CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

213793Orig1s000

PRODUCT QUALITY REVIEW(S)

QUALITY ASSESSMENT

Recommendation: Approval

NDA 213793
Review 1

Drug Name/Dosage Form	IMCIVREE (setmelanotide) injection
Strength	10 mg/mL
Route of Administration	Subcutaneous injection
Rx/OTC Dispensed	Rx
Applicant	Rhythm Pharmaceuticals
US agent, if applicable	-

SUBMISSION(S) REVIEWED	DOCUMENT DATE	DISCIPLINE(S) AFFECTED
Pre-submission, Original submission, and amendments	Pre-submission: (8/23/2019). Pre-sub amendments: 10/08/2019 (Facility information); 11/25/2019 and 2/07/2020 (microbiology). Original submission: 3/27/2020 Amendments: 5/13/2020 (Microbiology), 5/18/2020 and 5/29/2020 (Drug Substance, drug product, and process), 6/9/2020 (DMF LOA), 8/13/2020 (Drug product), 8/7/20 (Label)8/7/20 (Process), 8/14/20 (Comparability protocol), 8/17/2020 (Pkg. Batch record); 8/20/2020 (Drug substance, Drug product, Label)	Quality modules 3, 1.14, and 1.11

Quality Review Team

Discipline	Reviewer/Secondary	Branch/division
Drug Substance	Joseph Leginus/ Suong Tran	Branch III/Division of New Drug Active pharmaceutical
Drug Product	Theodore Carver / David J Claffey	Branch V/New Drug Products III
Process/ Facility	Kumar Janoria/ Vidya Pai	Branch II/ Office of Pharmaceutical Manufacturing Assessment (OPMA)
Microbiology	Yan Zheng/ Jesse Wells	OPMA
Regulatory Business Process Manager	Leeza Rahimi/ Hamet Toure	Branch I/Regulatory Business Process Management I
Application Technical Lead	Muthukumar Ramaswamy	Branch V/New Drug Products III
Environmental Analysis (EA)	Theodore Carver/ David J Claffey	Branch V/New Drug Products III of New Drug Products

Quality Review Data Sheet

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	III		(b) (4)	Active	*	LOA dated 4/20/2018
	V			Active	3/04/2019	LOA dated 3/28/2018
	IV			Active	*	LOA dated 7/26/2018
	III			Active	*	LOA dated 3/28/2018

*Sufficient information provided in the NA

B. Other Documents: *IND, RLD, or sister applications*

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	112595	Setmelanotide

2. CONSULTS: None

DISCIPLINE	STATUS	RECOMMENDATION	DATE	REVIEWER
Pharmacology/Toxicology	Complete	Acceptable	8/24/20	Shaji Theodore
Biopharmaceutics	Complete	Acceptable	8/06/2020	Kimberly Raines

Executive Summary

I. Recommendations and Conclusion on Approvability

The recommendation from the Office of Pharmaceutical Quality (OPQ) for NDA 213793 is approval, which includes an acceptable recommendation for the facilities listed in the application.

II. Summary of Quality Assessments

A. Product Overview

IMCIVREE (setmelanotide) injection, 10 mg/mL is for subcutaneous administration to treat obesity (b) (4) associated with pro-opiomelanocortin (POMC) deficiency obesity or leptin receptor (LEPR) deficiency obesity in adults and children 6 years and older. The proposed maximum dose is 3 mg/daily in adults and (b) (4) mg/day in children.

Setmelanotide is a melanocortin-4 (MC4) receptor agonist and an analog of endogenous melanocortin peptide, alpha-melanocyte stimulating hormone (α-MSH). It is a cyclic octapeptide containing one intramolecular disulfide bond.

IMCIVREE injection is a solution provided as a 1 mL multiple dose vial sealed with (b) (4) stopper, a flip-off seal, and an aluminum overseal. The dose will be administered using a (b) (4) syringe. Each mL of IMCIVREE contains 10 mg of setmelanotide, 100 mg of mPEG-200-DSPE (b) (4) 8.0 mg of carboxymethyl cellulose (b) (4) 11.0 mg of mannitol (b) (4) 5.0 mg of phenol (b) (4), 10.0 mg of benzyl alcohol (preservative), and 1.0 mg of sodium edetate (b) (4) water for injection.

Unopened IMCIVREE should be stored at 2ºC to 8ºC (36ºF to 46ºF) in the original carton. Opened vials can be stored (b) (4)

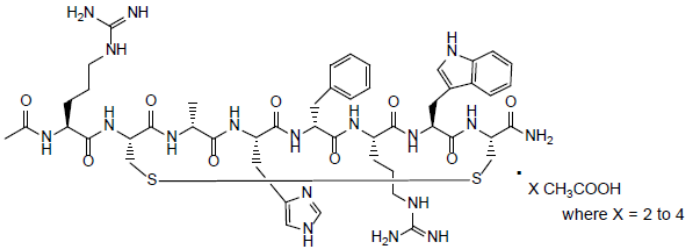
Proposed Indication(s) including Intended Patient Population	(b) (4) in adults and children 6 years and older
Duration of Treatment	*Chronic*
Maximum Daily Dose	*3 mg (adults); (b) (4) mg (children).*
Alternative Methods of Administration	*Not applicable*

B. Quality Assessment Overview

Drug Substance

The drug substance, setmelanotide acetate is a cyclic octapeptide, (b) (4)

Thee chemical name for setmelanotide acetate is acetyl-L-arginyl-L-cysteinyl-D-alanyl-L-histidinyl-D-phenylalanyl-L-arginyl-L-tryptophanyl-L-cysteinamide cyclic (2→8)-disulfide acetate. The molecular formula of anhydrous, free base is $C_{49}H_{68}N_{18}O_9S_2$ with a molecular weight of 1117.3 Daltons. Setmelanotide acetate is a white to off-white amorphous powder and is freely soluble in water. The drug substance (DS) has the following structural formula:



Dr. Joseph Leginus reviewed the chemistry, manufacturing, and control information for the drug substance including manufacturing process description, the proposed starting material specifications, control strategy for impurities, characterization data for drug substance and its impurities, reference standard information, test method descriptions and methods validation, drug substance specifications, and stability data. His review concluded that the drug substance information is adequate to control the identity, purity, strength, and quality of the drug substance used for manufacturing the drug product. The proposed drug substance specifications are consistent with batches used in clinical, nonclinical, and registration stability studies.

The applicant proposed to use (b) (4) as drug substance manufacturers and analytical comparability assessment for the two sources. Dr. Leginus' s review concluded that the physical and chemical quality of setmelanotide drug substance produced by each manufacturer are comparable with indistinguishable quality attributes. Based on review of the stability information, the drug substance reviewer granted a retest period of (b) (4) months for the drug substance when stored in (b) (4) at (b) (4) °C.

Dr. Leginus's recommendation for this application is adequate based on CMC review of drug substance section. For additional details, please refer to Dr. Leginus's CMC review dated 7/16/2020 in Panorama.

Drug Product

Drug Product Formulation: The established name for this product is setmelanotide injection. The proposed product is a clear to opalescent, colorless, sterile, (b) (4) solution packaged in a 1mL multiple-dose vial. Each mL of IMCIVREE contains 10 mg

of setmelanotide, 100 mg of mPEG-2000-DSPE (b) (4), 8.0 mg of carboxymethyl cellulose (b) (4) 11.0 mg of mannitol (b) (4) 5.0 mg of phenol (b) (4), 10.0 mg of benzyl alcohol (preservative), and 1.0 mg of sodium edetate (b) (4) water for injection. The pH of the formulation is 5 to 6. A (b) (4) syringe will be used to administer from the vial. The recommended maximum dose is 3 mg (0.3 mL) per day for adults.

The drug substance has adequate solubility at the proposed pH (b) (4) The choice and the levels of each excipient proposed for use in the drug product are based on developmental and clinical studies. Specifically, carboxymethyl cellulose and mPEG-2000-DSPE were chosen for use in the product, as it affected the drug release profile. All excipients present in the drug product are USP/NF grade and present in approved products. The viscosity of the product is 20cP. The osmolality of the product (~300 mOsm/kg).

(b) (4)

The proposed product is provided in a (b) (4) mL Type (b) (4) glass vial sealed with a (b) (4) stopper, a flip-off seal, and an aluminum crimp. The final product is provided in a carton. The container closure components proposed for use in the product are known for use in approved products and the applicant provided leachable study assessment to assure the safety of the proposed container closure system.

The vial head space contains (b) (4) Storage of the product in the carton is recommended to prevent exposure to light during shelf-life. The applicant also provided in-use study data to support the storage of the opened vial at (b) (4)

Dr. Ted Carver reviewed the drug product information including drug product composition, drug product specification, excipient information, analytical methods, container closure system, compatibility information, and stability data. The compatibility of the active ingredient with excipients and the container closure components is supported by drug product stability data.

The drug product is tested for visual clarity, color, appearance, identity, particulate matter, pH, osmolality, assay, impurities, (b) (4) closure integrity, endotoxin content, and sterility. The drug product conforms to USP <1> injection, USP <788> particulate matter, US<71> sterility, USP <785> osmolality, USP <697> container content for injections,

and USP <85> bacterial endotoxin. Dr. Carver concluded that the proposed specification is adequate to support the quality of the proposed product. Please refer to the drug product review dated 8/21/20 for additional information.

Manufacturing Process and Controls: The manufacturing process involves (b) (4)

(b) (4)

Microbiological control information: Microbiology reviewer, Dr. Zheng reviewed the microbiological controls used in the drug product manufacturing process including (b) (4)

. Her

review concluded that the proposed microbiological controls are adequate to support the NDA. Refer to CMC (Microbiology) review by Dr. Zheng dated 2/04/19 in Panorama.

Control Strategy: The critical quality attributes of the product are controlled through batch records instructions, process design, excipient specifications including bioburden and endotoxin control, drug substance specification, component specifications for incoming container closure components, (b) (4) .

The proposed control strategy is adequate to assure the quality of the product. Limits proposed for individual impurities were discussed with the Pharm. Tox. reviewer. No safety concerns were identified. For additional information, please refer to the following CMC reviews in Panorama: Dr. Leginus drug substance review dated 7/16/2020, Dr. Zheng's microbiology review dated 2/04/2020, Dr. Carver's drug product review dated 8/21/2020 and Dr. Janoria' s process reviews dated 8/19/2020.

Risk Assessment: CMC Reviewer's risk assessment for critical attributes is shown at the end of the review. In conclusion, the final risk is low for the proposed product. No further mitigation is necessary (Attachment 1).

Facility compliance information: Facility compliance information for the drug product and drug substance facilities was reviewed by Dr. Kumar Janoria. His facility review concluded that the proposed facilities are acceptable to support the approval of this NDA. Please refer to her review in Panorama dated 8/19/2020.

Environmental assessment: The applicant sought exemption from environmental impact analysis per 21CFR 25.31(b) as the action on this NDA may not significantly affect the quality of the human environment. The estimated concentration of the drug substance at the point of entry into the aquatic environment would be below 1 part per billion (1 ppb). Dr. Ted Carver granted categorical exclusion from submitting environmental assessment. Please refer to drug product review dated 8/20/20 for additional information.

Expiration Date & Storage Conditions: The application contains 24 months of long-term stability data (5°C), 12 month accelerated stability (25°C/65% RH), and 1 month of in-use stability data (30°C/65% RH) for 3 primary stability batches manufactured at (b) (4) L scale. Dr. Ted Carver reviewed the stability information. The product is sensitive light and should not be frozen. *Based on available stability data, an expiration period of 24 months is granted when stored at 2 to 8°C in commercial packaging. After first use, the drug product can be stored in* (b) (4) . Please refer to the drug product review dated 8/21/20 in Panorama for additional information.

Container and Carton Label Review: The drug product reviewer completed review of container and carton label. The dosage form description, strength, established name,

NDC #, Lot #/Expiry, and storage conditions are adequately described in the carton and container label, which meets relevant regulatory requirements for labeling. Refer to the Dr. Carver's labeling review dated 8/21/2020 for additional information.

OVERALL ASSESSMENT AND SIGNATURES:

At present, there are no outstanding deficiencies related to the drug substance, drug product, process/facilities, microbiology, environmental analysis, and container/ carton label sections of the NDA. *OPQ overall CMC recommendation for NDA 213793 is approval.*

Muthukumar Ramaswamy, Ph.D. 8/25/2020

Application Technical Lead Name and Date:

Attachment I: Final Risk Assessment

From Initial Risk Identification			*Review Assessment*		
Attribute/ CQA	***Factors that can impact the CQA***	***Initial Risk Ranking***	***Risk Mitigation Approach***	***Final Risk Ranking***	***Lifecycle Considerations/ Comments***
Drug content (assay)	Formulation, Process, Container/ Stability/Method	M	(b) (4)	Acceptable	None
(b) (4)	Formulation, Process, Container/ Stability/Method	M		Acceptable	None
Particulate Matter	Formulation/Excipients/Stability/ Components/ Container closure system	M		Acceptable	none
Impurities	Formulation, Stability, Process, Container closure	L		Acceptable	none
Appearance (Color and clarity)	Formulation, process, Container closure, stability	L		Acceptable	none
(b) (4)	Formulation/Excipients/Stability/sterility	M		Acceptable	none
pH	Drug substance, Formulation/Excipients/Stability/ Components	L		Acceptable	none
Sterility	Container closure Process/ (b) (4)	L		Acceptable	none
Endotoxin	Excipients, Container closure and Process	M		Acceptable	none
Leachable/ Extractables	Formulation, Process, and container closure	M		L	None

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CHAPTER IV: LABELING

IQA NDA Assessment Guide Reference

1.0 PRESCRIBING INFORMATION

Assessment of Product Quality Related Aspects of the Prescribing Information: *Summary of issues*.

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

Item	Information Provided in the NDA	Assessor's Comments
Product Title in Highlights		
Proprietary name	IMCIVREE (setmelanotide) (b) (4) for subcutaneous injection	Revise to IMCIVREE (setmelanotide) injection, for subcutaneous use
Established name(s)		Adequate.
Route(s) of administration		Adequate.
Dosage Forms and Strengths Heading in Highlights		
Summary of the dosage form(s) and strength(s) in metric system.	Injection: 10 mg/mL solution in a (b) (4) dose vial.	Adequate
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"		N/A

For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient use). Other package terms include pharmacy bulk package and imaging bulk package.		Revise highlighted to "multiple dose"

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2 (DOSAGE AND ADMINISTRATION)

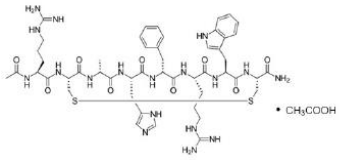
Item	Information Provided in the NDA	Assessor's Comments
DOSAGE AND ADMINISTRATION section		

Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents, storage conditions needed to maintain the stability of the reconstituted or diluted product)	**2.2 Administration Instructions** (b) (4)	Revise highlighted to use metric units: (b) (4)

1.2.2 Section 3 (DOSAGE FORMS AND STRENGTHS)

Item	Information Provided in the NDA	Assessor's Comments
DOSAGE FORMS AND STRENGTHS section		
Available dosage form(s)	Injection: 10 mg/mL (b) (4) Clear to slightly opalescent, colorless to slightly colored solution (b) (4)	Revise to state: "Injection: 10 mg/mL of setmelanotide, (b) (4) clear to slightly opalescent, colorless to slightly colored solution in a multiple-dose vial (b) (4)
Strength(s) in metric system		Adequate.
If the active ingredient is a salt, apply the USP Salt Policy per FDA Guidance		Adequate.
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting		Adequate.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"		N/A
For injectable drug products for parental administration, use appropriate labeling term (e.g., single-dose, multiple-dose, single-patient-use). Other package type terms include pharmacy bulk package and imaging bulk package.		Adequate.

1.2.3 Section 11 (DESCRIPTION)

Item	Information Provided in the NDA	Assessor's Comments
DESCRIPTION section		
Proprietary and established name(s)	(b) (4) 8 amino acid cyclic peptide analog of endogenous melanocortin peptide α-MSH (alpha-melanocyte stimulating hormone) (b) (4) The chemical name for setmelanotide acetate is acetyl-L-arginyl-L-cysteinyl-D-alanyl-L-histidinyl-D-phenylalanyl-L-arginyl-L-tryptophanyl-L-cysteinamide cyclic (2→8)-disulfide acetate. Its molecular formula is $C_{49}H_{68}N_{18}O_9S_2$ (anhydrous, free-base), and molecular mass is 1117.3 Daltons (anhydrous, free-base). The chemical structure of setmelanotide is:  IMCIVREE is a sterile clear to slightly opalescent, colorless to slightly colored solution. Each 1 mL of IMCIVREE (b) (4) contains 10 mg of setmelanotide (anhydrous, free-base) and the following inactive ingredients: N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-glycero-3-phosphoethanolamine sodium salt,	Adequate.
Dosage form(s) and route(s) of administration		Adequate.
If the active ingredient is a salt, apply the USP Salt Policy and include the equivalency statement per FDA Guidance.		Revise second highlighted section below to use "injection" instead of (b) (4) and include equivalency statement. IMCIVREE injection is a solution of pH 5 to 6 containing 10 mg of setmelanotide, provided as setmelanotide acetate, which is a salt with 2.1 to 4.7 molar equivalents of acetate, and the following inactive ingredients:…"
List names of all inactive ingredients. Use USP/NF names. Avoid Brand names.		Adequate.
For parenteral injectable dosage forms, include the name and quantities of all inactive ingredients. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect.		Inadequate. Include pH (see above). Quantities of each component should be included in the description. Revise to: " … the following inactive ingredients: 100 mg N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl- glycero-3-phosphoethanolamine sodium salt, 8 mg carboxymethylcellulose sodium (average MWt 90,500), 11 mg mannitol, 5 mg phenol, 10 mg benzyl alcohol, 1 mg

	carboxymethylcellulose sodium (average MWt 90,500), mannitol, phenol, benzyl alcohol, (b) (4) and Water for Injection.	edetate disodium dihydrate, and Water for Injection."
If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol		N/A
Statement of being sterile (if applicable)		Adequate.
Pharmacological/ therapeutic class		Revise to "IMCIVREE contains setmelanotide, a melanocortin 4 (MC4) receptor agonist. Setmelanotide is (b) (4) analog of α-MSH (alpha-melanocyte stimulating hormone)."
Chemical name, structural formula, molecular weight		Adequate.
If radioactive, statement of important nuclear characteristics.		N/A
Other important chemical or physical properties (such as pKa or pH)		N/A

Section 11 (DESCRIPTION) Continued

Item	Information Provided in the NDA	Assessor's Comments
For oral prescription drug products, include gluten statement if applicable	None.	N/A
Remove statements that may be misleading or promotional (e.g., "synthesized and developed by Drug Company X," "structurally unique molecular entity"	None.	Adequate.

1.2.4 Section 16 (HOW SUPPLIED/STORAGE AND HANDLING)

Item	Information Provided in the NDA	Assessor's Comments
HOW SUPPLIED/STORAGE AND HANDLING section		
Available dosage form(s)	IMCIVREE (b) (4) Package of 1 multiple dose vial. NDC 72829-010-01 (b) (4)	Revise to (b) (4)
Strength(s) in metric system		Adequate.

Available units (e.g., bottles of 100 tablets)	**Table 9: IMCIVREE Recommended Storage** [redacted] (b) (4) **Storage Condition** / **Unopened Vial** / **Opened Vial** [redacted] (b) (4) — Until the expiration date — Up to 30 days, *OR* Until the expiration date (whichever is earlier) [redacted] — Up to 30 days, *OR* Until the expiration date (whichever is earlier) — Up to 30 days, *OR* Until the expiration date (whichever is earlier) [redacted] — Discard and do not use — Discard and do not use [redacted] (b) (4)	Adequate.
Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number		Adequate.
Assess if the tablet is scored. If product meets guidelines and criteria for a scored tablet, state "functionally scored"	N/A	N/A
For injectable drug products for parental administration, use appropriate package type term (e.g., single-dose, multiple-dose, single-patient-use). Other package terms include pharmacy bulk package and imaging bulk package.	See above.	Adequate.

Section 16 (HOW SUPPLIED/STORAGE AND HANDLING) (Continued)

Item	Information Provided in the NDA	Assessor's Comments

Special handling about the supplied product (e.g., protect from light, refrigerate). If there is a statement to “Dispense in original container,” provide reason why (e.g. to protect from light or moisture, to maintain stability, etc.)		Adequate. The shelf life and in-use conditions are supported by stability results.
If the product contains a desiccant, ensure the size and shape differ from the dosage form and desiccant has a warning such as “Do not eat.”	N/A	
Storage conditions. Where applicable, use USP storage range rather than storage at a single temperature.	See above.	Revise highlighted temperature statements to use metric units with Fahrenheit in parentheses. Excursion condition is supported by in-use stability data at 30 ^{o}C.
Latex: If product does not contain latex and manufacturing of product and container did not include use of natural rubber latex or synthetic derivatives of natural rubber latex, state: “Not made with natural rubber latex. Avoid statements such as “latex-free.”	No information included.	N/A

Include information about child-resistant packaging	No Information included.	Not applicable

1.2.5 Other Sections of Labeling Section 17. Revise end of sentence to read

(b) (4)

1.2.6 **Manufacturing Information After Section 17 (for drug products)**

Item	Information Provided in the NDA	Assessor's Comments
Manufacturing Information After Section 17		
Name and location of business (street address, city, state and zip code) of the manufacturer, distributor, and/or packer	(b) (4) **Manufactured for:** Rhythm Pharmaceuticals, Inc. 222 Berkeley Street, Suite 1200 Boston, MA 02116 (b) (4)	Adequate.

2.0 PATIENT LABELING

Assessment of Product Quality Related Aspects of Patient Labeling (e.g., Medication Guide, Patient Information, Instructions for Use):
To be assessed

3.0 CARTON AND CONTAINER LABELING

Assessment of Container and Carton labeling:
Revise the list of ingredients in the carton side panel to describe the active ingredient as "setmelanotide, 10 mg, provided as setmelanotide acetate, which is a salt with 2.1 to 4.7 molar equivalents of acetate".

3.1 Container Label

3.2 Carton Labeling

ITEMS FOR ADDITIONAL ASSESSMENT

N/A

Overall Assessment and Recommendation:

The labeling/labels will be adequate from a quality perspective after the recommended changes have been made.

Theodore Carver

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David Claffey

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CHAPTER VII: MICROBIOLOGY

IQA NDA Assessment Guide Reference

Product Information	
NDA Number	213793
Assessment Cycle Number	01
Drug Product Name/ Strength	Setmelanotide / 10mg/mL
Route of Administration	Subcutaneous injection
Applicant Name	Rhythm Pharmaceuticals, Inc
Therapeutic Classification/ OND Division	CDER/OND/ODEII/DMEP
Manufacturing Site	(b) (4)
Method of Sterilization	

Assessment Recommendation: **Adequate**

Assessment Summary:

Document(s) Assessed	Date Received
Original submission	08/23/2019
Response to IR	11/25/2019
Response to IR	02/07/2020
CMC submission 2	03/27/2020
Response to IR	05/13/2020

List Submissions being assessed (table):

Highlight Key Issues from Last Cycle and Their Resolution: N/A

Remarks: This is eCTD submission. This is a rolling submission. Submission dated 11/25/2019 contains response to the Agency's information request dated 10/25/2019. Submission dated 02/07/2020 is submitted in response to the Agency's information request dated 01/09/2020. CMC rolling submission 2 is submitted on 03/27/2020, which contains batch stability data, comparability protocol, and labeling information. Submission dated 05/13/2020 is provided in response to the Agency's information request dated 04/29/2020.

Concise Description of Outstanding Issues
(List bullet points with key information and update as needed): None.

Supporting Documents:

Endotoxins reduction requalification study performed in May 2018 using the worst-case configuration for [redacted] was reviewed and found adequate in D[redacted] on 03/04/2019.

[redacted] on 09/24/2018.

S DRUG SUBSTANCE

The manufacturing process for the drug substance is not reviewed because the drug substance is [redacted]

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

Product description

The subject drug product is 1mL-fill sterile, multi-dose, clear to slightly opalescent solution packaged in a 2mL vial. The recommended dose is 0.5mg-3mg (0.05mL-0.3mL). The product is administered by subcutaneous injection using a [redacted] syringe and 29G×12.7 mm needles (2.3.P).

Product composition

Component	Function	Reference	Quantity (mg per mL and mg/vial)
Setmelanotide	Active	3.2.S.4.1	10.0[a]
mPEG-2000-DSPE[b]	[redacted]	3.2.P.4.1	100.0
Mannitol		USP/Ph. Eur.	11.0
Carboxymethylcellulose sodium[c]		USP/Ph. Eur.	8.0
Phenol		USP/Ph. Eur.	5.0
Benzyl alcohol	Preservative	NF/Ph. Eur.	10.0
Sodium Edetate	[redacted]	USP/Ph. Eur.	1.0
Water for Injection		USP/Ph. Eur.	q.s. to 1.0 mL[d]
[redacted]		USP/Ph. Eur.	N/A

(Table reproduced from the submission, 3.2.P.1, pg. 2)

Container closure system

Components	Description	Supplier
Vial	[redacted] USP Type [redacted] glass	[redacted]
Stopper	[redacted] grey	
Cap	[redacted]	

Assessment: Adequate

The description of drug product is acceptable.

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Yan Zheng

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