

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

761349Orig1s000

PRODUCT QUALITY REVIEW(S)



**U.S. FOOD & DRUG
ADMINISTRATION**

Center for Drug Evaluation and Research
Office of Pharmaceutical Quality
Office of Biotechnology Products

LABELS AND LABELING ASSESSMENT

Date of Assessment:	September 20, 2023
Assessor:	Diana Pei, PharmD Labeling Assessor Office of Biotechnology Products (OBP)
Through:	Qiong Fu, PhD Product Quality Assessor OBP/Division of Biotechnology Review and Research II
Application:	BLA 761349
Applicant:	Novartis Pharmaceuticals Corporation
Submission Date:	December 7, 2022
Product:	COSENTYX (secukinumab)
Dosage form(s):	Injection
Strength and Container-Closure:	Proposed: 125 mg/5 mL solution in a single-dose vial for dilution prior to intravenous infusion (for healthcare professional use only) Approved: 150 mg/mL solution in a single-dose Sensoready® pen and in a single-dose prefilled syringe. 75 mg/0.5 mL solution in a single-dose prefilled syringe (for pediatric patients). 300 mg/ (b) (4) solution in a single-dose prefilled syringe and single-dose UnoReady® pen
Purpose of assessment:	The Applicant submitted a biologics license application for secukinumab to support a new formulation for intravenous use provided as solution in single-dose 125 mg/5 mL vial.
Recommendations:	The prescribing information, medication guide, instructions for use container label, and carton labeling are acceptable from an OBP labeling perspective.

Materials Considered for this Label and Labeling Assessment	
Materials Assessed	Appendix Section
Proposed Label and Labeling	A
Evaluation Tables	B
Acceptable Label and Labeling	C

n/a = not applicable for this assessment

DISCUSSION

We assessed the proposed labels and labeling for compliance with applicable requirements in the Code of Federal Regulations. Also, we assessed the proposed labels and labeling for consistency with recommended labeling practices (see Appendix B).

CONCLUSION

The prescribing information, medication guide, instructions for use submitted on September 25, 2023 and the container label and carton labeling submitted on August 14, 2023 were assessed and found to be acceptable (see Appendix C) from an OBP Labeling perspective.

APPENDICES

Appendix A: Proposed Labeling

- Prescribing Information, Medication Guide, and Instructions for Use (submitted on 12/7/2022)

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- Container Label (submitted on 12/7/2022)

(b) (4)

Appendix B: Evaluation Tables

Evaluation Tables: Label^{1,2} and Labeling³ Standards

Container⁴ Label Evaluation

Proper Name (container label)	Acceptable
Regulations: 21 CFR 610.60(a)(1), 21 CFR 201.10(g)(2), 21 CFR 610.62(a), 21 CFR 610.62(b), 21 CFR 610.62(c), 21 CFR 610.60(c), 21 CFR 201.50(b), 21 CFR 201.10(a), 21 CFR 201.10(h)(2)(i)(1)(i)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices (placement of dosage form outside of parenthesis and/or below the proper name)</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Manufacturer name, address, and license number (container label)	Acceptable
Regulations: 21 CFR 610.60(a)(2), 21 CFR 201.1(a), 21 CFR 610.60(c), 21 CFR 201.10(h)(2)(i)(1)(iv), 21 CFR 201.100(e)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices (using the qualifying phrase "Manufactured by:")</i>	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices (U.S license number for container bearing a partial label⁵)</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Lot number or other lot identification (container label)	Acceptable
Regulations: 21 CFR 610.60(a)(3), 21 CFR 610.60(c), 21 CFR 201.18, 21 CFR 201.100(b)(6), 21 CFR 201.10(h)(2)(i)(1)(iii)	☒ Yes ☐ No

¹ Per 21 CFR 1.3(b) *Label* means any display of written, printed, or graphic matter on the immediate container of any article, or any such matter affixed to any consumer commodity or affixed to or appearing upon a package containing any consumer commodity.

² Per CFR 600.3(dd) *Label* means any written, printed, or graphic matter on the container or package or any such matter clearly visible through the immediate carton, receptacle, or wrapper.

³ Per 21 CFR 1.3(a) *Labeling* includes all written, printed, or graphic matter accompanying an article at any time while such article is in interstate commerce or held for sale after shipment or delivery in interstate commerce.

⁴ Per 21 CFR 600.3(bb) *Container* (referred to also as "final container") is the immediate unit, bottle, vial, ampule, tube, or other receptacle containing the product as distributed for sale, barter, or exchange.

⁵ Per 21 CFR 610.60(c) *Partial Label*. If the container is capable of bearing only a partial label, the container shall show as a minimum the name (expressed either as the proper or common name), the lot number or other lot identification and the name of the manufacturer; in addition, for multiple dose containers, the recommended individual dose. Containers bearing partial labels shall be placed in a package which bears all the items required for a package label."

	☐ N/A
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Comment/Recommendation:

Expiration date (container label)	Acceptable
Regulations: 21 CFR 610.60(a)(4), 21 CFR 201.17	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices references: USP General Chapters <7> Labeling, Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 lines 178-184, which, when finalized, will represent FDA's current thinking on topic</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:
Verify on month format to clarify digits or letters

Beyond Use Date (Multiple-dose containers) (container label)	Acceptable
<i>Recommended labeling practices: USP General Chapters: <659> Packaging and Storage Requirements and <7> Labeling</i>	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Product Strength (container label)	Acceptable
Regulations: 21 CFR 201.10(d)(1), 21 CFR 201.100(b)(4)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices (expression of strength for injectable drugs) references: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 line 176, which, when finalized, will represent FDA's current thinking on topic USP General Chapters: <7> Labeling</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Multiple-dose containers (container label)	Acceptable
Regulations: 21 CFR 610.60(a)(5), 21 CFR 201.55 <i>(recommended individual dose)</i>	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Statement: "Rx only" (container label)	Acceptable
Regulations: 21 CFR 610.60(a)(6), 21 CFR 201.100(b)(1)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices (prominence of Rx Only statement) reference: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 line 147, which, when finalized, will represent FDA's current thinking on topic</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Medication Guide (container label)	Acceptable
Regulations: 21 CFR 610.60(a)(7), 21 CFR 208.24(d)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation: Label is small and could be considered a partial label. The required statement is found on the package label.

No Package for container (container label)	Acceptable
Regulation: 21 CFR 610.60(b)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

No container label (container label)	Acceptable
Regulation: 21 CFR 610.60(d)	☐ Yes ☐ No ☒ N/A

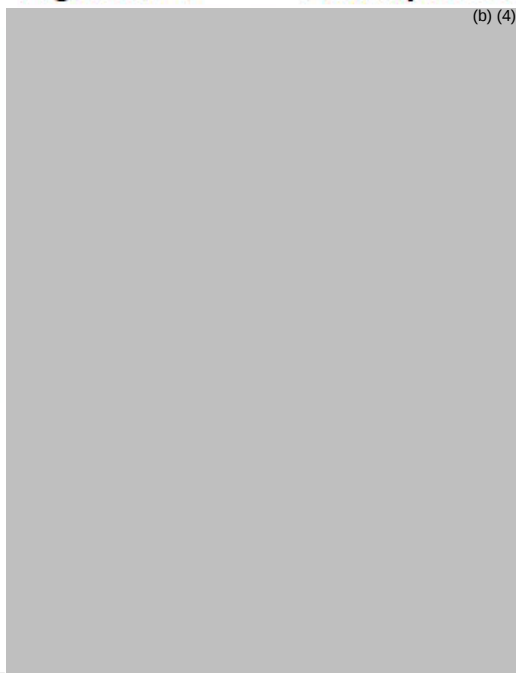
Comment/Recommendation:

Ferrule and cap overseal (for vials only)	Acceptable
<i>Recommended labeling practices references: United States Pharmacopeia (USP) General Chapters: <7> Labeling (Ferrules and Cap Overseals)</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

To Applicant: Confirm there is no text on the ferrule and cap overseal of the vials.

Applicant's response: Novartis confirms there is no text on the ferrule and cap overseal of the vials. Please see Figure b-1 below for an example vial.

Figure b-1**Example for secukinumab 125 mg/5mL liquid in vial**

Visual inspection	Acceptable
Regulation: 21 CFR 610.60(e)	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

To Applicant: Confirm that sufficient area of the container remains uncovered for its full length or circumference to allow for visual inspection when the label is affixed to the container and indicate where the visual area of inspection is located.

Applicant's response: Novartis confirms there is sufficient area on the container uncovered for its full length to allow for visual inspection. The area is located on the vial, as a space between the two ends of the label. Please see Figure b-1 above for an example vial. The space between the ends of the label for the secukinumab 125 mg/5 mL liquid in vial is approximately 9 mm.

Route of administration (container label)	Acceptable
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Regulations: 21 CFR 201.5(f), 21 CFR 201.100(b)(3), 21 CFR 201.100(d)(1)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices (route of administration statement to appear after the strength statement on the principal display panel)</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

<u>NDC numbers (container label)</u>	<u>Acceptable</u>
Regulations: 21 CFR 201.2, 21 CFR 207.35	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

<u>Preparation instructions (container label)</u>	<u>Acceptable</u>
Regulation: 21 CFR 201.5(g)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (lines 426-430), which, when finalized, will represent FDA's current thinking on topic</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation: Label is small and could be considered a partial label.

<u>Package type term (container label)</u>	<u>Acceptable</u>
<i>Recommended labeling practices: Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018) USP chapter <659> Packaging and Storage Requirements</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

<u>No misleading statements (container label)</u>	<u>Acceptable</u>
Regulation: 21 CFR 201.6	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Prominence of required label statements (container label)	Acceptable
Regulation: 21 CFR 201.15	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Spanish-language (Drugs) (container label)	Acceptable
Regulation: 21 CFR 201.16	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

FD&C Yellow No. 5 and/or FD&C Yellow No. 6 (container label)	Acceptable
Regulation: 21 CFR 201.20	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Bar code label requirements (container label)	Acceptable
Regulations: 21 CFR 201.25, 21 CFR 610.67	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices references: Guidance for Industry: Bar Code Label Requirements Questions and Answers, August 2011 Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (lines 511-512), lines 780-786), which, when finalized, will represent FDA's current thinking on topic</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Strategic National Stockpile (exceptions or alternatives to labeling requirements for human drug products) (container label)	Acceptable
Regulations: 21 CFR 610.68, 21 CFR 201.26	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Net quantity (container label)	Acceptable
Regulation: 21 CFR 201.51	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices references: Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (line 461- 463) which, when finalized, will represent FDA's current thinking on topic</i> <i>Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products Guidance for Industry, June 2015 (line 68, 93-99)</i> <i>USP General Chapters <1151> Pharmaceutical Dosage Forms (Excess volume in injections).</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Statement of Dosage (container label)	Acceptable
Regulations: 21 CFR 610.60(a)(5), 21 CFR 610.60(c), 21 CFR 201.55, 21 CFR 201.100(b)(2)	☒ Yes ☐ No ☐ N/A

Comment/Recommendation: Label is small and could be considered a partial label.

Inactive ingredients (container label)	Acceptable
Regulation: 21 CFR 201.100	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices reference: USP General Chapters <1091> Labeling of Inactive Ingredients and USP General Chapters <7> Labeling</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation: Label is small and could be considered a partial label.

Storage requirements (container label)	Acceptable
<i>Recommended labeling practices references: USP General Chapters <7> Labeling, USP General Chapters <659> Packaging and Storage Requirements</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Dispensing container (container label)	Acceptable
Regulation: 21 CFR 201.100(b)(7)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Package⁶ Labeling Evaluation

Proper name (package labeling)	Acceptable
Regulations: 21 CFR 610.61(a), 21 CFR 201.50(b), 21 CFR 201.10(g)(2)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices (placement of dosage form outside of parenthesis and/or below the proper name)</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Manufacturer name, address, and license number (package labeling)	Acceptable
Regulations: 21 CFR 610.61(b), 21 CFR 201.1(a), 21 CFR 201.1(i), 21 CFR 201.100(e)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices (using the qualifying phrase "Manufactured by:")</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Lot number or other lot identification (package labeling)	Acceptable
Regulation: 21 CFR 610.61(c), 21 CFR 201.18	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Expiration date (package labeling)	Acceptable
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⁶ Per 21 CFR 600.3(cc) *Package* means the immediate carton, receptacle, or wrapper, including all labeling matter therein and thereon, and the contents of the one or more enclosed containers. If no package, as defined in the preceding sentence, is used, the container shall be deemed to be the package. Thus, this includes the carton, prescribing information, and patient labeling.

Regulations: 21 CFR 610.61(d), 21 CFR 201.17	☒ Yes ☐ No ☐ N/A
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Comment/Recommendation:

Beyond Use Date (Multiple-dose containers) (package labeling)	Acceptable
<i>Recommended labeling practices: USP General Chapters: <659> Packaging and Storage Requirements and <7> Labeling</i>	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Preservative (package labeling)	Acceptable
Regulation: 21 CFR 610.61(e)	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Number of containers (package labeling)	Acceptable
Regulation: 21 CFR 610.61(f)	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Product Strength (package labeling)	Acceptable
Regulations: 21 CFR 610.61(g), 21 CFR 201.10(d)(1), 21 CFR 201.100(b)(4)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices references: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (line 176), which, when finalized, will represent FDA's current thinking on topic USP General Chapters: <7> Labeling</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

<u>Storage temperature/requirements (package labeling)</u>	<u>Acceptable</u>
Regulation: 21 CFR 610.61(h)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices reference: USP General Chapters: <7> Labeling, USP General Chapters <659> Packaging and Storage Requirements</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

<u>Handling: "Do Not Shake", "Do not Freeze" or equivalent (package labeling)</u>	<u>Acceptable</u>
Regulation: 21 CFR 610.61(i)	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

<u>Multiple dose containers (recommended individual dose) (package labeling)</u>	<u>Acceptable</u>
Regulation: 21 CFR 610.61(j)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

<u>Route of administration (package labeling)</u>	<u>Acceptable</u>
Regulations: 21 CFR 610.61(k), 21 CFR 201.5(f), 21 CFR 201.100(d)(1)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices (route of administration statement to appear after the strength statement on the principal display panel)</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Known sensitizing substances (package labeling)	Acceptable
Regulations: 21 CFR 610.61(l), 21 CFR 801.437 (User labeling for devices that contain natural rubber)	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Inactive ingredients (package labeling)	Acceptable
Regulations: 21 CFR 610.61, 21 CFR 201.100	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices references: USP General Chapters <1091> Labeling of Inactive Ingredients, USP General Chapters <7> Labeling</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Source of the product (package labeling)	Acceptable
Regulation: 21 CFR 610.61(p)	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Minimum potency of product (package labeling)	Acceptable
Regulation: 21 CFR 610.61(r)	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

To Applicant: Based on CDER's current interpretation of 21 CFR 610.61(r) and after consultation with OBP Product Quality assessors, this regulation does not apply to this product because 1) no U.S. standard of potency has been prescribed for secukinumab products (i.e., there is no specific test method described in regulation for secukinumab products that establishes an official standard of potency) and 2) Product Quality assessors have determined that potency is not a factor within the meaning of § 610.61(r) for COSENTYX because lot variability is not a concern as the manufacturing process is

appropriately controlled to ensure the consistency and quality of the final product. Accordingly, the phrase "No U.S. standard of potency" is not required to appear on the carton labeling.

You may request removal of the "No U.S. standard of potency" statement for your other approved carton labeling when you submit mockups in future supplement(s) that involve these other approved carton labeling presentation(s).

Applicant's response: Novartis is making this change and it is reflected in the updated artwork documents in Module 1.14.1.1.

Rx only (package labeling)	Acceptable
Regulations: 21 CFR 610.61(s), 21 CFR 201.100(b)(1)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices references: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (line 147-149), which, when finalized, will represent FDA's current thinking on topic</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Divided manufacturing (package labeling)	Acceptable
Regulation: 21 CFR 610.63 (Divided manufacturing responsibility to be shown)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Distributor (package labeling)	Acceptable
Regulation: 21 CFR 610.64, 21 CFR 201.1(h)(5)	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Bar code (package labeling)	Acceptable
Regulations: 21 CFR 610.67, 21 CFR 201.25	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices references: Guidance for Industry: Bar Code Label Requirements Questions and Answers, August 2011</i>	☒ Yes ☐ No

<i>Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (lines 511-512), lines 780-786)</i>	☐ N/A
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Comment/Recommendation:

Strategic National Stockpile (exceptions or alternatives to labeling requirements for human drug products) (package labeling)	Acceptable
Regulations: 21 CFR 610.68, 21 CFR 201.26	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

NDC numbers (package labeling)	Acceptable
Regulations: 21 CFR 201.2, 21 CFR 207.35	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Preparation instructions (package labeling)	Acceptable
Regulation: 21 CFR 201.5(g) and 21 CFR 610.61(i)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices references: Draft Guidance Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013 (lines 426-430), which, when finalized, will represent FDA's current thinking on topic</i> <i>USP General Chapters <7> Labeling</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Package type term (package labeling)	Acceptable
<i>Recommended labeling practices: Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018)</i> <i>USP chapter <659> Packaging and Storage Requirements</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

No misleading statements (package labeling)	Acceptable
Regulation: 21 CFR 201.6	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Prominence of required label statements (package labeling)	Acceptable
Regulation: 21 CFR 201.15	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Spanish-language (Drugs) (package labeling)	Acceptable
Regulation: 21 CFR 201.16	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

FD&C Yellow No. 5 and/or FD&C Yellow No. 6 (package labeling)	Acceptable
Regulation: 21 CFR 201.20	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Phenylalanine as a component of aspartame (package labeling)	Acceptable
Regulation: 21 CFR 201.21(c)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

<u>Sulfites; required warning statements (package labeling)</u>	<u>Acceptable</u>
Regulation: 21 CFR 201.22(b)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

<u>Net quantity (package labeling)</u>	<u>Acceptable</u>
Regulation: 21 CFR 201.51	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices references: Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (line 461- 463) which, when finalized, will represent FDA's current thinking on topic</i> <i>Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products Guidance for Industry, June 2015 (line 68, 93-99)</i> <i>USP General Chapters <1151> Pharmaceutical Dosage Forms (Excess volume in injections).</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

<u>Statement of Dosage (package labeling)</u>	<u>Acceptable</u>
Regulations: 21 CFR 201.55, 21 CFR 201.100(b)(2)	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

<u>Dispensing container (package labeling)</u>	<u>Acceptable</u>
Regulation: 21 CFR 201.100(b)(7)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Medication Guide (package labeling)	Acceptable
Regulations: 21 CFR 610.60(a)(7), 21 CFR 208.24(d)	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Other (package labeling)	Acceptable
	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Prescribing Information Evaluation

PRESCRIBING INFORMATION

Highlights of Prescribing Information	
PRODUCT TITLE	Acceptable
Regulation: 21 CFR 201.57(a)(2)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices reference: Draft Guidance for Industry on Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products - Content and Format (January 2018), which, when finalized, will represent FDA's current thinking on topic</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:
 To applicant: FDA does not recommend the use of the word " (b) (4) for injectable products. Ensure the word " (b) (4) is deleted throughout.
Applicant revised as recommended.

Highlights of Prescribing Information	
DOSAGE AND ADMINISTRATION	Acceptable
<i>Recommended labeling practices reference: USP nomenclature for diluents and intravenous solutions</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

To Applicant: The statement (b) (4) " was removed to have a more concise highlight section.

Applicant revised as recommended.

Highlights of Prescribing Information**DOSAGE FORMS AND STRENGTHS****Acceptable**

Regulations: 21 CFR 201.57(a)(8), 21 CFR 201.10, 21 CFR 201.100

☒ Yes
☐ No
☐ N/A

*Recommended labeling practices references: Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018)
USP chapter <659> Packaging and Storage Requirements
USP General Chapters: <7> Labeling*

☒ Yes
☐ No
☐ N/A

Comment/Recommendation:

To Applicant: We typically do not include (b) (4). We do not recommend use of (b) (4). Consider the revision provided.

The Applicant revised as recommended.

Full Prescribing Information**2 DOSAGE AND ADMINISTRATION****Acceptable**

Regulation: 21 CFR 201.57(c)(3)(iv)]

Confirm appropriateness of specific direction on dilution, preparation, and administration of the dosage form and storage conditions for stability of the reconstituted or diluted drug; ensure verbatim statement for parenterals: "Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."

☒ Yes
☐ No
☐ N/A

Recommended labeling practices reference: USP nomenclature for diluents and intravenous solutions and storage instructions for reconstituted and diluted products; confirm the appropriateness of infusion bags, infusion sets (e.g., tubing, infusion aids, or filter membranes) incompatibilities with these components

☒ Yes
☐ No
☐ N/A

Comment/Recommendation:

To applicant: Revised to include the required verbatim statement per 21 CFR 201.57(c)(3)(iv).

The Applicant revised as recommended.

Full Prescribing Information**3 DOSAGE FORMS AND STRENGTHS****Acceptable**

Regulation: 21 CFR 201.57(c)(4)

☒ Yes
☐ No
☐ N/A

*Recommended labeling practices references: Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018)
USP chapter <659> Packaging and Storage Requirements
USP General Chapters: <7> Labeling*

☒ Yes
☐ No
☐ N/A

Comment/Recommendation:

To applicant: Added the identifying characteristics of the dosage form.

The Applicant revised as recommended.

Full Prescribing Information**11 DESCRIPTION****Acceptable**

Regulations: 21 CFR 201.57(c)(12), 21 CFR 610.61 (m), 21 CFR 610.61(o), 21 CFR 610.61 (p), 21 CFR 610.61 (q)

☒ Yes
☐ No
☐ N/A

*Recommended labeling practices references: USP General Chapters <1091>,
USP General Chapters <7>*

☒ Yes
☐ No
☐ N/A

Comment/Recommendation:**Full Prescribing Information****15 & 16 Hazardous Drug****Acceptable**

Regulation: 21 CFR 201.57(c)(17)(iv)

☐ Yes
☐ No

Section 15: References 1. OSHA Hazardous Drugs. OSHA. http://www.osha.gov/SLTC/hazardousdrugs/index.html Section 16: xxxx is a hazardous drug. Follow applicable special handling and disposal procedures.¹	☒ N/A
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Comment/Recommendation:

Full Prescribing Information	
16 HOW SUPPLIED/ STORAGE AND HANDLING	Acceptable
Regulation: 21 CFR 201.57(c)(17)	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices: to ensure placement of detailed storage conditions for reconstituted and diluted products</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Full Prescribing Information	
MANUFACTURER INFORMATION	Acceptable
Regulations: 21 CFR 201.100(e), 21 CFR 201.1	☒ Yes ☐ No ☐ N/A
<i>Recommended labeling practices references: 21 CFR 610.61(b) (add the US license number for consistency with the carton labeling), and 21 CFR 610.64 (Name and address of distributor may appear and use a qualifying phrase for consistency with the carton labeling, when applicable)</i>	☒ Yes ☐ No ☐ N/A

Comment/Recommendation:

Medication Guide Evaluation

MEDICATION GUIDE	
TITLE (NAMES AND DOSAGE FORM)	Acceptable
Regulation for Medication Guide: 21 CFR 208.20(a)(7)	☒ Yes ☐ No ☐ N/A

Comment/Recommendation: To Applicant: FDA does not recommend the use of the word “(b) (4)” for injectable products. Ensure the word “(b) (4)” is deleted throughout.

The Applicant revised as recommended.

MEDICATION GUIDE

STORAGE AND HANDLING

Acceptable

Regulation for Medication Guide: 21 CFR 208.20(a)(2)

☒ Yes
☐ No
☐ N/A

Comment/Recommendation:

MEDICATION GUIDE

INGREDIENTS

Acceptable

Recommended labeling practice: To ensure labeling of inactive ingredients are in alphabetical order (see USP General Chapters <1091>)

☒ Yes
☐ No
☐ N/A

Comment/Recommendation:

MEDICATION GUIDE

MANUFACTURER INFORMATION

Acceptable

21 CFR 208.20(b)(8)(iii)

☒ Yes
☐ No
☐ N/A

21 CFR 610.61 (add the US license number for consistency with the carton labeling), 21 CFR 610.64 (Name and address of distributor may appear and use a qualifying phrase for consistency with the carton labeling, when applicable)

☒ Yes
☐ No
☐ N/A

Comment/Recommendation:

Instructions for Use Evaluation

INSTRUCTIONS FOR USE

TITLE (NAMES AND DOSAGE FORM)

Recommended Labeling Practices references: Proprietary name in upper case letters on line 1, proper name (line 2) in lower case letters in parentheses, and dosage form followed by the route of administration (line 3) in lower case letters (see Draft Instructions for Use – Patient Labeling for Human

☒ Yes
☐ No
☐ N/A

Prescription Drug and Biological products and Drug-Device and Biologic-Device Combination Products – Content and Format Guidance for Industry (July 2019). For the recommended dosage form (see USP General Chapters: <1> Injections, Nomenclature and Definitions, Nomenclature form).

Comment/Recommendation:

INSTRUCTIONS FOR USE

STORAGE AND HANDLING

Acceptable

Recommended labeling practices for IFU: Draft Instructions for Use – Patient Labeling for Human Prescription Drug and Biological products and Drug-Device and Biologic-Device Combination Products – Content and Format Guidance for Industry (July 2019). To ensure that applicable storage and handling requirements are consistent with the information provided in the PI (Reference: Section 2 (Dosage and Administration) and Section 16 (How Supplied Storage and Handling) of the PI)

✓ Yes
☐ No
☐ N/A

Comment/Recommendation:

INSTRUCTIONS FOR USE

INGREDIENTS

Acceptable

Recommended labeling practice: To ensure labeling of inactive ingredients are in alphabetical order (see USP General Chapters <1091>)

✓ Yes
☐ No
☐ N/A

Comment/Recommendation:

INSTRUCTIONS FOR USE

MANUFACTURER INFORMATION

Acceptable

21 CFR 201.1, 19 CFR 134.11

✓ Yes
☐ No
☐ N/A

*Draft Instructions for Use – Patient Labeling for Human Prescription Drug and Biological products and Drug-Device and Biologic-Device Combination Products – Content and Format Guidance for Industry (July 2019).
 21 CFR 610.61 (add the US license number for consistency with the carton labeling),
 21 CFR 610.64 (Name and address of distributor may appear and use a qualifying phrase for consistency with the carton labeling, when applicable)*

✓ Yes
☐ No
☐ N/A

Comment/Recommendation:

APPENDIX C. Acceptable Labels and Labeling

- Prescribing Information, Medication Guide, and Instructions for Use (submitted on September 25, 2023)

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- Container Label (submitted on August 14, 2023)





Diana
Pei

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Qiong
Fu

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Date: 9/26/2023 04:45:48PM

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BLA Executive Summary

Assessment Date: August 29, 2023

1. Application/Product Information

BLA number	761349
Submission Type	Original
Regulatory Pathway	351 (a)
Associated IND/BLA	BLA 125504, IND 012678
Review Designation	Standard
Applicant	Novartis Pharmaceutical Corporation
Indication	Treatment of adult patients with Psoriatic Arthritis (PsA), Ankylosing Spondylitis (AS) and Non-radiographic axial spondyloarthritis (nr-axSpA)
Rx/OTC dispensed	Rx
Drug Product Name	Proprietary Name : Cosentyx
	Non-proprietary Name/Code Name : Secukinumab/AIN457
	OBP Naming : MAB HUMANIZED (IGG1) ANTI_Q16552 (IL17_HUMAN) [SECUKINUMAB]
Drug Product Description	AIN457 125 mg/5 mL concentrate for solution for infusion is a sterile, single-use, preservative-free, clear to opalescent, colorless to slightly yellowish solution for infusion
Dosage Form	Injection
Strength	125 mg/ 5mL
Route of Administration	Intravenous infusion

Primary Container Closure System	6 mL glass vial with a grey (b) (4)-rubber stopper (b) (4) and an aluminum cap seal with a flip-off disk.		
Device Information	N/A (vial product only)		
Co-packaged Product Information	N/A		
OPQ Review Team	Discipline	Primary	Secondary
	Drug substance	Qiong Fu	Anjali Shukla
	Drug product	Qiong Fu	Anjali Shukla
	Immunogenicity Assay	Qiong Fu	Anjali Shukla
	Facility	Michael Shanks	Virginia Carroll
	Microbiology	Reyes Candau-Chacon	Virginia Carroll
	RBPM	Anika Lalmansingh	
	ATL	Anjali Shukla	
OPQ Issued Consults	None		

2. Recommendation and Conclusion on Approvability

Recommendation: Approval

The Office of Pharmaceutical Quality, CDER, recommends approval of BLA 761349 for Cosentyx (intravenous formulation) manufactured by Novartis Pharmaceutical Corporation. The data submitted in this application are adequate to support the conclusion that the manufacture of Cosentyx is well-controlled and leads to a product that is pure and potent. It is recommended that this product be approved for human use under conditions specified in the package insert.

3. CMC Information for Action Letter

a. Manufacturing Location:

- **Drug Substance:** (cross referenced to BLA 125504)

Novartis Pharma S.A.S.
Centre de Biotechnologie
8 rue de l'Industrie
68330 Huningue
France
(FEI: 3007198645)



- **Drug Product:**
Novartis Pharma Stein AG
Schaffhauserstrasse
4332 Stein
Switzerland
(FEI: 3002653483)

b. Fill size and dosage form: 125 mg/ 5mL, injection

c. Dating Period:

- **Drug Product:** 24 months when stored at 2-8°C
- **Drug Substance:** (b) (4) months when stored at ≤ (b) (4) °C
- **Intermediate Substance, if applicable:** Not applicable
- **For packaged products:** Not packaged
- **Stability Option:**
 - For stability protocols:
 - We have approved the stability protocol(s) in your license application for the purpose of extending the expiration dating of your drug product under 21 CFR 601.12.

d. Exempt from lot release:

- Yes
- Rationale, if exempted: Cosentyx is exempted from lot release per FR 95-29960.

4. Basis for Recommendation

a. Summary: Secukinumab is a recombinant, fully human monoclonal anti-human interleukin-17A (IL-17A) antibody of the IgG1/κ-class that binds to human IL-17A and neutralizes the activity of this cytokine. IL-17 is a lymphokine of the Th17 subset of inflammatory T cells, that are involved in several autoimmune and inflammatory processes. IL-17 antagonism is aimed at interference with the chronic inflammatory process by selectively targeting the proinflammatory cytokine IL-17 of the Th17 cell subset. Secukinumab by subcutaneous administration is currently licensed for the treatment of adults with plaque psoriasis (PsO), AS, nr-AxSpA, PsA; pediatric patients (6 to <18 years old) with moderate to severe psoriasis, juvenile PsA (2 years and older) and enthesitis-related arthritis (ERA; 4 years and older). A new formulation of secukinumab (125 mg/5 mL) is proposed in this BLA, that allows for weight-based intravenous dosing in adult patients with PsA, AS, and nr-AxSpA. A cell-based bioassay is used to control the potency of secukinumab. IL-17 stimulates the release of IL-6 from target cells. Secukinumab binds and neutralizes human IL-17. The biological activity of secukinumab is measured based on its capacity to inhibit the IL-17-induced release of IL-6 from the immortalized human C-20/A4 chondrocyte cell line. Potency results are reported as percentage relative to the reference standard. The drug substance used for the intravenous formulation is the same as that used for the subcutaneous Cosentyx product. Drug substance information is cross referenced to BLA 125504. The drug product (DP) manufacturing process includes (b) (4)

(b) (4)

The overall Cosentyx control strategy incorporates controls over raw materials, facilities and equipment, the manufacturing process, adventitious agents, microbial contamination, and release and stability of the drug substance and drug product. The manufacturing processes and overall control strategies for Cosentyx are appropriately established to ensure consistency and quality of the final product; therefore, lot variability is not a concern. The assays used for immunogenicity assessment in the clinical studies to support this BLA are adequately validated and suitable for their intended purpose. Adequate descriptions of the facilities, equipment, environmental controls, cleaning and contamination control strategy were provided for Novartis Pharma S.A.S, Huningue, France (FEI: 3007198645) and (b) (4)

(b) (4) for the secukinumab DS manufacture and Novartis Pharma Stein AG, Switzerland (FEI: 3002653483) proposed for the

secukinumab DP manufacture. All proposed manufacturing and testing facilities are acceptable based on their currently acceptable CGMP compliance status and recent relevant inspectional coverage. The BLA is recommended for approval from a product quality, facility, product quality microbiology and sterility assurance perspectives.

b. Subdiscipline Recommendation:

Drug Substance	-	Adequate
Drug Product	-	Adequate
Immunogenicity Assay	-	Adequate
Facilities	-	Adequate
Microbiology	-	Adequate

c. Environmental Assessment (EA):

Categorical exclusion is claimed by the applicant and deemed acceptable.

d. Potency Assessment for Labeling:

As an initial matter, we determined that no U.S. standard of potency has been prescribed for Cosentyx (i.e., there is no specific test method described in regulation for Cosentyx that establishes an official standard of potency). We next considered whether potency is a factor for Cosentyx within the meaning of 21 CFR 610.61(r), which requires a statement about potency on the package (carton) label if "potency is a factor" and "no U.S. standard of potency has been prescribed." We have determined that potency is not a factor for Cosentyx for purposes of § 610.61(r) because lot variability is not a concern for Cosentyx as Cosentyx's manufacturing process is appropriately controlled to ensure the consistency and quality of the final product.

5. Life-Cycle Considerations

a. Established Conditions based on ICH Q12 principles: No

b. Drug Substance:

- i. Protocols approved: Refer to BLA 125504 (cross referenced for the drug substance)
- ii. Residual risk: None
- iii. Future inspection points to consider: None

c. Drug Product:

- i. Protocols approved:
 - Post-approval annual stability protocol
 - Stability protocol for post-approval changes

- Comparability protocol for post-approval changes to introduce a new product into the manufacturing line
 - Protocol for extension of drug product shelf-life
- ii. Residual risk: None
- iii. Future inspection points to consider: None

FOIA statement: More detailed assessments of the BLA submission, which are not included in this integrated quality assessment, may be requested via a Freedom of Information Act (FOIA) request.



Anjali
Shukla

Digitally signed by Anjali Shukla

Date: 8/29/2023 01:46:59PM

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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/

ANIKA A LALMANSINGH
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ANJALI A SHUKLA
08/29/2023 02:29:12 PM