CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761134Orig1s000

PRODUCT QUALITY REVIEW(S)

BLA Executive Summary
Assessment Date: 9/6/2023

1. Application/Product Information

BLA number	761134
Submission Type	Original Submission
Regulatory Pathway	351(a)
Associated IND(s)/BLA	IND 112198
Review Designation	Standard
Applicant	Evive Biotechnology Singapore PTE. Ltd.
Indication	Decrease in the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia
Rx/OTC dispensed	Rx
Drug Product Name	Proprietary name: Ryzneuta
	Established name: Efbemalenograstim alfa-vuxw)
	OBP systematic name: FUS: MABFRAG HUMAN (IGG2 FC); RPROT P09919 (CSF3_HUMAN) [F627]
Drug Product Description	Ryzneuta drug product (DP) is a sterile, preservative-free solution supplied in a single-dose Pre-filled syringe with a needle safety device. Each DP prefilled syringe contains 20 mg of Efbemalenograstin alpha at a concentration of 20mg/mL formulated in a solution containing (b) (4) mM sodium (b) (4) % (w/v) sorbitol, (b) (4) % (w/v) polysorbate 20, and (b) (4) mM EDTA, pH 5.2.
	Efbemalenograstin alpha is a fusion protein consisting of human granulocyte colony-stimulating factor (G-CSF) and the Fc fragment of human IgG2. The two proteins are connected via a 16 amino acid linker between G-CSF and Fc. The G-CSF portion functions to stimulate the proliferation, differentiation, release and survival of granulocytes, mainly that of neutrophils and the Fc portion functions to prolong the half-life of G-CSF through binding to Fc neonatal receptor (FcRn).

Dosage Form	Injection.		
Strength	20 mg/mL		
Route of Administration	subcutaneous injection		
Primary container closure system	pre-filled syringe		
Device Information	N/A		
Co-packaged Product Information	N/A		
OPQ Review Team	Subdiscipline	Primary	Secondary
	Drug substance	Jee Chung	Chana Fuchs
	Drug product	Jee Chung	Chana Fuchs
	Immunogenicity Assay	Jee Chung	Chana Fuchs
	Facility	Yun Wu (DS) Wayne Seifert (DP)	Zhong Li
	Microbiology	Yun Wu (DS) Wayne Seifert (DP)	Maxwell Van Tassell
	RBPM	Kristine Leahy	
	ATL	Chana Fuchs	
OPQ Issued Consults	CDRH		

2. Recommendation and Conclusion on Approvability

The Office of Pharmaceutical Quality, CDER, recommends approval of BLA STN 761134 for Ryzneuta (Efbemalenograstin alpha-vuxw) manufactured by Evive Biotechnology Singapore PTE. Ltd. The data submitted in this application are adequate to support the conclusion that the manufacture of Ryzneuta 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:

- EVIVE Biopharmaceutical (Beijing), Ltd, Beijing, China; FEI: 3013430082

Drug Product:

- Aji BioPharma Services, San Diego, CA; FEI: (b) (4) manufactures the DP.
- Catalent Pharma Solutions, LLC, Schorndorf, Germany; FEI (b) (4) conducts plunger rod and safety device assembly, DP packaging, labeling and serialization.

b. Fill size and dosage form: 20 mg/mL prefilled syringe, injection

c. Dating Period:

- Drug Product: Expiration dating period is 36 months for Ryzneuta drug product when stored at 2-8°C protected from light.

- Drug Substance: Expiration dating period is (b) (4) months for efbemalenograstim alfa drug substance when stored at (b) (4) °C

- For packaged products: Not packaged

- Stability Option:
  None

d. Exempt from lot release:

- Yes
- Ryzneuta is exempted from lot release per FR 95-29960 and 21 CFR 610.2(b).

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

None

4. Basis for Recommendation

a. Summary:

- Efbemalenograstim alfa is a recombinant fusion protein consisting of human granulocyte colony-stimulating factor (G-CSF) and the Fc fragment of human IgG2. The two proteins are connected via a 16 amino acid linker between G-CSF and Fc. The fusion protein consists of 413 amino acids (including C-terminal lysine residue) and due to disulfide linkages between Fc regions, two molecules of G-CSF are present in one molecule of Efbemalenograstim alfa. A total of 8 intra-disulfide bonds (2 in each G-CSF molecule and 2 in Fc regions) and 2 inter-disulfide bonds are present in Efbemalenograstim alfa. Two free cysteine residues are also present on residue 17. Each heavy chain portion of Fc contains the consensus glycosylation site on asparagine residue 263 (Asn303) and a serine to proline substitution on residue 297 (S297P) to

reduce effector function. Efbemalenograstim alfa is also glycosylated on Thr133 (O-linked) located within the G-CSF portion. The mechanism of action and mechanism of activity are directly associated with the components of the fusion protein. The G-CSF part of the molecule binds to the G-CSF receptor and activates the STAT 3 signaling pathway, resulting in cell proliferation, differentiation, and release and survival of granulocytes, mainly neutrophils. The IgG2Fc part of the molecule functions to prolong the half-life of the G-CSF portion of the molecule by binding to the Fc neonatal receptor (FcRn) and mediating cellular recycling , as well as by adding to the molecular weight of the protein which is through to decrease renal clearance.

- The potency is a cell proliferation assay using M-NFS-60 Cell, a murine cell line derived from myelogenous leukemia cells. The cells are responsive to G-CSF stimulus. Cell proliferation is measured using Cell Titer Blue reagent that contains resazurin to measure cell viability. Resazurin is reduced by live cells into fluorescent resorufin, and the relative potency is calculated through the comparison of fluorescent signal from the test sample and the reference standard.

- A single primary reference standard (PRS) is currently being used. The current primary reference standard (b) (4) was derived from DS batch #627S150603. A protocol for requalification/stability of the primary standard was provided in the BLA. The Applicant is intending to qualify a working reference standard (WRS) for a two-tiered reference material system. A qualification protocol for new reference standards (WRS and PRS) was included in the BLA.

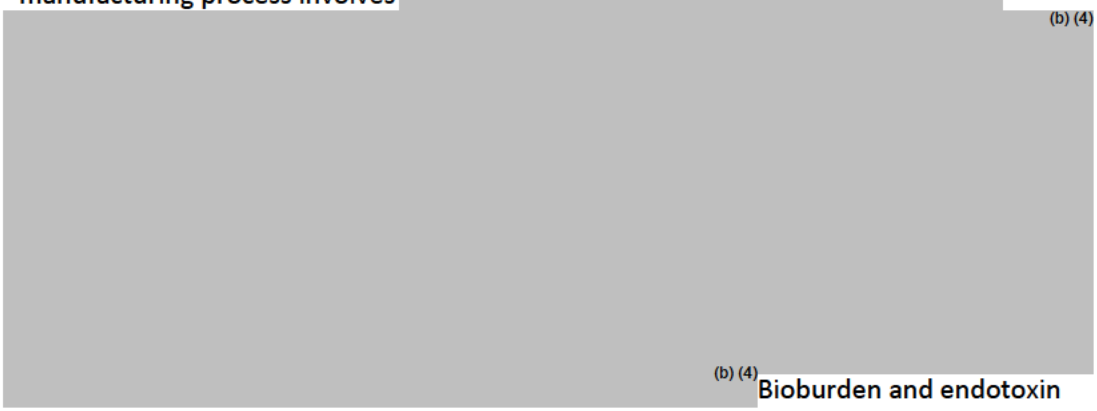
- The Efbemalenograstim alfa expressing cell line was derived (b) (4) (b) (4) The long-term stability of the cell banks will be assessed in accordance with a protocol provided in the BLA.

- Efbemalenograstim alfa drug substance is (b) (4)

(b) (4)

- The DP is manufactured at Aji BioPharma Services, San Diego, CA. The DP manufacturing process involves (b) (4)

(b) (4)



(b) (4) Bioburden and endotoxin are tested during manufacture, and sterility and endotoxin are tested at release. Sterility of the DP is assured within the stability program by container closure integrity testing using a validated method. Validation of the shipping system to assure temperature control and stability of the product during shipment was provided. The plunger movement simulation of the PFS under worst case conditions assessing transport conditions and manufacturing capability provided evidence that the sterile boundary is maintained.

- The overall Ryzneuta (Efbemalenograstim alfa) control strategy incorporates control (b) (4)

(b) (4) The manufacturing processes and overall control strategies for Ryzneuta 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 a product quality, facility, microbiology and sterility assurance perspectives.

- An inspection of Evive Biopharmaceutical (Beijing) Ltd (FEI: 3013430082, Beijing, China) was required before this application could be approved. Due to restrictions on travel, OPQ was unable to conduct an inspection during the initial review cycle, and therefore, FDA deferred action on the application until inspection activities were completed.

- The immunogenicity assays used to assess immunogenicity to efbemalenograstim alpha are sufficiently sensitive to detect anti-drug antibodies (ADA) in presence of efbemalenograstim alpha at plasma concentrations. The screening and Neutralizing Antibody assays for F-627 and G-CSF are adequately validated.

b. Subdiscipline Recommendation:

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

c. Environmental Assessment (EA):
A categorical exclusion is claimed by Evive Biotechnology Singapore PTE. Ltd. from the requirement to prepare an environmental assessment in accordance with 21 CFR 25.31(c) and is deemed acceptable.

d. Potency Assessment for Labeling:
Potency is not a factor.
As an initial matter, we determined that no U.S. standard of potency has been prescribed for Efbemalenograstim alfa-vuxw) (i.e., there is no specific test method described in regulation for Efbemalenograstim alfa-vuxw) that establishes an official standard of potency). We next considered whether potency is a factor for Efbemalenograstim alfa-vuxw) 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 Ryzneuta for purposes of § 610.61(r) because lot variability is not a concern for Ryzneuta as Ryzneuta'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:

- (b) (4) Validation Protocol
- (b) (4) Validation Protocol
- (b) (4) Validation Protocol
- (b) (4) Study Protocol
- Primary reference standard stability protocol
- Qualification of new Primary and Working Reference Standard
- Drug Substance annual stability protocol
- (b) (4) protocol (b) (4)
- (b) (4) protocol (b) (4)

ii. Residual risk: none.

iii. Future inspection points to consider: Verify that deviations and appropriate steps are taken to evaluate impact to product quality for excursions of any key process parameters (KPP) and non-KPPs. This verification is related to Generon's Quality System and follow-up to FDA Form 483 Observation 4: Deviation root cause analyses, CAPAs implementation, and preventative actions are inadequate to prevent recurring event (s). (b) (4)

c. Drug Product:

i. Protocols approved:

- Drug product annual stability protocol
- Comparability Protocol for scale-up of DP PFS manufacturing at Ajinomoto Biopharma Serices, San Diego, CA

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.

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/

CHANA FUCHS
09/06/2023 03:52:00 PM

JENNIFER F SWISHER
09/06/2023 07:26:21 PM

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

LABELS AND LABELING ASSESSMENT – AMENDED
ADDENDUM (see pages 30 - 32)

Date of Assessment:	October 3, 2023
Assessor:	Diana Pei, PharmD Labeling Assessor Office of Biotechnology Products (OBP)
Through:	Jee Chung, PhD Product Quality Assessor OBP/Division of Biotechnology Review and Research IV
Application:	BLA 761134
Applicant:	EVIVE BIOTECHNOLOGY SINGAPORE PTE. LTD.
Submission Date:	March 30, 2021 May 13, 2021 October 20, 2021 December 16, 2021 August 30, 2023 September 6, 2023 September 28, 2023 October 3, 2023
Product:	Ryzneuta (efbemalenograstim alfa-vuxw)
Dosage form(s):	injection
Strength and Container-Closure:	20 mg/mL single-dose prefilled syringe
Purpose of assessment:	The Applicant submitted a biologics license application for the approval of efbemalenograstim alfa for decreasing the incidence of infections as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.
Recommendations:	The prescribing information, patient labeling, container labels, and carton labeling are acceptable from an OBP 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). Current and previous versions (b) (4) have been deleted from the submission and was not included in the acceptable labeling (Appendix C).

CONCLUSION

The prescribing information and patient labeling submitted on August 30, 2023 and the container label and carton labeling submitted on September 6, 2023 were assessed and found to be acceptable (see Appendix C) from an OBP Labeling perspective.

APPENDICES

Appendix A: Proposed Labeling

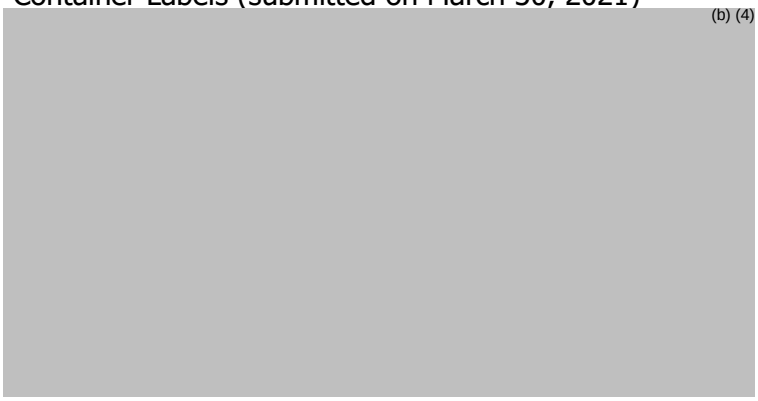
- Prescribing Information (submitted on May 13, 2021)
  \\CDSESUB1\evsprod\bla761134\0008\m1\us\114-labeling\114a-draft-label\united-states-prescribing-information.docx

- (b) (4) (submitted on May 13, 2021)
  \\CDSESUB1\evsprod\bla761134\0008\m1\us\114-labeling\114a-draft-label\instructions-for-use-tracked.docx

- Patient Information (submitted on May 13, 2021)
  \\CDSESUB1\evsprod\bla761134\0008\m1\us\114-labeling\114a-draft-label\patient-information-leaflet-tracked.docx

- Container Labels (submitted on March 30, 2021)

  (b) (4)

- Carton Labeling (submitted on March 30, 2021)

1 Page of Draft Labeling has been Withheld in Full as B4 (CCI/TS) immediately following this page

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(h)(2)(i)(1)(i)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (placement of dosage form outside of parenthesis and/or below the proper name)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
To Applicant: add the dosage form after or below the proper name.

Applicant's added the dosage form after the proprietary name.

To Applicant: The layout of the finished dosage form is not consistent with the presentation of the proprietary name, proper name, and dosage form for biological products. See Draft Guidance: Container and Carton, April 2013 (lines 344-349)5. Move the finished dosage to the line below the proper name. For example:

Ryzneuta
(efbemalenograstim alpha-xxxx)
Injection

Applicant revised labeling so the dosage form is under the proper name. The revision is acceptable.

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[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] Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors. Food and Drug Administration. 2013. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM349009.pdf.

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
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[6])	☐ Yes ☐ No ☒ N/A

Comment/Recommendation: The label is small and could be considered a partial label. Thus, the qualifying phrase "Manufactured by" and the U.S. license number are not required per 21 CFR 610.60(c).

To Applicant: the manufacturer's name should be presented on the labeling as it appears on your 356h form. The Applicant's name on the 356h form is considered the manufacturer.

Applicant changed manufacturer's name to (b) (4) *This does not match the Applicant's name on the FDA 356h form.*

To Applicant: The applicant's name on the 356h form is considered the manufacturer. The manufacturer's name should be presented on the labeling as it appears on your 356h form, "EVIVE BIOTECHNOLOGY SINGAPORE PTE. LTD."

Applicant's response: Evive has changed the manufacturer's name to "EVIVE BIOTECHNOLOGY SINGAPORE PTE. LTD" on the carton and tray lid labels. However, to avoid over-crowding, Evive proposes to retain the original abbreviated format of manufacturer as (b) (4) *on the container label.*

To Applicant: To avoid over-crowding, the US license number can be omitted on the partial labeling to make room for the complete name of the manufacturer. Please refer to 21 CFR 610.60(c) for additional information.

Applicant did not change the manufacturer's name on the labeling. The carton labeling still has the manufacturer listed as (b) (4)

To Applicant: The FDA Form 356h lists the applicant's name as "EVIVE BIOTECHNOLOGY SINGAPORE PTE. LTD.", where as your labeling displays (b) (4) The presentation of the applicant's name should be consistent and appear the same (including

[6] 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."

capitalization and punctuation) between the FDA Form 356h and the labeling. If space is limited, consider removing the US license number. See 21 CFR 610.60(c) which states "If the container is capable of bearing only a partial label, the container shall show as a minimum … the name of the manufacturer." *Applicant revised 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(h)(2)(i)(1)(iii)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

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

Comment/Recommendation:

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

Comment/Recommendation:

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:
To Applicant: The strength presentation is not presented per total volume in the highlighted yellow box. We recommend revising the strength in the box to "20 mg/ml". *Applicant revised the product strength to 20 mg/mL. The revision is acceptable.*

Multiple-dose containers (container label)	**Acceptable**
Regulations: 21 CFR 610.60(a)(5), 21 CFR 201.55 *(recommended individual dose)*	☐ 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
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

Comment/Recommendation: The label is small and could be considered a partial label. Thus, a "Rx only" statement is not required per 21 CFR 610.60(c).

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

Comment/Recommendation:

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: The product contains a container label.

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

Comment/Recommendation:

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: Evive confirms that the entire syringe barrel post-fill and stoppering is uncovered and allows for visual inspection of the bulk drug product (BDP). The BDP is assembled with the plunger rod, label, and safety device. At the end of labeling and assembly, the area near the stopper and label edge also allows full circumference visualization. In addition, the label is opaque. Photos of Ryzneuta BDP and full packaged product (FPP) are provided (Figure 1).

Figure 1. Photos of Ryzneuta BDP (A) and FPP (B - D)

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

Comment/Recommendation:
To Applicant: We recommend adding the route of administration. The route of administration is not present on the principal display panel (PDP). The route of administration is critical information that should be available to users at the time or product administration. Therefore, we recommend you add a statement similar to, "For Subcutaneous Use Only" on the PDP.

Applicant made the recommended revisions and added "For Subcutaneous Use Only". The revision is acceptable.

NDC numbers **(container label)**	**Acceptable**

Regulations: 21 CFR 201.2, 21 CFR 207.35	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
To Applicant: We recommend adding the NDC number.

Applicant made the recommended revision, and the revision is acceptable.

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

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

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:
To Applicant: Replace (b) (4) with "single dose".

Applicant made the recommended revision, and the revision is acceptable.

No misleading statements (container label)	**Acceptable**
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: The label does not display text in Spanish.

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: The drug product does not contain FD&C Yellow No. 5 or 6.

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

Comment/Recommendation:
To Applicant: we recommend adding a barcode. The linear barcode is absent. The drug barcode is often used as an additional verification before drug administration in the hospital setting; therefore, it is an important safety feature that should be part of the label whenever possible. Therefore, we request you add the product's linear barcode to each individual container as required per 21 CFR 201.25(c)(2). Ensure the barcode is surrounded by sufficient white space to allow scanners to correctly read the barcode in accordance with 21 CFR 201.25(c)(i).

Applicant made the recommended revision, and the revision is acceptable.

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
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

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: The label is small and could be considered a partial label. Thus, a dosage statement is not required.

Inactive ingredients (container label)	**Acceptable**
Regulation: 21 CFR 201.100	☐ 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

Comment/Recommendation:

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

Comment/Recommendation:

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

Comment/Recommendation:

Package[7] 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
Recommended labeling practices (placement of dosage form outside of parenthesis and/or below the proper name)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
To Applicant: add the dosage form after or below the proper name.

Applicant's added the dosage form below the proprietary name.

To Applicant: The layout of the finished dosage form is not consistent with the presentation of the proprietary name, proper name, and dosage form for biological products. See Draft Guidance: Container and Carton, April 2013 (lines 344-349)8. Move the finished dosage to the line below the proper name. For example:

Ryzneuta
(efbemalenograstim alpha-xxxx)
Injection

Applicant revised labeling so the dosage form is under the proper name. The revision is acceptable.

[7] 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.
[8] Draft Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors. Food and Drug Administration. 2013. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM349009.pdf.

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:
To Applicant: the manufacturer's name should be presented on the labeling as it appears on your 356h form. The Applicant's name on the 356h form is considered the manufacturer.

Applicant changed manufacturer's name to (b) (4) *This does not match the Applicant's name on the FDA 356h form.*

To Applicant: The applicant's name on the 356h form is considered the manufacturer. The manufacturer's name should be presented on the labeling as it appears on your 356h form, "EVIVE BIOTECHNOLOGY SINGAPORE PTE. LTD."

Applicant's response: Evive has changed the manufacturer's name to "EVIVE BIOTECHNOLOGY SINGAPORE PTE. LTD" on the carton and tray lid labels. However, to avoid over-crowding, Evive proposes to retain the original abbreviated format of manufacturer as (b) (4) *on the container label.*

To Applicant: The FDA Form 356h lists the applicant's name as "EVIVE BIOTECHNOLOGY SINGAPORE PTE. LTD.", where as your labeling does not have a period after "LTD". The presentation of the applicant's name should be consistent and appear the same (including capitalization and punctuation) between the FDA Form 356h and the labeling. Please revise the manufacturer's name so it is exactly the same as the Applicant's name on the FDA 356h Form.

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

Comment/Recommendation:

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

	☐ N/A

Comment/Recommendation:

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

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
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

Comment/Recommendation: To Applicant: The strength presentation is not presented per total volume in the highlighted yellow box. We recommend revising the strength in the box to "20 mg/ml". *Applicant revised the product strength to 20 mg/mL. The revision is acceptable.*

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

Comment/Recommendation:

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

Comment/Recommendation:

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

Comment/Recommendation:

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

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:

To Applicant: Add "This product contains dry natural rubber" in bold print consistent with the tray lid labeling.

Applicant made the recommended revision, and the revision is acceptable.

Inactive ingredients (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61, 21 CFR 201.100	✓ 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:
To Applicant: The statement, "Each 1 mL prefilled syringe contains: 20 mg efbemalenograstim alfa in a sterile, clear, colorless solution (pH 5.2) containing acetate (0.60 mg), (b) (4) (b) (4) Remove (b) (4) to avoid a (b) (4) (b) (4) misinterpretation. We also recommend listing the inactive ingredients in alphabetical order.

Applicant revised as requested.

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

Comment/Recommendation:

(b) (4) **(package labeling)**	**Acceptable**
Regulation: (b) (4)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
To Applicant: Remove the statement (b) (4) from the carton labeling because our view is that (b) (4) is not applicable. Based on CDER's current interpretation (b) (4) and after consultation with OBP Product Quality assessors, this regulation does not apply to this product (b) (4) (b) (4)

(b) (4) (b) (4) Accordingly, the phrase (b) (4) is not required to appear on the carton labeling. Remove the statement (b) (4) from the carton labeling because our view is that (b) (4) is not applicable. *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

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
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

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
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

Comment/Recommendation:

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

Comment/Recommendation: To Applicant: Replace (b) (4) with "single dose". *Applicant made the recommended revision, and the revision is acceptable.*

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: The label does not display text in Spanish.

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: The drug product does not contain FD&C Yellow No. 5 or 6.

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

Comment/Recommendation: The drug product does not contain phenylalanine.

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

Comment/Recommendation: The drug product does not contain sulfites.

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) 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

Comment/Recommendation:

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

Comment/Recommendation: To Applicant: A "Recommended Dosage" statement is absent. We recommend you include a statement that reads, "Dosage: See Prescribing Information". *Applicant made the recommended revision, and the revision is acceptable.*

Dispensing container (package labeling)	**Acceptable**
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
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

Comment/Recommendation:

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

Comment/Recommendation:

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*	✓ Yes ☐ No ☐ N/A

USP General Chapters: <7> Labeling	

Comment/Recommendation:
To Applicant: Revise (b) (4) to "20 mg/mL".

Applicant revised as requested.

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:

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: Revise (b) (4) to "20 mg/mL".

Applicant revised as requested.

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:

To Applicant:

1. Please include pH [redacted]
2. According to mass spec data in the CMC section, the [redacted] molecular weight is [redacted] kDa. Please clarify the molecular weight.
3. Revised "sodium 0.23 mg" [redacted]

Applicant's response:

1. *Evive clarifies that the pH is [redacted] (pH 5.2).* [redacted]
2. *Evive would like to clarify that the molecular weight of 89.5 kDa is correct* [redacted]
3. *Evive would like to clarify that the sodium concentration of **0.23 mg** per syringe is correct. The sodium of the formulation is* [redacted] *0.23 mg.*

Below is a table summarizing the amounts of excipients in F-627 DP. The table is aPlease refer to Evive's response to IR submitted on Jan 24, 2022 (Seq 0041) for

Excipient	**Compound Concentration**	**Ion Concentration**	**Label Claim**
Sodium [redacted]	[redacted]		

Acetate	(b) (4) mg/mL	Acetate: (b) (4) mg/mL	• Sodium: (b) (4) (b) (4) Label claim: 0.23mg • EDTA: 0.293 mg/mL, Label claim: 0.29mg • Polysorbate 20: 0.1 mg/mL • Sorbitol, 50 mg/mL
Polysorbate 20	0.1 mg/mL	Polysorbate 20: 0.1 mg/mL	
Sorbitol	50 mg/mL	Sorbitol, 50 mg/mL	
(b) (4) EDTA	(b) (4) mg/mL	(b) (4) EDTA: 0.293 mg/mL	

Evive respectfully requests that no changes be made to 3.2.P.1 and the PI.

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

Comment/Recommendation:

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:
To Applicant:

We acknowledge the freeze/thaw studies were conducted with drug substance; however, we are not aware of any freeze/thaw studies with the drug product. Added in "Do not freeze." Revised to remove [redacted] (b) (4) and deleted [redacted] (b) (4) from "Discard syringe if frozen [redacted] (b) (4)" *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: To Applicant: The name of the applicant on the 356h form is considered the manufacturer. Please refer to 21 CFR 600.3(t). *Applicant revised as requested.*

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

Comment/Recommendation:

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

Comment/Recommendation:

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:

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:
To Applicant:
The name of the applicant on the 356h form is considered the manufacturer. Please refer to 21 CFR 600.3(t).

Applicant revised as requested.

APPENDIX C. ~~Acceptable~~ Labels and Labeling (See Addendum)

- Prescribing Information (submitted on August 30, 2023)
  \\CDSESUB1\EVSPROD\bla761134\0059\m1\us\114-labeling\114a-draft-label\united-states-prescribing-information-30aug2023.docx

- Patient Information (submitted on August 30, 2023)
  \\CDSESUB1\EVSPROD\bla761134\0059\m1\us\114-labeling\114a-draft-label\patient-information-leaflet-30aug2023.docx

- Container Label (submitted on September 5, 2023)

2 Pages of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

ADDENDUM
October 3, 2023

On September 28, 2023, EVIVE BIOTECHNOLOGY SINGAPORE PTE. LTD. submitted a revised carton label and tray lid labeling which included the suffix for the proper name.

During a review of the carton and tray lid labeling, the inactive ingredient was missing the suffix for the proper name. Thus, EVIVE BIOTECHNOLOGY SINGAPORE PTE. LTD. was requested to revise the proper name to include the missing suffix. EVIVE BIOTECHNOLOGY SINGAPORE PTE. LTD. submitted revised carton and tray lid labeling displaying the proper name with the suffix.

On September 28, 2023, Division of Medication and Error Prevention and Analysis (DMEPA) had also requested EVIVE BIOTECHNOLOGY SINGAPORE PTE. LTD. to relocate the strength statement in the orange box to directly underneath the dosage form and to reduce the size of the manufacturer logo for the carton and tray lid labeling. The route of administration was also requested to be relocated to be directly underneath the strength statement on the principal display panel on the tray lid labeling. On October 3, 2023, DMEPA requested the statement "One Single-Dose Prefilled Syringe" be relocated to its own separate line to improve readability of the statement.

The revised carton labeling submitted on September 28, 2023 and tray lid labeling submitted on October 3, 2023 is acceptable from an OBP labeling perspective.

Revised carton and tray lid labeling is displayed in Appendix D.

Appendix D: Accepted Labeling

- Prescribing Information (submitted on August 30, 2023)
  \\CDSESUB1\EVSPROD\bla761134\0059\m1\us\114-labeling\114a-draft-label\united-states-prescribing-information-30aug2023.docx

- Patient Information (submitted on August 30, 2023)
  \\CDSESUB1\EVSPROD\bla761134\0059\m1\us\114-labeling\114a-draft-label\patient-information-leaflet-30aug2023.docx

- Container Label (submitted on September 5, 2023)

2 Pages of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

Diana Pei

Digitally signed by Diana Pei
Date: 10/03/2023 04:02:13PM
GUID: 6352da2c009ad0777a2c3b47ec094b9a

Jee Chung

Digitally signed by Jee Chung
Date: 10/03/2023 04:06:52PM
GUID: 508da6da000265c6b990d788ce889c0b