division of Medical Policy Programs (DMPP)

From: Mary Carroll, BSN, RN
Patient Labeling Reviewer
Division of Medical Policy Programs (DMPP)

Kyle Snyder, Pharm.D.
Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

Subject: Review of Patient Labeling: Medication Guide (MG)

Drug Name (established name): COSENTYX (secukinumab)

Dosage Form and Route: injection, for intravenous use

Application Type/Number: BLA 761349

Applicant: Novartis Pharmaceuticals Corporation

1 INTRODUCTION

On December 7, 2022, Novartis Pharmaceuticals Corporation submitted for the Agency's review a Biologics License Application (BLA) 761349 for COSENTYX (secukinumab) injection, for intravenous use. The purpose of this submission is to seek market approval for:

- Psoriatic Arthritis (PsA), Ankylosing Spondylitis (AS), and Non-radiographic Axial Spondyloarthritis (nr-axSpA) for intravenous use provided as solution in single-dose 125mg/5mL vial.

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 Rheumatology and Transplant Medicine (DRTM) on February 7, 2023 for DMPP and OPDP to review the Applicant's proposed Medication Guide (MG) for COSENTYX (secukinumab) injection, for intravenous use.

2 MATERIAL REVIEWED

- Draft COSENTYX (secukinumab) MG received on December 7, 2022, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on August 31, 2023.
- Draft COSENTYX (secukinumab) Prescribing Information (PI) received on December 7, 2022, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on August 31, 2023.
- Approved COSENTYX (secukinumab) labeling dated [REDACTED] (b) (4).

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.

In our collaborative review of the MG we:

- simplified wording and clarified concepts where possible
- ensured that the MG is consistent with the Prescribing Information (PI)
- rearranged information due to conversion of the PI to Physicians Labeling Rule (PLR) format
- removed unnecessary or redundant information

- ensured that the MG is 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 meet the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006).

4 CONCLUSIONS

The MG is 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 is 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.

Please let us know if you have any questions.

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/s/

MARY E CARROLL
09/14/2023 11:54:11 AM

KYLE SNYDER
09/14/2023 11:58:41 AM

MARCIA B WILLIAMS
09/14/2023 12:01:17 PM

LASHAWN M GRIFFITHS
09/14/2023 12:19:52 PM

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

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

Memorandum

Date: September 11, 2023

To: Saharat Patanavanich, Regulatory Project Manager
Division of Rheumatology and Transplant Medicine (DRTM)

From: Kyle Snyder, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Adewale Adeleye, Team Leader, OPDP

Subject: OPDP Labeling Comments for COSENTYX® (secukinumab) injection, for subcutaneous or intravenous use (Cosentyx)

BLA: 761349

Background:

In response to DRTM's consult request dated February 6, 2023, OPDP has reviewed the proposed Prescribing Information (PI), Medication Guide, and carton and container labeling for the original BLA submission for Cosentyx.

PI/PPI/Medication Guide/IFU:

OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on August 31, 2023, and we do not have any comments at this time.

A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed for the proposed Medication Guide, and comments will be sent under separate cover.

Carton and Container Labeling:

OPDP's review of the proposed carton and container labeling is based on the draft labeling submitted by the sponsor to the electronic document room on August 14, 2023, and we do not have any comments at this time.

Thank you for your consult. If you have any questions, please contact Kyle Snyder at 240-402-8792 or kyle.snyder@fda.hhs.gov.

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/s/

KYLE SNYDER
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DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Drug Evaluation and Research
Office of New Drugs
Division of Pediatrics and Maternal Health
Silver Spring, MD 20993
Telephone 301-796-2200
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M E M O R A N D U M

From: Ndidi Nwokorie, MD, Medical Officer
Division of Pediatrics and Maternal Health (DPMH)
Office of Rare Diseases, Pediatrics, Urologic & Reproductive
Medicine (ORPURM)
Office of New Drugs (OND)

Through: Mona Khurana, MD, Pediatric Team Leader
DPMH, ORPURM, OND

John J. Alexander, MD, MPH, Deputy Director
DPMH, ORPURM, OND

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

Subject: Pediatric Study Plan Review and Development of Pediatric
Research Equity Act Postmarketing Requirements

Drug: secukinumab

Proprietary Name: COSENTYX

Application Number: BLA 761349

Applicant: Novartis Pharmaceuticals¹

Proposed Indications: (b) (4)

Approved Indication: Adult and pediatric psoriasis in patients 6 years of age and older
Adult and pediatric psoriatic arthritis (PsA) in patients 2 years of age and older
Adult ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA)
Adult and pediatric enthesitis-related arthritis (ERA) in patients at least 4 years of age and older

Dosage Form solution for intravenous infusion

Dosage Strength: 125 mg/5 mL

Route of Administration: Intravenous (i.v.)

Materials Reviewed:

- Accessed from the Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations
 - Approval Letter_BLA125504/0 from January 21, 2015_ accessed on 06-13-2023
 - Approval letter BLA 125504/S-001 and 002 from January 15, 2016_ access on 06-20-2023

¹ Hereafter referred to as “the Applicant”.

- Approval Letter BLA 125504/s-050 and 051 from December 22, 2021 accessed on 06-20-2023
- Approved USPI² for Cosentyx_BLA-125504 accessed on 06-13-2023
- BLA 761349 secukinumab IV_DPMH Consult Request Form in DARRTS on 05-31-2023
- Documents submitted to DocuBridge under BLA 761349
 - Cover Letter dated 12-7-2022
 - Pediatric Study Plan submitted 05-22-2023

Consult Request:

DRTM consulted DPMH to opine on the pediatric safety of a new proposed i.v. dosage form of secukinumab, which has a higher predicted maximum concentration (C_{max}) compared to the approved subcutaneous (s.c.) dosage form. DRTM also asked DPMH for assistance in developing post marketing requirements (PMRs) to address the Pediatric Research Equity Act (PREA) for this new dosage form.

I. Regulatory Background of Secukinumab

DRTM approved the subcutaneous administration of Cosentyx (secukinumab) under BLA 125504 on 1/21/2015 for the **treatment of moderate to severe plaque psoriasis** in adult patients who are candidates for systemic therapy or phototherapy³. At the time of approval, the Division granted a partial waiver in patients from birth to 6 years of age because necessary studies are impossible or highly impracticable and issued the following PREA PMR:

PMR 2848-1 Conduct a study to evaluate the safety and efficacy of secukinumab in pediatric subjects ≥ 6 years of age with plaque psoriasis.

Final Protocol Submission:	1/2022
Study Completion:	12/2025
Final Report Submission:	2/2026

FDA subsequently approved s.c. secukinumab for the **treatment of psoriatic arthritis (PsA)(S-001) and ankylosing spondylitis (AS)(S-002)** in adults on January 15, 2016. With these approvals, the Division granted a full waiver of PREA requirements for both indications on the basis that necessary studies are impossible or highly impracticable. The adult dosing for all three approved indications is 150 mg or 300 mg s.c., given on weeks 0, 1, 2, 3, and 4 and then every 4 weeks thereafter.

On December 22, 2021, the Division approved the s.c. dosage form of secukinumab in pediatric patients **2 years of age and older for the treatment of active juvenile psoriatic arthritis (JPsA) (S-051) and in pediatric patients 4 years of age and older with active enthesitis-related arthritis (ERA)**. Support for both approvals was based on a double-blind, placebo-controlled, event-driven, randomized withdrawal design, phase 3 trial that demonstrated the

² United States Prescribing Information

³ Approval Letter 1-21-2015

clinical safety and efficacy of secukinumab compared with placebo in active JPsA or active ERA. The approved s.c. dosing for pediatric patients is 75 mg (for patients weighing >15 kg and <50 kg) and 150 mg (for patients weighing \geq 50 kg) to be administered at weeks 0, 1, 2, 3, and 4 and then every 4 weeks thereafter.

The Applicant is developing a new i.v. infusion dosage form of secukinumab for **treatment of PsA, AS and nr-axSpA**. The Division issued an Agreed initial Pediatric Study Plan (iPSP) to the Applicant on July 30, 2019, that includes a plan to request a full waiver of PREA requirements for all three indications on the basis that necessary studies are impossible or highly impracticable to complete. Since the initial iPSP agreement, the Division's thinking regarding the feasibility of studies in pediatric patients with juvenile psoriatic arthritis (JPsA) has evolved due to recent understanding of the high degree of similarity between adults and pediatric patients with PsA.⁴ The Division conveyed this new thinking to the Applicant at a Type B meeting held on December 8, 2021⁵ where the Division stated that waivers for pediatric assessments on the basis that necessary studies in patients with JPsA are impossible or highly impracticable are no longer acceptable and recommended Applicant consider an exposure-matching approach to support extrapolation of efficacy established in adults with PsA to pediatric patients with JPsA.

Subsequently, the Applicant submitted an amended Agreed iPSP containing a plan to request full waivers for the AS and nr-axSpA indications and a Pediatric Study Plan (PSP) detailing a plan to request a partial waiver in patients less than 2 years of age and a deferral of assessment in patients 2 years and older for JPsA based on an extrapolation strategy relying on data from adult PsA patients and pediatric juvenile arthritis (JIA) patients.

II. Pediatric Development Strategy for JPsA

(b) (4)

⁴ [Accelerating Drug Development for Polyarticular Juvenile Idiopathic Arthritis \(pJIA\) | Center of Excellence in Regulatory Science and Innovation \(umd.edu\)](#)

⁵ Pediatric Study Plan submitted to BLA 761349 on 5/22/2023

(b) (4)

III. Conclusion

The Applicant has proposed:

(b) (4)

IV. Recommendation

DPMH recommends, based on the review of this PSP for a new i.v. dosage of secukinumab, the Applicant should:

1. plan to request a partial waiver in pediatric patients from birth to less than 2 years of age on the basis that necessary studies are impossible or highly impracticable.

⁸ Presentation by DDD medical officer, Maryjoy Mejia, MD, at Internal Meeting on July 12, 2023.

2. plan to request a deferred assessment in patients 2 years to 17 years of age because the product is expected to be ready for approval in adults before the pediatric study(ies) will be completed.

Therefore, DPMH recommends that the Division issue the following PREA PMR at the time of adult approval:

A deferred pediatric assessment consisting of PK analysis of the [REDACTED] (b) (4)
[REDACTED] in pediatric patients 2
to 17 years of age with JPsA, [REDACTED] (b) (4)
pending PK analysis.

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/s/

NDIDI N NWOKORIE
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JOHN J ALEXANDER
08/23/2023 11:24:12 AM
Signing for Dr. Mona Khurana

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)

Date of This Memorandum: August 15, 2023
Requesting Office or Division: Division of Rheumatology and Transplant Medicine (DRTM)
Application Type and Number: BLA 761349
Product Name, Dosage Form, and Strength: Cosentyx
(secukinumab)
injection,
125 mg/5 mL
Applicant/Sponsor Name: Novartis
TTT ID #: 2022-2997-1
DMEPA 1 Safety Evaluator: Sarah K. Vee, PharmD
DMEPA 1 Team Leader: Idalia E. Rychlik, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container label and carton labeling received on August 14, 2023 for Cosentyx. The Division of Rheumatology and Transplant Medicine (DRTM) requested that we review the revised container label and carton labeling for Cosentyx (Appendix A) to determine if it is 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 Vee, S. Label and Labeling Review for Cosentyx (BLA 761349). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2023 AUG 04. TTT ID No.: 2022-2997.

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/s/

SARAH K VEE
08/15/2023 01:17:08 PM

IDALIA E RYCHLIK
08/15/2023 01:49:42 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:	August 4, 2023
Requesting Office or Division:	Division of Rheumatology and Transplant Medicine (DRTM)
Application Type and Number:	BLA 761349
Product Name, Dosage Form, and Strength:	Cosentyx (secukinumab) injection, 125 mg/5 mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Novartis
FDA Received Date:	December 7, 2022 and July 28, 2023
TTT ID #:	2022-2997
DMEPA 1 Safety Evaluator:	Sarah K. Vee, PharmD
DMEPA 1 Team Leader:	Idalia E. Rychlik, PharmD

1 REASON FOR REVIEW

As part of the approval process for Cosentyx (secukinumab) injection, the Division of Rheumatology and Transplant Medicine (DRTM) requested that we review the proposed Cosentyx prescribing information, container label, and carton labeling for areas of vulnerability that may lead to medication errors.

2 REGULATORY HISTORY

The original BLA 125504 was approved on January 21, 2015, for the indication of moderate to severe plaque psoriasis. Supplemental BLAs were later approved for the indications of Psoriatic Arthritis (PsA), Ankylosing Spondylitis (AS), Non-radiographic Axial Spondyloarthritis (nr-axSpA), pediatric plaque psoriasis, and most recently juvenile idiopathic arthritis (juvenile PsA and enthesitis-related arthritis). Currently 300 mg/2 mL UnoReady pen, 150 mg/mL Sensoready pen, 75 mg/0.5 mL and 150 mg/mL prefilled syringe are approved for subcutaneous injection.

Novartis submitted BLA 125504/S-055 on 25-Feb-2022 to propose to remove the lyophilized powder formulation from the label. Supplement 055 was approved on July 24, 2023.

Novartis submitted Cosentyx (secukinumab) injection for intravenous use under BLA 761349 on December 7, 2022.

3 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 Review	
Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B – N/A
ISMP Newsletters*	C – N/A
FDA Adverse Event Reporting System (FAERS)*	D – N/A
Other	E – N/A
Labels and Labeling	F

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

4 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

Novartis submitted BLA 761349 to propose a new intravenous formulation (125 mg/5 mL) for the indications of PsA, AS, and nr-axSpA for secukinumab. Novartis proposes to share the currently approved prescribing information (PI) for BLA 125504 for the new intravenous formulation.

We reviewed the proposed label and labeling for Cosentyx to determine whether there are deficiencies that may lead to medication errors and other areas of improvement. The proposed PI, container labels, and carton labeling may be improved to promote the safe use of the product from a medication error perspective. We provide our recommendations below in Section 5.1 for the Division and Section 5.2 for Novartis.

5 CONCLUSION & RECOMMENDATIONS

We conclude that the proposed PI, container labels and carton labeling for Cosentyx may be improved to promote the safe use of the product. We provide specific recommendations to the Division in Section 5.1 and the Applicant in Section 5.2 below.

5.1 RECOMMENDATIONS FOR DIVISION OF RHEUMATOLOGY AND TRANSPLANT MEDICINE (DRTM)

A. Prescribing Information

1. Dosage and Administration Section



5.2 RECOMMENDATIONS FOR NOVARTIS

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

A. General Comments (Container labels & Carton Labeling)

1. As currently presented the lot number and expiration date are not defined. Confirm the location of this information and include the format of the expiration date. We recommend 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.
2. Revise the route of administration statement from “(b) (4)
(b) (4) to read “For Intravenous Infusion After Dilution”

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Cosentyx received on July 28, 2023 from Novartis.

Table 2. Relevant Product Information for Cosentyx	
Initial Approval Date	N/A
Nonproprietary Name	secukinumab
Indication	<ul style="list-style-type: none"> • moderate to severe plaque psoriasis in patients 6 years and older who are candidates for systemic therapy or phototherapy • active psoriatic arthritis (PsA) in patients 2 years of age and older • adults with active ankylosing spondylitis (AS) • adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation • active enthesitis-related arthritis (ERA) in patients 4 years of age and older
Route of Administration	Subcutaneous injection and intravenous infusion
Dosage Form	For injection and injection
Strength	<p>Subcutaneous Injection</p> <ul style="list-style-type: none"> • <u>Injection</u>: 300 mg/2 mL solution in a single-dose UnoReady[®] pen and in a single-dose prefilled syringe. • <u>Injection</u>: 150 mg/mL solution in a single-dose Sensoready[®] pen and in a single-dose prefilled syringe. • <u>Injection</u>: 75 mg/0.5 mL solution in a single-dose prefilled syringe (for pediatric patients). <p>Intravenous Infusion</p> <p><u>Injection</u>: 125 mg/5 mL (b) (4) solution in a single-dose vial (for healthcare professional use only).</p>
Dose and Frequency	<ul style="list-style-type: none"> • Plaque Psoriasis: <ul style="list-style-type: none"> ○ <i>Adults</i>: Recommended dosage is 300 mg by subcutaneous injection at Weeks 0, 1, 2, 3, and 4 followed by 300 mg every 4 weeks. For some patients, a dose of 150 mg may be acceptable. ○ <i>Pediatric Patients 6 Years and Older</i>: Recommended weight-based dosage is administered by subcutaneous injection at Weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter. <ul style="list-style-type: none"> ▪ For patients < 50 kg (at the time of dosing), the dose is 75 mg.

	<ul style="list-style-type: none"> ▪ For patients ≥ 50 kg (at the time of dosing), the dose is 150 mg. • Psoriatic Arthritis: <p>Recommended Adult Subcutaneous Dosages:</p> <ul style="list-style-type: none"> ○ For PsA patients with coexistent moderate to severe plaque psoriasis, use the dosage and administration for plaque psoriasis. ○ For other PsA patients, administer with or without a loading dosage. <ul style="list-style-type: none"> ▪ <u>With a loading dosage</u>: 150 mg at Weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter ▪ <u>Without a loading dosage</u>: 150 mg every 4 weeks ▪ If a patient continues to have active PsA, consider a dosage of 300 mg every 4 weeks. <p>Recommended Pediatric Subcutaneous Dosages: Patients 2 years and older, administer by subcutaneous injection at Weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter.</p> <ul style="list-style-type: none"> ○ For patients ≥ 15 kg and < 50 kg the dose is 75 mg. ○ For patients ≥ 50 kg the dose is 150 mg. <p>Recommended Adult Intravenous Dosage: The recommended intravenous dosage regimen is 6 mg/kg given at Week 0 as a loading dose, followed by 1.75 mg/kg every 4 weeks thereafter.</p> <p>Total doses exceeding 300 mg per infusion are not recommended for the 1.75 mg/kg maintenance dose in patients with PsA.</p> • Ankylosing Spondylitis: <p>Recommended Subcutaneous Dosage Regimen: Administer with or without a loading dosage.</p> <p>The recommended dosages are:</p> <ul style="list-style-type: none"> ○ <u>With a loading dosage</u>: 150 mg at Weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter. ○ <u>Without a loading dosage</u>: 150 mg every 4 weeks. ○ If a patient continues to have active ankylosing spondylitis, consider a dosage of 300 mg every 4 weeks. <p>Recommended Intravenous Dosage The recommended intravenous dosage regimen is 6 mg/kg given at Week 0 as a loading dose, followed by 1.75 mg/kg every 4 weeks thereafter.</p> <p>Total doses exceeding 300 mg per infusion are not recommended for the 1.75 mg/kg maintenance dose in patients with AS.</p> • Non-Radiographic Axial Spondyloarthritis: <p>Recommended Subcutaneous Dosage</p>
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	<p>Administer with or without a loading dosage. The recommended dosage is:</p> <ul style="list-style-type: none"> ○ <u>With a loading dosage</u>: 150 mg at Weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter. ○ <u>Without a loading dosage</u>: 150 mg every 4 weeks. <p>Recommended Intravenous Dosage</p> <p>The recommended intravenous dosage regimen is 6 mg/kg given at Week 0 as a loading dose, followed by 1.75 mg/kg every 4 weeks thereafter.</p> <p>Total doses exceeding 300 mg per infusion are not recommended for the 1.75 mg/kg maintenance dose in patients with nr-axSpA.</p> <ul style="list-style-type: none"> • Enthesitis-Related Arthritis: Recommended weight-based dosage is administered by subcutaneous injection at Weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter. <ul style="list-style-type: none"> ○ For patients \geq 15 kg and $<$ 50 kg the dose is 75 mg. ○ For patients \geq 50 kg the dose is 150 mg. <p>Administration of Intravenous Formulation COSENTYX solution in vial requires dilution prior to administration. Administer as an intravenous infusion over a period of 30 minutes. (b) (4)</p> <p>(b) (4)</p>
How Supplied	<p>COSENTYX 300 mg/2 mL UnoReady pen:</p> <ul style="list-style-type: none"> • Carton of one 300 mg/2 mL (300 mg dose) single-dose UnoReady pen (injection) <p>COSENTYX 300 mg/2 mL (150 mg/mL) prefilled syringe:</p> <ul style="list-style-type: none"> • Carton of one 300 mg/2 mL (150 mg/mL) single-dose prefilled syringe (injection) <p>COSENTYX 150 mg/mL Sensoready pen:</p> <ul style="list-style-type: none"> • Carton of two 150 mg/mL (300 mg dose) single-dose Sensoready pens (injection) • Carton of one 150 mg/mL single-dose Sensoready pen (injection) <p>COSENTYX 150 mg/mL prefilled syringe:</p> <ul style="list-style-type: none"> • Carton of two 150 mg/mL (300 mg dose) single-dose prefilled syringes (injection) • Carton of one 150 mg/mL single-dose prefilled syringe (injection) <p>COSENTYX 75 mg/0.5 mL prefilled syringe (for pediatric patients less than 50 kg):</p> <ul style="list-style-type: none"> • Carton of one 75 mg/0.5 mL single-dose prefilled syringe (injection)

	<p>COSENTYX vial:</p> <ul style="list-style-type: none"> • Carton containing one 125 mg/5 mL (25 mg/mL) solution in a single-dose vial for dilution prior to intravenous infusion.
Storage	<p>Refrigerate COSENTYX at 2°C to 8°C (36°F to 46°F). Keep the product in the original carton to protect from light until the time of use. Do not freeze. To avoid foaming, do not shake. COSENTYX does not contain a preservative; discard any unused portion.</p> <p><u>COSENTYX 150 mg/mL Sensoready Pens, and 150 mg/mL and 75 mg/0.5 mL Prefilled Syringes:</u></p> <ul style="list-style-type: none"> • May be stored for up to 4 days at room temperature not to exceed 30°C (86°F).

APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,^a along with postmarket medication error data, we reviewed the following Cosentyx labels and labeling submitted by Novartis.

- Container label received on December 7, 2022
- Carton labeling received on December 7, 2022
- Prescribing Information (Image not shown) received on December 7, 2022, available from <\\CDSESUB1\evsprod\BLA761349\0000>
- Medication Guide received on December 7, 2022, available from <\\CDSESUB1\evsprod\BLA761349\0000>

F.2 Label and Labeling Images

(b) (4)



^a Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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/s/

SARAH K VEE
08/04/2023 11:06:17 AM

IDALIA E RYCHLIK
08/07/2023 06:21:57 AM

MEMORANDUM

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

DATE: 5/12/2023

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: BLA 761349

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

OSIS conducted a Remote Regulatory Assessment (RRA) for the site in (b) (4). The inspection was conducted under the following submissions: BLA Non-responsive

The following objectionable conditions were observed:

Non-responsive

After review of the objectionable conditions and the written response from the site, OSIS determined that the observations impacted the reliability of some data from study Non-responsive but that the observations were isolated in nature and did not impact the reliability of data from other reviewed studies ([Final OSIS Review - \(b\) \(4\) RRA](#)).

Site

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

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/s/

FOLAREMI ADEYEMO
05/12/2023 12:07:46 PM

MEMORANDUM

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

DATE: 3/28/2023

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 an on-site inspection**

RE: BLA 761349

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

OSIS conducted a Remote Regulatory Assessment (RRA) for the site in (b) (4). The RRA was conducted under the following submission: BLA (b) (4) NON-RESPONSIVE.

OSIS concluded that data from the reviewed studies were reliable.

Site

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

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/s/

JAMES J LUMALCURI
03/28/2023 09:50:03 AM