CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761434Orig1s000

PRODUCT QUALITY REVIEW(S)

LABELS AND LABELING ASSESSMENT

Date of Assessment:	November 6, 2025
Assessor:	Vicky Borders-Hemphill, PharmD Labeling Assessor Office of Product Quality Assessment III (OPQA III)
Through:	Dilip Devineni, PhD Product Quality Assessor OPQA III/Division of Product Quality Assessment XV
Application:	BLA 761434
Applicant:	Otsuka Pharmaceutical Company, Ltd. Tokyo, Japan
Submission Date:	March 28, 2025
Product:	sibeprenlimab-szsi
Dosage form(s):	Injection
Strength and Container-Closure:	400 mg/2 mL (200 mg/mL) in a single-dose prefilled syringe
Purpose of assessment:	The Applicant submitted a biologics license application for Agency assessment.
Recommendations:	The prescribing information, patient labeling, instructions for use (submitted on October 27, 2025), container labels (submitted on October 7, 2025), and carton labeling (submitted on September 24, 2025) were assessed and found to be acceptable (see Appendix C) from an OPQA III Labeling perspective.

Materials Considered for this Label and Labeling Assessment	
Materials Assessed	**Appendix Section**
Proposed Labels and Labeling	A
Evaluation Tables	B
Acceptable Labels 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, patient labeling, instructions for use (submitted on October 27, 2025), container labels (submitted on October 7, 2025), and carton labeling (submitted on September 24, 2025) were assessed and found to be acceptable (see Appendix C) from an OPQA III Labeling perspective.

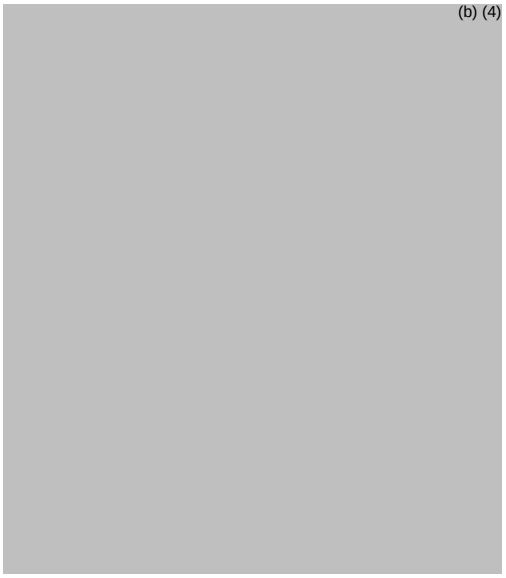
APPENDICES

Appendix A: Proposed Labeling

Prescribing Information/Patient Information Labeling (submitted on March 28, 2025 \\CDSESUB1\EVSPROD\bla761434\0001\m1\us\114-labeling\draft\labeling\draft-labeling-text-clean.pdf)

Instructions for Use (submitted on March 28, 2025 \\CDSESUB1\EVSPROD\bla761434\0001\m1\us\114-labeling\draft\annotated\voyxact-pfs-ifu-annotated-v11-10mar2025.pdf)

Container Labels (submitted on March 28, 2025)



Carton Labeling (submitted on March 28, 2025)

Appendix B: Evaluation Tables
Evaluation Tables: Label[1,2] and Labeling[3] Standards

Container[4] 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(i), 21 CFR 600.3(k)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (placement of dosage form outside of parenthesis and/or below the proper name)	✓ Yes ☐ No ☐ N/A

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(i), 21 CFR 201.100(e)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (using the qualifying phrase "Manufactured by:")	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (U.S license number for container bearing a partial label[5])	✓ Yes ☐ No ☐ N/A

Comment/Recommendation: Revise to the applicant's name provided on line 2 of Form FDA 356h, Otsuka Pharmaceutical Company, Ltd., and include a placeholder for the US license number as follows: Otsuka Pharmaceutical Company, Ltd. U.S. license No. XXXX.

Applicant's response: The label is too small to include the manufacturer information. The distributor information (aligned with NDC number) is included. The license number will not fit onto the label due to lack of space. Per 21CFR201.100 (b)(7), this product is packaged within

[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."

an outer container from which it is removed for dispensing or use, the information required by paragraphs (b) (2), (3), and (5) of this section may be placed on such outer container only. OPQA III Labeling' s response: We refer you to labeling standards for biologics. FDA's biological product regulations (21 CFR 600.3(t)) define "manufacturer" as "any legal person or entity engaged in the manufacture of a product subject to license under the PHS Act," including "any legal person or entity who is an applicant for a license where the applicant assumes responsibility for compliance with the applicable product and establishment standards". A manufacturer thus includes a license applicant, who may or may not own the facilities engaged in significant manufacturing steps, when such an applicant assumes responsibility for compliance with the applicable product and establishment standards, including, but not limited to, 21 CFR Parts 210, 211, 600 through 680, and 820. Therefore, we find the applicant written on Form FDA 356h to be considered the following terms: license applicant, license manufacturer, or manufacturer. Revise to the applicant's name provided on line 2 of Form FDA 356h, Otsuka Pharmaceutical Company, Ltd. Per 21 CFR 610.60(c), for a partial label, the manufacturer's names must appear on the container label. Your container label provides only the distributor information which is not in compliance with 21 CFR 610.64. The US license number is requested if space permits but is not required for a partial label. This requested revision for the manufacturer's name will provide consistency with your carton labeling and prescribing information. *The Applicant revised the name as requested.*

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(i)	✓ Yes ☐ No ☐ N/A

Expiration date (container label)	**Acceptable**
Regulations: 21 CFR 610.60(a)(4), 21 CFR 201.17	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: USP General Chapters <7> Labeling, Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)	✓ Yes ☐ No ☐ N/A

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

Product Strength (container label)	**Acceptable**
Regulations: 21 CFR 201.10(d)(1), 21 CFR 201.100(b)(4)	✓ Yes ☐ No

	☐ N/A
Recommended labeling practices (expression of strength for injectable drugs) references: Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022) *USP General Chapters: <7> Labeling*	✓ Yes ☐ No ☐ N/A

Comment/Recommendation: Partial label space considerations for the exclusion of parenthetical mg/mL presentation.

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

Statement: "Rx only" (container label)	**Acceptable**
Regulations: 21 CFR 610.60(a)(6), 21 CFR 201.100(b)(1)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (prominence of Rx Only statement) reference: Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)	✓ Yes ☐ No ☐ N/A

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

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

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

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

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

Comment/Recommendation: 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: The area at the top of the label is transparent and when wrapped around the syringe, it creates a window into the syringe.

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

NDC numbers **(container label)**	**Acceptable**
Regulations: 21 CFR 201.2, 21 CFR 207.35	✓ Yes ☐ No ☐ N/A

Preparation instructions (container label)	**Acceptable**
Regulation: 21 CFR 201.5(g)	☐ Yes ☐ No ☒ N/A
Recommended labeling practices: Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)	☐ Yes ☐ No ☒ N/A

Package type term (container label)	**Acceptable**
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*	☐ Yes ☐ No ☒ N/A

Comment/Recommendation: Partial label space considerations for the exclusion of package type term

No misleading statements (container label)	**Acceptable**
Regulation: 21 CFR 201.6	✓ Yes ☐ No ☐ N/A

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

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

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

Bar code label requirements (container label)	**Acceptable**
Regulations: 21 CFR 201.25, 21 CFR 610.67	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Guidance for Industry *Bar Code Label Requirements Questions and Answers* (August 2011) Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)	✓ Yes ☐ No ☐ N/A

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

Net quantity (container label)	**Acceptable**
Regulation: 21 CFR 201.51	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022) Guidance for Industry *Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products* (June 2015) *USP General Chapters <1151> Pharmaceutical Dosage Forms (Excess volume in injections).*	✓ Yes ☐ No ☐ N/A

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

Inactive ingredients (container label)	**Acceptable**
Regulation: 21 CFR 201.100, FD&C Act section 502(e)	☐ Yes ☐ No ☒ N/A
Recommended labeling practices reference: USP General Chapters <1091> Labeling of Inactive Ingredients and USP General Chapters <7> Labeling	☐ Yes ☐ No ☒ N/A

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

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

Package[6] Labeling Evaluation

Proper name (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(a), 21 CFR 201.50(b), 21 CFR 201.10(g)(2), 21 CFR 600.3(k)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (placement of dosage form outside of parenthesis and/or below the proper name)	✓ Yes ☐ No ☐ N/A

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
Recommended labeling practices (using the qualifying phrase "Manufactured by:")	✓ Yes ☐ No ☐ N/A

Comment/Recommendation: Revise to the applicant's name provided on line 2 of Form FDA 356h, 'Otsuka Pharmaceutical Company, Ltd.'. *Applicant revised as requested*

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

Expiration date (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(d), 21 CFR 201.17	✓ Yes ☐ No ☐ N/A

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

[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.

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

Comment/Recommendation: Add "No Preservative." to appear on the back panel with the ingredient information. *Applicant revised as requested*

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

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
Recommended labeling practices references: Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022) *USP General Chapters: <7> Labeling*	✓ Yes ☐ No ☐ N/A

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

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

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

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

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: The product is not made with latex (natural rubber latex, dry natural rubber or synthetic derivatives of natural rubber latex).

Inactive ingredients (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61, 21 CFR 201.100, FD&C Act section 502(e)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: USP General Chapters <1091> Labeling of Inactive Ingredients, USP General Chapters <7> Labeling	✓ Yes ☐ No ☐ N/A

Comment/Recommendation: FDA approved labeling is required to use the established names for drugs (i.e., drug products and ingredients) per 21 CFR 299.4. Ensure that the established names for inactive ingredients in your product are the USP/NF monographs titles: arginine, glutamic acid, histidine, polysorbate 80, and sorbitol. The common name for L-histidine hydrochloride monohydrate is sufficient for labeling. Ensure that the inactive ingredients names appear in alphabetical order. Ensure that the number of significant figures reported for the amount(s) in the inactive ingredient list in labeling are consistent with the composition statement in the 3.2.P.1 table.

Revise the ingredient information to read as follows: "Each 2 mL prefilled syringe delivers 400 mg sibeprenlimab-szsi and the inactive ingredients: arginine (17.6 mg), glutamic acid (14.8

mg), histidine (4.34 mg), L-histidine hydrochloride monohydrate (4.62 mg), polysorbate 80 (0.40 mg), and sorbitol (36.4 mg), and Water for Injection, USP. The pH is 6.2." *Applicant revised as requested.*

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

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

Comment/Recommendation: Based on CDER's current interpretation of 21 CFR 610.61(r) and after consultation with OPQA III Product Quality assessors, this regulation does not apply to this product because 1) no U.S. standard of potency has been prescribed for sibeprenlimab products (i.e., there is no specific test method described in regulation for sibeprenlimab 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 **Voyxact** 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.

(b) (4)

(b) (4) *Applicant revised as requested*

Rx only (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(s), 21 CFR 201.100(b)(1)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)	✓ Yes ☐ No ☐ N/A

Divided manufacturing (package labeling)	**Acceptable**
Regulation: 21 CFR 610.63 (Divided manufacturing responsibility to be shown) (Also refer to the Guidance for Industry, Cooperative Manufacturing Arrangements for Licensed Biologics)	☐ Yes ☐ No ☒ N/A

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

Bar code (package labeling)	**Acceptable**
Regulations: 21 CFR 610.67, 21 CFR 201.25	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Guidance for Industry *Bar Code Label Requirements Questions and Answers* (August 2011) Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)	✓ Yes ☐ No ☐ N/A

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

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

Preparation instructions (package labeling)	**Acceptable**
Regulation: 21 CFR 201.5(g) and 21 CFR 610.61(i)	☐ Yes ☐ No ☒ N/A
Recommended labeling practices references: Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022) *USP General Chapters <7> Labeling*	✓ Yes ☐ No ☐ N/A

Package type term (package labeling)	**Acceptable**
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*	✓ Yes ☐ No ☐ N/A

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

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

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

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

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

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

Net quantity (package labeling)	**Acceptable**
Regulation: 21 CFR 201.51	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)	✓ Yes ☐ No ☐ N/A

Guidance for Industry *Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products* (June 2015) *USP General Chapters <1151> Pharmaceutical Dosage Forms (Excess volume in injections).*	

Statement of Dosage (package labeling)	**Acceptable**
Regulations: 21 CFR 201.55, 21 CFR 201.100(b)(2)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation: Revise from "Usual Dosage:…" to "Dosage: See Prescribing Information". *Applicant revised similarly as requested*

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

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

Comment/Recommendation: Remove the statement (b) (4) (b) (4) from the principal display panel (b) (4) (b) (4) *Applicant revised as requested*

Prescribing Information Evaluation

PRESCRIBING INFORMATION

Highlights of Prescribing Information	
PRODUCT TITLE	**Acceptable**
Regulation: 21 CFR 201.57(a)(2)	✓ Yes ☐ No ☐ N/A
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	✓ Yes ☐ No ☐ N/A

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

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

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 Draft Guidance *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products - Content and Format Guidance for Industry* (January 2023)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation: Added the clarity to the identifying characteristics in the visually inspect statement. *The Applicant revised as requested.*

Visually inspect the prefilled syringe for particulate matter and discoloration. The solution should be clear to opalescent and colorless to yellow. Do not use the prefilled syringe if the solution contains visible particulate matter, is cloudy or discolored (other than clear to opalescent, colorless to yellow).

Relocated from section 16 and revised the instructions for removal of syringe from refrigerated conditions prior to administration. *The Applicant revised as requested and added the statement - do not use Voyxact if it has been at RT for 7 days or longer. Product quality assessor determined data support.*

Provide the minimum time required for the prefilled syringe to equilibrate to room temperature prior to administration and the maximum allowable time the syringe may be held at room temperature after equilibration. *The Applicant added "15 to 30 minutes".*

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

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), FD&C Act Section 502(e)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: USP General Chapters <1091>, USP General Chapters <7>	✓ Yes ☐ No ☐ N/A

Comment/Recommendation: Revised to read as the pharmacological class instead of mechanism of action. *The Applicant revised as requested.*

FDA approved labeling is required to use the established names for drugs (i.e., drug products and ingredients) per 21 CFR 299.4. Ensure that the established names for inactive ingredients in your product are the USP/NF monographs titles: arginine, glutamic acid, histidine, polysorbate 80, and sorbitol. The common name for L-histidine hydrochloride monohydrate is sufficient for labeling. Ensure that the inactive ingredients names appear in alphabetical order. Ensure that the number of significant figures reported for the amount(s) in the inactive ingredient list in labeling are consistent with the composition statement in the 3.2.P.1 table. *The Applicant revised as requested.*

Full Prescribing Information	
15 & 16 Hazardous Drug	**Acceptable**
Regulation: 21 CFR 201.57(c)(17)(iv) 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]	☐ Yes ☐ No ☒ N/A

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

Comment/Recommendation: Revised handling instructions for readability. *The Applicant revised as requested.*

Relocated sentences describing storage requirements before administration to section 2 (Preparation and Administration). *The Applicant revised as requested.*

Full Prescribing Information	
MANUFACTURER INFORMATION	**Acceptable**
Regulations: 21 CFR 201.100(e), 21 CFR 201.1	✓ Yes ☐ No ☐ N/A
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)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation: Revise to the applicant's name provided on line 2 of Form FDA 356h, Otsuka Pharmaceutical Company, Ltd. *The Applicant revised as requested.*

(b) (4)

Distributed by:
Otsuka America Pharmaceutical, Inc.
Rockville, MD 20850, USA

Patient Information Labeling Evaluation

PATIENT INFORMATION LABELING	
TITLE (NAMES AND DOSAGE FORM)	**Acceptable**
Recommended Labeling Practices references: To ensure consistency with the product title in the Highlights of Prescribing Information (see Draft Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products - Content and Format Guidance for Industry (January 2018). For the recommended dosage form (see USP General Chapters: <1> Injections, Nomenclature and Definitions, Nomenclature form).	✓ Yes ☐ No ☐ N/A

PATIENT INFORMATION LABELING	
STORAGE AND HANDLING	**Acceptable**
Recommended labeling practices for Patient Labeling: 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

PATIENT INFORMATION LABELING	
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: Revised ingredient names to align with your Prescribing Information. *Applicant revised as requested*

(b) (4)

PATIENT INFORMATION LABELING	
MANUFACTURER INFORMATION	**Acceptable**
21 CFR 201.1, 19 CFR 134.11	✓ 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: Revise to the applicant's name provided on line 2 of Form FDA 356h, Otsuka Pharmaceutical Company, Ltd. *Applicant revised as requested*

(b) (4)

Distributed by:
Otsuka America Pharmaceutical, Inc.
Rockville, MD 20850, USA

Instructions for Use Evaluation

INSTRUCTIONS FOR USE	
TITLE (NAMES AND DOSAGE FORM)	**Acceptable**
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 Guidance for Industry *Instructions for Use – Patient Labeling for Human Prescription Drug and Biological products – Content and Format (*July 2022*). For the recommended dosage form (see USP General Chapters: <1> Injections, Nomenclature and Definitions, Nomenclature form).*	✓ Yes ☐ No ☐ N/A

INSTRUCTIONS FOR USE	
STORAGE AND HANDLING	**Acceptable**
Recommended labeling practices for IFU: Guidance for Industry *Instructions for Use – Patient Labeling for Human Prescription Drug and Biological products – Content and Format (*July 2022*). 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

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

INSTRUCTIONS FOR USE	
MANUFACTURER INFORMATION	**Acceptable**
21 CFR 201.1, 19 CFR 134.11	✓ Yes ☐ No ☐ N/A
Guidance for Industry *Instructions for Use – Patient Labeling for Human Prescription Drug and Biological products – Content and Format (*July 2022). *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: Revise to the applicant's name provided on line 2 of Form FDA 356h, Otsuka Pharmaceutical Company, Ltd. *The Applicant revised as requested.*

(b) (4)

Distributed by:
Otsuka America Pharmaceutical, Inc.
Rockville, MD 20850 USA

APPENDIX C. Acceptable Labels and Labeling

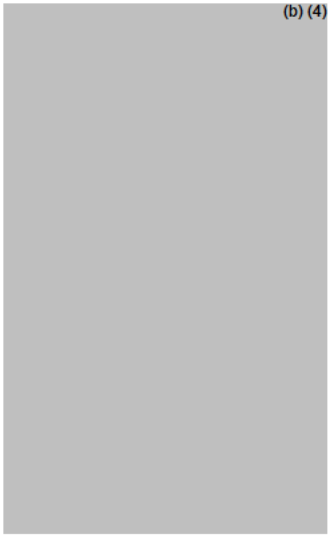
To note, additional non-product quality-related revisions may be submitted at a future date within this review cycle. Product quality-related information in this version of the labeling is acceptable from OPQA III labeling perspective.

Prescribing Information (submitted on October 27, 2025 \\CDSESUB1\EVSPROD\bla761434\0033\m1\us\114-labeling\draft\labeling\draft-labeling-text-clean.pdf)

Instructions for Use (submitted on October 27, 2025 \\CDSESUB1\EVSPROD\bla761434\0033\m1\us\114-labeling\draft\labeling\voyxact-pfs-ifu-clean-23oct2025.pdf)

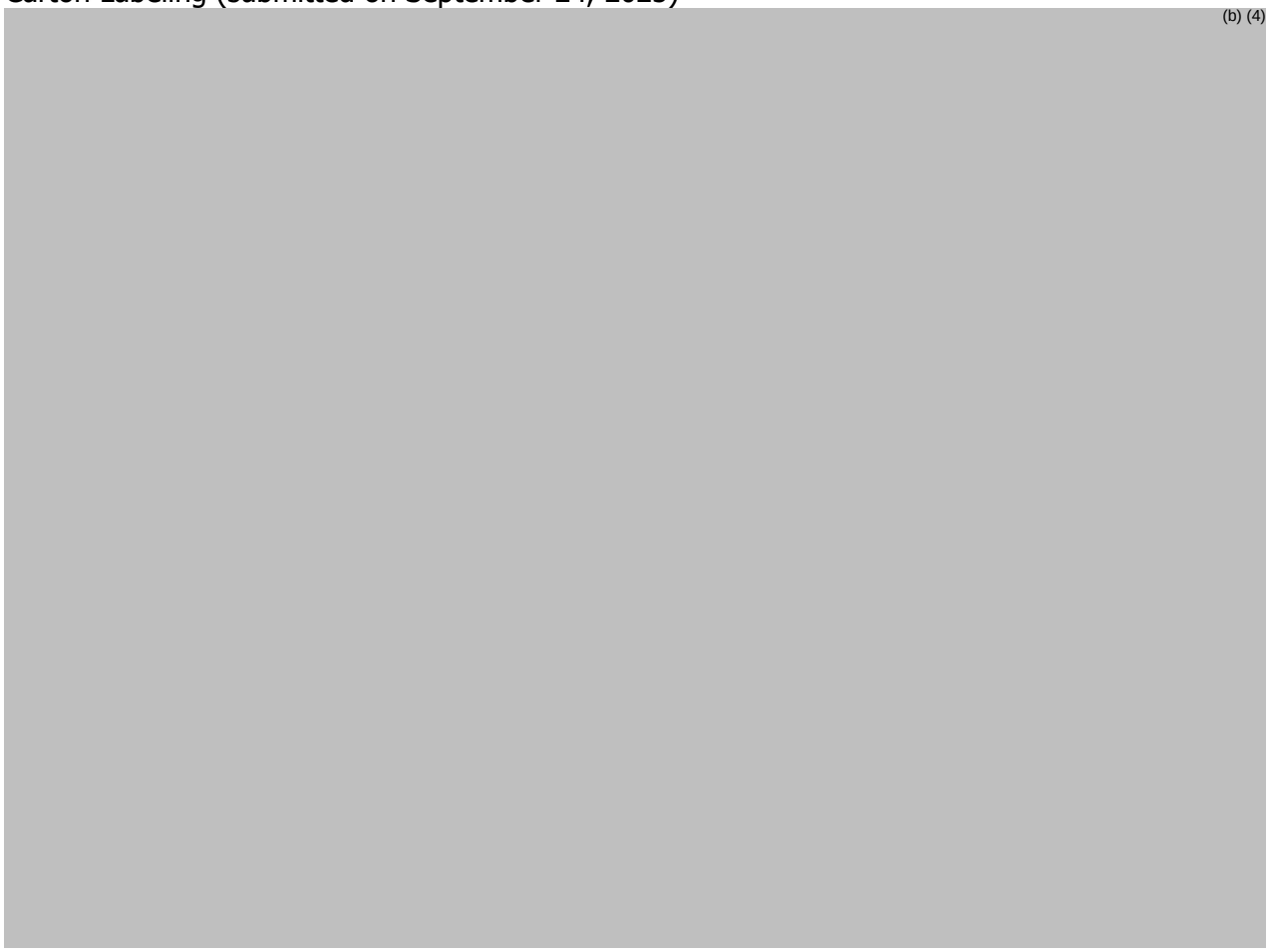
Patient Information (submitted on submitted on October 27, 2025 \\CDSESUB1\EVSPROD\bla761434\0033\m1\us\114-labeling\draft\labeling\voyxact-ppi-clean-24oct2025.pdf)

Container Labels (submitted on October 7, 2025)



Carton Labeling (submitted on September 24, 2025)

(b) (4)



Vicky Borders-Hemphill

Digitally signed by Vicky Borders-Hemphill
Date: 11/06/2025 07:34:45AM
GUID: 50814c7000007a3d59329f660d8ddf02

Dilip Devineni

Digitally signed by Dilip Devineni
Date: 11/06/2025 08:18:35AM
GUID: 5f2d768200266ce23091f4d27463e444

BLA Executive Summary
Assessment Date: 10/09/2025

1. Application/Product Information

BLA number	761434
Submission Type	Original Submission
Regulatory Pathway	NME 351(a)
Associated IND/BLA	IND 158899, IND 135282
Review Designation	Priority Review
Applicant	Otsuka Pharmaceutical Company, Ltd.
Indication	Treatment of immunoglobulin A nephropathy (IgAN)
Rx/OTC dispensed	Rx
Drug Product Name	Proprietary Name: VOYXACT
	Non-proprietary Name/Code Name: sibeprenlimab-szsi
	OBP Naming: MAB HUMANIZED (IGG2) ANTI O75888 (TNF13_HUMAN) [VIS649]
Drug Product Description	VOYXACT (sibeprenlimab-szsi) injection is a sterile, preservative-free, clear to opalescent, colorless to yellow solution, supplied in a single-dose prefilled syringe (PFS) designed to deliver 2.0 mL solution containing 400 mg sibeprenlimab-szsi in (b) (4) mM L-histidine, (b) (4) mM sorbitol, (b) (4) mM (b) (4) arginine, (b) (4) mM (b) (4) glutamic acid, and (b) (4) % (w/v) polysorbate 80, with a pH of 6.2. Sibeprenlimab-szsi is a humanized IgG2 monoclonal antibody that binds and blocks the biological actions of the cytokine A Proliferation Inducing Ligand (APRIL). The molecular weight is approximately 146 kDa.

	Sibeprenlimab-szsi is produced using recombinant DNA technology in Chinese hamster ovary (CHO) cells.		
Dosage Form	Solution, injection		
Strength	400 mg/2 mL (200 mg/mL) solution in a single-dose PFS		
Route of Administration	Subcutaneous (SC) injection		
Primary Container Closure System	(b) (4) clear (b) (4) glass syringe (b) (4) (b) (4) with 27G ½ inch stainless steel needle; closed with (b) (4) rubber plunger stopper (b) (4)		
Device Information	The PFS is further assembled with (b) (4) (b) (4) plunger rod (b) (4) (b) (4) finger flange (b) (4) and (b) (4) (b) (4) needle safety device (b) (4)		
Co-packaged Product Information	Not applicable		
OPQ Review Team	Discipline	Primary	Secondary
	Drug Substance (DS) and Drug Product (DP)	Dilip Devineni	Nailing Zhang
	Immunogenicity Assay	Davinna Ligons	
	Facility and Microbiology	Maria Gutierrez-Hoffman	Madushini Dharmasena
	RBPM	Shazma Aftab	RBPM

	ATL	Nailing Zhang
	Review Chief	Maria-Teresa Gutierrez-Lugo
OPQ Issued Consults	A CDRH consult for the needle safety device (NSD) was requested and the review will be documented separately.	

2. Recommendation and Conclusion on Approvability
Recommendation: Approval with PMCs/PMRs

The Office of Pharmaceutical Quality, CDER, recommends approval of BLA 761434 for VOYXACT (sibeprenlimab-szsi) manufactured by Otsuka Pharmaceutical Company, Ltd. The data submitted in this application are adequate to support the conclusion that the manufacture of VOYXACT (sibeprenlimab-szsi) 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:**

  (b) (4)

- **Drug Product:**
  - Manufacturing: (b) (4) (b) (4) (FEI: (b) (4)).
  - Device assembly, secondary packaging and labeling:
    - (b) (4) (FEI: (b) (4))
    - (b) (4) (FEI: (b) (4))

b. Fill size and dosage form:

400 mg/2 mL (200 mg/mL) solution in a single-dose prefilled syringe

c. Dating Period:

- **Drug Product:** 24 months at 5°C ± 3°C, protected from light

- Drug Substance: (b) (4) months at (b) (4) °C
- 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 substance and drug product under 21 CFR 601.12.

d. Exempt from lot release:
   - Yes
   - VOYXACT is exempted from lot release per FR 95-29960.

e. Draft Phase 4 (Post-Marketing) Commitments, Requirements, Agreements, and/or Risk Management Steps, as applicable

Three OPMA microbiology PMCs are listed below:

PMC 4907-2: Conduct a Low Endotoxin Recovery hold time study, with at least 3 batches of sibeprenlimab drug product, at temperatures that reflect the relevant temperatures of the drug product manufacturing process (b) (4) (b) (4) for a duration greater than the proposed hold times during the manufacturing process.

Final Report Submission: 08/31/2026

PMC 4907-3: Implement and qualify bioburden testing, with appropriate limits (b) (4)

Final Report Submission: 08/31/2026

PMC 4907-4: Conduct bioburden method qualification for sibeprenlimab drug substance and associated in-process samples using two additional drug substance batches.

Final Report Submission: 12/31/2025

4. Basis for Recommendation

a. Summary:

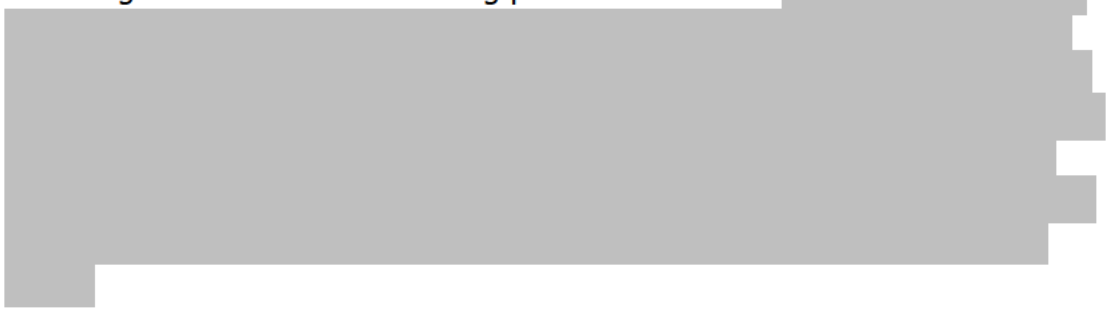
VOYXACT (sibeprenlimab-szsi) is indicated for the treatment of immunoglobulin A nephropathy (IgAN). It is a humanized IgG2 monoclonal antibody that binds and blocks the biological actions of the cytokine A Proliferation Inducing Ligand (APRIL), preventing APRIL from engaging with

its receptors B cell maturation antigen (BCMA) and transmembrane activator and calcium modulator and cyclophilin ligand interactor (TACI). Inhibition of APRIL results in reduced levels of galactose-deficient immunoglobulin A1 (Gd-IgA1), which is implicated in the pathogenesis of IgAN.

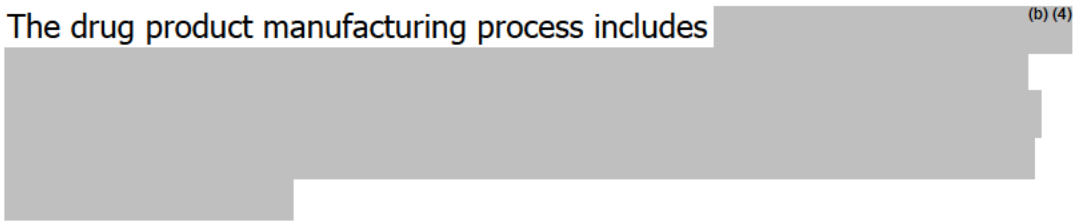
Two assays are used to control the potency of VOYXACT (sibeprenlimab-szsi). The first is an ELISA assay to measure its binding affinity to APRIL. The second is a cell-based inhibition assay that measures the luciferase signal emitted by the NF-κB reporter in HEK293 cells that are engineered to express luciferase enzyme upon binding of APRIL to BCMA and activation of the NF-κB pathway; the ability of VOYXACT (sibeprenlimab-szsi) to prevent APRIL from binding to BCMA is determined by the inhibition of the luminescence signal. Potency results are reported as percentage relative to a qualified reference material.

As VOYXACT (sibeprenlimab-szsi) binds to a functionally conserved binding epitope on APRIL that is shared by both BCMA and TACI receptors, measuring its ability to inhibit APRIL-BCMA interaction reflects its ability to inhibit APRIL-TACI interaction. Therefore, it is acceptable to have a cell-based assay that only measures the inhibition of APRIL-BCMA interaction.

The drug substance manufacturing process consists of (b) (4)



The drug product manufacturing process includes (b) (4)



No approvability issues were identified from a sterility assurance or microbiology product quality perspective. Three PMCs were issued to mitigate residual risks of microbial control. All facilities used for the manufacture and quality control testing were found acceptable for the proposed operations.

The onsite pre-license inspections for the drug substance manufacturing facility (b) (4) and the drug product manufacturing facility (b) (4) (b) (4) were waived based on compliance history.

Two anti-drug antibody (ADA) assays and one neutralizing antibody (NAb) assay used for immunogenicity assessment in the clinical studies to support this BLA are adequately validated and suitable for their intended purpose. Drug tolerance and APRIL interference issues were identified for the NAb assay; however, NAb-positive samples were detected across all clinical studies in which neutralizing ADA evaluations were conducted. OPQ defers to the clinical pharmacology team for assessment of the clinical data and the evaluation of the impact of drug tolerance and APRIL interference limitations on NAb assay clinical analysis.

The overall VOYXACT (sibeprenlimab-szsi) control strategy incorporates control 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 are appropriately established to ensure consistency and quality of the final product; therefore, lot variability is not a concern. The BLA is recommended for approval from the product quality, facility, microbiology and sterility assurance perspectives.

b. Subdiscipline Recommendation:

Drug Substance	**-**	**Adequate**
Drug Product	**-**	**Adequate**
Immunogenicity Assay	**-**	**Adequate**
Facilities	**-**	**Adequate**
Microbiology	**-**	**Adequate with PMCs/PMRs**

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 VOYXACT (i.e., there is no specific test method described in regulation for VOYXACT that establishes an official standard of potency). We next considered whether potency is a factor for VOYXACT 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 VOYXACT for purposes of § 610.61(r) because lot variability is not a concern for VOYXACT as VOYXACT'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:

- Concurrent validation (b) (4)
- Concurrent validation (b) (4)
- Concurrent validation (b) (4)
- Stability monitoring for master cell bank and working cell bank
- Stability monitoring for primary and working reference standards
- Stability protocol for drug substance shelf-life extension
- Post-approval stability protocol for drug substance

ii. Residual risk:
See PMC 4907-3 and PMC 4907-4 in Section 3.e. for residual microbial control issues covered by the PMCs.

iii. Future inspection points to consider: None

c. Drug Product:

i. Protocols approved:

- Stability protocol for drug product shelf-life extension
- Post-approval stability protocols for drug product

ii. Residual risk:
See PMC 4907-2 in Section 3.e. for residual microbial control issue covered by the PMC.

iii. Future inspection points to consider:

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.

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/

DILIP D DEVINENI
10/09/2025 07:28:37 AM

NAILING ZHANG
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MARIA T GUTIERREZ LUGO
10/09/2025 09:21:43 AM