CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761092Orig1s000

OTHER REVIEW(S)

Division of Transplant and Ophthalmology Products
Associate Director for Labeling Recommendations
of the Prescribing Information

Product Title	REVCOVI (elapegademase-lvlr) injection, for intramuscular injection
Applicant	Leadiant Biosciences, Inc.
Application/Supplement Number	BLA 761092
Type of Application/Submission	New BLA
Approved Indications	Treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID)
Date FDA Received Application	Rolling submission: July 14, 2017 (1st section- Nonclinical); August 15, 2017 (2nd section- Chemistry); September 15, 2017 (Chemistry); October 24, 2017 (4th section- Clinical and Labeling)
Review Date	September 20, 2018
Reviewer	Jane Filie, MD
Project Manager	Jacqueline Smith

This Associate Director for Labeling (ADL) memorandum provides recommendations for consideration by the management of the Division of Transplant and Ophthalmology Products (DTOP), on the content and format of the prescribing information (PI) to help ensure that the PI:

- Is compliant with Physician Labeling Rule (PLR) and Pregnancy and Lactation Labeling Rule (PLLR) requirements[1]
- Is consistent with labeling guidance recommendations[2] and with CDER/OND best labeling practices and policies
- Conveys the essential scientific information needed for safe and effective use of the product
- Is clinically meaningful and scientifically accurate
- Is a useful communication tool for health care providers
- Is consistent with other PI with the same active moiety, drug class, or similar indication

[1] See *January 2006 Physician Labeling Rule*; 21 CFR 201.56 and 201.57; and *December 2014 Pregnancy and Lactation Labeling Rule* available at https://www.federalregister.gov/documents/2014/12/04/2014-28241/content-and-format-of-labeling-for-human-prescription-drug-and-biological-products-requirements-for

[2] See *PLR Requirements for PI* website for PLR labeling guidances.

LABELING FORMATTING AND CONTENT

This is an original biologic license application (BLA) for elapegademase-lvlr, a recombinant bovine adenosine deaminase, replacement enzyme therapy for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID). Formatting and content recommendations were made with the aim of improving clarity and readability of labeling. Key elements of the labeling discussions regarding the Prescribing Information of REVCOVI are summarized below at a high level.

For detailed information of the labeling review by discipline please refer to the following:

- review by the Office of Biotechnology Products by Vicky Borders-Hemphill, Pharm.D.
- clinical review by Dr. Marc Cavaille-Coll
- nonclinical review by Dr. Maria Rivera
- clinical pharmacology review by Dr. Abhay Joshi.

Labeling Related Consults and Reviews

The Office of Biotechnology Products reviewed the carton and container labels as well as the prescribing information and offered many comments and recommendations which were accepted by the applicant. The container labels and carton labeling submitted on July 12, 2018 were considered acceptable. Please refer to the review by Vicky Borders-Hemphill, Pharm.D. and Zhenzhen Liu, PhD.

The Office of Prescription Drug Promotion provided comments which are incorporated to the Prescribing Information. Please refer to consult by the Regulatory Review Officer, Carrie Newcomer, Pharm.D. Please refer to the consult dated August 2, 2018.

The Division of Medication Error Prevention and Analysis (DMEPA) evaluated the proposed proprietary name “REVCOVI”. The DMEPA Safety Evaluator, Madhuri Patel, Pharm.D. and Team Leader, Sarah K. Vee, Pharm.D.. concluded that the proposed proprietary name REVCOVI is acceptable since it will not misbrand the product and does not raise safety concerns. Please refer to the review by DMEPA dated October 12, 2017. The proprietary name was granted on October 13, 2017. On June 7, 2018, DMEPA reviewer Nasim Roosta, Pharm. D., concluded that the suffix -lvlr for the nonproprietary name was acceptable.

DMEPA also reviewed the proposed label and labeling for REVCOVI. The DMEPA Safety Evaluator, Nasim Roosta, Pharm.D., and DMEPA Team Leader, Otto Townsend, Pharm.D. provided recommendations. Please refer to the review dated June 28, 2018). The recommendations were included in the Prescribing Information, except for a few as follows:

- In **Highlights**, under **Dosage and Administration**, and section 2 of the **Full Prescribing Information**, subsection **2.1 Recommended Dosage,** the safety evaluator expressed concern that the instructions did not clearly instruct prescribers to divide the total weekly

dose in half, potentially resulting in dosing errors and recommended the following statement: "Adagen-naïve patients: (b) (4) " In the opinion of the clinical team, it is important to provide the total weekly dose of 0.4 mg/kg. The instruction was revised to provided clearer information and reconcile with the recommendation as follows:

"Adagen-naïve patients: (b) (4) "

- In section 2 of the **Full Prescribing Information**, subsection **2.1 Recommended Dosage,** the safety evaluator notes that under "Patients transitioning from Adagen" the labeling states "The total weekly dose may be divided into multiple intramuscular administrations" and that the information does not provide clear instruction on dosing. The clinical team contends here are no specific recommendations as to how to divide the weekly dose because this will be patient specific and adjusted based on the clinician's assessment of the patient's local tolerability and clinical status. This product is meant to be titrated according to therapeutic drug monitoring.

- In section 2 of the **Full Prescribing Information,** subsection **2.1 Recommended Dosage,** the safety evaluated noted that it included the statement "…the dose may be gradually adjusted down" and in her opinion the lack of clear definition on how to calculate a reduced dose when dose reduction is necessary could pose a risk of dosing error. There are no defined algorithms or calculations for dose reductions. As per the clinical reviewer this drug is managed by specialists in the field and the dosing reductions are based on the therapeutic dose monitoring taking into consideration the patient's trough levels and clinical status.

Key Labeling Discussions and Recommendations

Following are key labeling discussions and recommendations made to the PI, by section.

HIGHLIGHTS OF PRESCRIBING INFORMATION

The subsections of the Highlights of Prescribing Information ("Highlights") follow the recommendations of content and formatting, to the extent possible, of the draft guidance for industry "Labeling for Human Prescription Drug and Biological Products- Implementing the PLR Content and Format Requirements", unless noted otherwise.

- **Product Title and Initial US Approval**: The formatting and contents of Product Title and Initial US Approval follows recommendations proposed by the draft guidance for industry "Product Title and Initial US Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products- Content and Format" will read as follows:

REVCOVI (elapegademase-lvlr) injection, for intramuscular use
Initial U.S. Approval: 2018

- **Indication and Usage**: Elapegademase-lvlr is not listed in the FDA Established Pharmacological Class (EPC) Text Phrases Database. The clinical, nonclinical and chemistry review teams concurred that the term "recombinant adenosine deaminase" best describes the pharmacological class of elapegademase. The term "bovine" was not included because this would be misleading as the product is not derived from bovine tissue as the currently marketed Adagen. The inclusion of this pharmacologic class term in FDA database has been requested to the National Drug File Reference Terminology Group, through Dr. Paul Brown the current OND liaison, as per process described in the MaPP 7400.13 Determining the Established Pharmacologic Class for Use in the Highlights of Prescribing Information. The following is the Indication and Usage as provided in Highlights of Prescribing Information.

(b) (6)

- **Dosage and Administration**: The dosing recommendation for Adagen-naïve patients is based on the patient's ideal body weight, justified by the applicant that patients with ADA-SCID are often underweight and common medical practice for such patients is to calculate doses based on their ideal body weight. This justification was deemed acceptable by the clinical team. This section will provide the dosing recommendations as follows:

----------DOSAGE AND ADMINISTRATION----------
- Patients transitioning from Adagen to REVCOVI: The starting dose of REVCOVI is 0.2 mg/kg weekly, intramuscularly. See full prescribing information (FPI) for conversion formula from Adagen to REVCOVI. (2.1)
- Adagen-naïve patients: The starting dose of REVCOVI is 0.4 mg/kg weekly based on ideal body weight, divided into two doses (0.2 mg/kg twice a week), intramuscularly. (2.1)
- For complete information, maintenance dosing and therapeutic monitoring, see FPI. (2.1, 2.3)
- REVCOVI is for intramuscular injection only. See FPI for administration instructions. (2.2)

FULL PRESCRIBING INFORMATION

- **2 DOSAGE AND ADMINISTRATION:** In subsection **2.2 Administration Instructions** because this is a lifelong treatment, starting in infancy through adulthood, this labeling merits general recommendations regarding intramuscular injections. The general recommendations were based on the labeling of other drugs for long-term intramuscular

use and on current medical literature[3,4] to alert the healthcare providers the need to adapt the administration technique to each patient according to age and anatomy, per current guidelines. The recommendations also take into consideration the recommendations by OPQ regarding the materials utilized (syringes and needles) for administration of the drug and the handling of the drug. This subsection will read as follows:

2.2 Administration Instructions

REVCOVI is for IM injection only. Follow sterile IM administration technique guidelines appropriate to the patient's age and anatomy (i.e. choice of needle gauge and length, site of administration). Take precautions not to inject into or near an artery or nerve. Alternate the injection site periodically.

Preparation of Injection and Procedure Instructions

- REVCOVI should not be diluted nor mixed with any other drug prior to administration.
- Visually inspect REVCOVI for particulate matter and discoloration prior to administration. REVCOVI is a clear, colorless solution; discard if solution is discolored, cloudy or contains particulate matter.
- Do not freeze or shake. REVCOVI should not be used if there are any indications that it may have been frozen. Once removed from refrigeration, allow REVCOVI to equilibrate to room temperature for 30 minutes.
- REVCOVI is to be administered using polypropylene syringes. Draw the solution from the vial with a 25- gauge needle or larger.
- Change the needle to a size and gauge appropriate for the patient's intramuscular administration.
- REVCOVI should be administered immediately after syringe preparation.
- Any remaining medication in the vial must be discarded immediately.

- **11 DESCRIPTION:** The description of REVCOVI will clarify that the amino acid sequence utilized for the recombinant DNA production of this product is of bovine origin as follows:

  Elapegademase-lvlr is a recombinant adenosine deaminase (rADA), based on bovine amino acid sequence, conjugated to monomethoxypolyethylene glycol (mPEG).

FINAL LABELING

Following is the agreed upon labeling submitted by the applicant as of October 1, 2018.

[3] Hopkins, U, Arias, CY. Large-volume IM injections: A review of best practices. Oncology Nurse Advisor. February 2013, p. 32-37

[4] Rishovd, A. Pediatric Intramuscular Injections: Guidelines for Best Practice. MCN, The American Journal of Maternal-Child Nursing. 2014. 39 (2);112-114

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/s/

JANE FILIE
10/01/2018

RENATA ALBRECHT
10/02/2018

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

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

Memorandum

Date: August 2, 2018

To: Jacquelyn Smith
Regulatory Project Manager
Division of Transplant and Ophthalmology Products (DTOP)

From: Carrie Newcomer, PharmD
Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

Subject: **BLA: 761092**
. **REVCOVI (elapegademase-lvlr) injection, for intramuscular use**

OPDP has reviewed the proposed Package Insert (PI) and carton and container labeling submitted for consult on January 16, 2018, for REVCOVI (elapegademase-lvlr) injection, for intramuscular use. Our review is based on the version of the proposed PI and carton and container labeling that was emailed to OPDP by Jacquelyn Smith on July 20, 2018 and August 2, 2018, respectively. OPDP's comments are provided directly on the attached version of the proposed PI. OPDP does not have any comments on the proposed carton and container labeling, also attached.

Thank you for your consult. If you have any questions on our comments for the proposed labeling, please contact Carrie Newcomer at 6-1233, or carrie.newcomer@fda.hhs.gov.

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/s/

CARRIE A NEWCOMER
08/02/2018

M E M O R A N D U M

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

DATE: July 13, 2018

TO: Edward M. Cox, M.D., M.P.H.
Director
Office of Antimicrobial Products (OAP)
Office of New Drugs (OND)

FROM: Yiyue Zhang, Ph.D.
Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

THROUGH: Arindam Dasgupta, Ph.D.
Deputy Director
DNDBE, OSIS

SUBJECT: Surveillance inspections (b) (4) (b) (4) (b) (4) covering BLA 761092 (b) (4)

Inspection Summary

The Office of Study Integrity and Surveillance (OSIS) and ORA inspected the analytical portion of **Study STP-2279-002** (**BLA 761092** (b) (4)) conducted at (b) (4) (b) (4)

Form FDA 483 was issued to both sites at the inspection close-out. The final inspection classification is Voluntary Action Indicated (VAI).

Objectionable conditions were observed during the inspections that could compromise the reliability of data from **Study STP-2279-002.** (b) (4) (b) (4)

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(b) (4)

Yiyue Zhang, Ph.D.
Visiting Associate

Final Classification:

Analytical

VAI – (b) (4)
FEI#: (b) (4)
VAI – (b) (4)
FEI#: (b) (4)

cc:
OTS/OSIS/Kassim/Choe/Kadavil/Fenty-Stewart/Nkah/CDER-OSIS-BEQ
OTS/OSIS/DNDBE/Bonapace/Dasgupta/Ayala/Biswas/Zhang
OTS/OSIS/DGDBE/Cho/Jang/Choi/Skelly/Au
ORA/OMPTO/OBIMO/DBIMOI/Garmendia

Draft: YZ 6/22/2018, 7/12/2018, 7/13/2018
Edit: RCA 7/11/2018, 7/12/2018; 7/13/2018; AD 7/11/2018, 7/13/2018

ECMS: Cabinets/CDER_OTS/Office of Study Integrity and Surveillance/INSPECTIONS/BE Program/ANALYTICAL/ (b) (4) (b) (4)
Cabinets/CDER_OTS/Office of Study Integrity and Surveillance/INSPECTIONS/BE Program/ANALYTICAL (b) (4) (b) (4)

OSIS File#: BE 7804
FACTS: (b) (4)

Attachments:

Attachment 1. Studies in support of pending applications
Attachment 2. Summary and chronology of events for Study STP-2279-002 provided by the sponsor
Attachment 3. Subject sample results generated (b) (4) as of (b) (4)
Attachment 4. Form FDA 483 issued (b) (4)
Attachment 5. (b) (4) response to Form FDA 483
Attachment 6. Subject sample results generated (b) (4)
Attachment 7. Authorization letter and affidavit
Attachment 8. Form FDA 483 issued (b) (4)

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/s/

YIYUE ZHANG
07/13/2018

RUBEN C AYALA
07/13/2018

ARINDAM DASGUPTA
07/13/2018

LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	June 27, 2018
Requesting Office or Division:	Division of Transplant and Ophthalmology Products (DTOP)
Application Type and Number:	BLA 761092
Product Name and Strength:	Revcovi (elapegademase-lvlr) Injection 1.6 mg/mL (2.4 mg/1.5 mL)
Product Type:	Single ingredient product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Leadiant Biosciences, Inc.
Submission Date:	October 24, 2017
OSE RCM #:	2017-2234
DMEPA Safety Evaluator:	Nasim Roosta, PharmD
DMEPA Team Leader:	Otto L. Townsend, PharmD

REASON FOR REVIEW

As part of the BLA approval process for Revcovi (elapegademase-lvlr) Injection, 1.6mg/mL, the Division of Transplant and Ophthalmology Products (DTOP) requested that we review the proposed packaging, label and labeling for areas that may lead to medication errors.

Leadiant Biosciences, Inc. submitted BLA 761092 to seek marketing approval of Revcovi (elapegademase-lvlr) Injection 1.6mg/mL indicated for enzyme replacement therapy for patients with severe combined immunodeficiency disease (ADA-SCID).

BACKGROUND/REGULATORY HISTORYMATERIALS REVIEWED

Table 1. Materials Considered for this Label and Labeling Review

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

N/A=not applicable for this review
*We do not typically search FAERS for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

1 FINDINGS AND RECOMMENDATIONS

Table 2 below includes the identified medication error issues with the submitted label and labeling, DMEPA's rationale for concern, and the proposed recommendation to minimize the risk for medication error.

Table 2: Identified Issues and Recommendations for the Division of Transplant and Ophthalmology Products (DTOP)

Prescribing Information			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
General Issues			
1.	We note (b) (4) throughout the PI.	Per FDA Guidance[a], the preferred package-type term is 'single dose'.	We defer to the Office of Pharmaceutical Quality (OPQ) on the determination of the appropriate package-type term for this product. If OPQ determines that 'single-dose' is appropriate, the package-type term should be updated in the PI and on the container label and carton labeling.
2.	Throughout the PI, the proprietary name placeholder, "TRADENAME", appears in place of the conditionally acceptable proprietary name, "Revcovi".	The proprietary name found conditionally acceptable, "Revcovi", should be used throughout the PI.	Replace the placeholder, "TRADENAME", with the conditionally acceptable proprietary name, "Revcovi".
3.	The nonproprietary name suffix, "lvlr" has been found conditionally acceptable.	The nonproprietary name suffix found conditionally acceptable, "lvlr", should be used included as part of the proper name throughout the PI.	Include the conditionally acceptable nonproprietary name suffix 'lvlr' (e.g., elapegademase-lvlr) throughout the PI.
4.	In the Dosage and Administration sections of both the Highlights and Full Prescribing Information, the dosage statement lists the route of administration prior to the dosage.	Customarily, the dosage is followed by the route of administration.	Consider changing dosage statements to list the dosage followed by the route of administration. For example, '*0.2 mg/kg intramuscularly twice weekly*'.
Highlights of Prescribing Information			

[a] 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

1.	Under *Dosage and Administration*, the statement, '*Adagen-naïve patients:* (b) (4) [redacted]' may be confusing to the provider when calculating the total weekly dose**.**	Failing to clearly instruct prescribers to divide the total weekly dose in half, may result in dosing errors.	Within the *Dosage and Administration* section of the Highlights, consider changing the statement to read, '*Adagen-naïve patients:* (b) (4) [redacted]'.
Full Prescribing Information			
1.	Section 2, subsection 2.1, under (b) (4) [redacted] the weight to be used to calculate the dose is not specified (i.e. actual body weight vs. ideal body weight), whereas under dosing for Adagen naïve patients, ideal body weight is specified.	Failing to clearly instruct the user which body weight to use when calculating the dose may result in dosing errors.	Indicate which body weight measurement (i.e. actual body weight or ideal body weight) should be used to calculate the dose in patients currently receiving treatment with Adagen.
2.	Section 2, subsection 2.1, under *Recommended Dosage*, the statement, '*Adagen-naïve patients:* (b) (4) [redacted]' may be misinterpreted by the prescriber when calculating weekly dosing.	Failing to clearly instruct prescribers to divide the total weekly dose in half, may result in dosing errors.	Change the statement to read, '*Adagen-naïve patients:* (b) (4) [redacted]'.
3.	Section 2, subsection 2.1 *Recommended Dosage states,* '*multiple IM administrations.*' This statement is vague and does not define clearly to the user	Failing to clearly define number of injections could result in dosing errors and improper use of the product.	Clearly define '*multiple IM administrations*' as either a number or a range (i.e., 'divided into XX IM administrations' OR 'divided into X to Y IM administrations').

	how many administrations is appropriate.		
4.	Section 2, subsection 2.1 *Recommended Dosage* includes the statement '*the dose may be gradually adjusted down*'. This statement does not give the provider specific instruction on how to reduce the dose.	Failing to provide clear instruction on dose reduction may result in dosing errors that could adversely affect the patient.	Clearly define to the prescriber how to calculate a reduced dose when dose reduction is necessary.
5.	Section 16 does not include the dosage form (i.e., injection).	This section should contain appropriate information to facilitate identification of the dosage form. Failure to properly identify the dosage form could result in administration errors.	For clarity and to prevent medication errors, in section 16, add the dosage form (i.e., injection) in the first line of the product description.
6.	Section 16 does not include the strength expressed as total quantity per total volume.	Failure to provide the strength clearly within this section could result in administration errors.	In accordance with 21 CFR 201.57(c)(17) and USP Chapter <7>, add the product strength as total quantity per total volume, before the concentration per mL in the first line of this section. For example: **2.4 mg/1.5 mL (1.6 mg/mL)**
7.	Section 16 does not include the corresponding product National Drug Codes (NDC).	The NDC is often used to facilitate identification of the product.	In accordance with 21 CFR 201.57(c)(17), add corresponding product NDCs to this section.

Table 3: Identified Issues and Recommendations for Leadiant Biosciences, Inc.

Container Labels			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
1.	The proprietary name placeholder, "TRADENAME", appears in place of the conditionally acceptable proprietary name, "Revcovi".	The proprietary name found conditionally acceptable, "Revcovi", should be used on the container label.	Replace the placeholder, "TRADENAME", with the conditionally acceptable proprietary name, "Revcovi".

2.	The nonproprietary name suffix, “lvlr” has been found conditionally acceptable.	The nonproprietary name suffix found conditionally acceptable, “lvlr”, should be used included on the container labels.	Include the conditionally acceptable nonproprietary name suffix ‘lvlr’ (e.g., elapegademase-lvlr) on the container labels.
3.	Only the strength per milliliter (1.6 mg/mL) is listed. The total strength per total volume is not included on the principal display panel.	Omission of the product’s strength may lead to preparation and administration errors.	Add the product strength expressed as total strength per total volume above the concentration per mL.[b] Display strength prominently, but in such a way so that it is not competing with the trade name. Example: **2.4 mg/1.5 mL** (1.6 mg/mL)
4.	The NDC is presented as 00000-000-00.	Since the NDC is often used as an additional verification prior to drug dispensing and product preparation in the pharmacy, it is an important safety feature that should be included on the container label and be consistent across labeling.	Ensure the assigned NDC is included on the container label and is consistent across labeling (i.e., Prescribing Information and 1-count carton labeling).
Carton Labeling			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
1.	See container label recommendation #1 above.		
2.	See container label recommendation #2 above.		
3.	Only the strength per milliliter (1.6 mg/mL) is listed. The total strength per total	Omission of the product’s strength may lead to administration errors.	Add the product strength expressed as total strength per total volume above the concentration per mL.[c] Display

[b] United States Pharmacopoeia (USP) General Chapter <7> Injections.

[c] United States Pharmacopoeia (USP) General Chapter <1> Injections.

	volume is not included on the principal display panel.		strength prominently, but in such a way so that it is not competing with the trade name. Example: **2.4 mg/1.5 mL** (1.6 mg/mL)
4.	Missing designated area for lot number and expiration date on side panels.	Lack of lot number or expiration date may result in dispensing errors.	Designate an area for inclusion of the lot number and expiration date. We recommend that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month.

2 CONCLUSION

DMEPA's evaluation of the proposed label and labeling identified areas of vulnerability that may lead to medication errors. We have provided recommendations for the Division in Table 2 above and in Table 3 above. We ask that the Division conveys the entire Table 3 to Leadiant Biosciences, Inc. so that recommendations are implemented prior to approval of this BLA.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 4 presents relevant product information for Revcovi (elapegademase-lvlr) Injection that Leadiant Biosciences, Inc. submitted on October 24, 2017.

Table 4. Relevant Product Information for Revcovi (elapegademase-lvlr)	
Initial Approval Date	N/A
Active Ingredient	Elapegademase-lvlr
Indication	enzyme replacement therapy for patients with severe combined immunodeficiency disease (ADA-SCID)
Route of Administration	Intramuscular
Dosage Form	Injection
Strength	2.4 mg/1.5 mL (1.6 mg/mL)
Dose and Frequency	(b) (4) The frequency of administration is at least once weekly; thus, the dosing interval is a maximum of one week. The maximum daily dose is 0.2 mg/kg.
How Supplied	1.5 mL single-dose vials
Storage	2°C to 8°C

APPENDIX B. PREVIOUS DMEPA REVIEWS

B.1 Methods

On January 5, 2018, we searched the L:drive and AIMS using the terms, Revcovi and elapegademase to identify reviews previously performed by DMEPA.

B.2 Results

Our search did not identify any previous reviews.

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APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[d] along with postmarket medication error data, we reviewed the following Revcovi (elapegademase-lvlr) Injection 1.6 mg/mL labels and labeling submitted by Leadiant Biosciences, Inc. on October 24, 2017.

- Container label
- Carton labeling
- Prescribing Information (Image not shown)

[d] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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/s/

NASIM N ROOSTA
06/27/2018

OTTO L TOWNSEND
06/28/2018

MEMORANDUM
NONPROPRIETARY NAME SUFFIX

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	June 7, 2018
Responsible OND Division:	Division of Transplant and Ophthalmology (DTOP)
Application Type and Number:	BLA 761092
Product Name and Strength:	SC-PEG rADA (elapegademase-lvlr) injection, 1.6 mg/mL
Product Type:	Single-ingredient product
Applicant/Sponsor Name:	Leadiant Biosciences, Inc.
FDA Received Date:	March 14, 2018
OSE RCM #:	2018-52
DMEPA Primary Reviewer:	Nasim Roosta, PharmD
DMEPA Deputy Director:	Danielle Harris, PharmD, BCPS

1 PURPOSE OF MEMO

This memorandum summarizes our evaluation of the four-letter suffixes proposed by Leadiant Biosciences, Inc. for inclusion in the nonproprietary name and communicates our recommendation for the nonproprietary name for BLA 761092.

1.1 REGULATORY HISTORY

Leadiant Biosciences was notified of the Agency's intention to designate a nonproprietary name that includes a four-letter distinguishing suffix that is devoid of meaning for their product in an Advice Letter[a].

2 ASSESSMENT OF THE NONPROPRIETARY NAME

On March 14, 2018, Leadiant Biosciences submitted a list of ten (10) suffixes, in their order of preference, to be used in the nonproprietary name of their product[b]. Leadiant Biosciences also provided findings from an external study conducted by (b) (4)[c], evaluating the proposed four-letter suffixes in conjunction with the nonproprietary name, for our consideration. Table 1 presents a list of suffixes submitted by Leadiant Biosciences:

Table 1. Suffixes submitted by Leadiant Biosciences***	
1.	-lvlr
2.	(b) (4)
3.	
4.	
5.	
6.	
7.	
8.	
9.	
10.	

We reviewed Leadiant Biosciences's proposed suffixes in order of preference listed by Leadiant Biosciences, along with the with the supporting data they submitted, using the principles described in the applicable guidance.[d]

2.1 Elapegademase-lvlr

Leadiant Biosciences's first proposed suffix, -lvlr, is acceptable.

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[a] Merchant, L. General Advice Letter for BLA 761092. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 JAN 22.

[b] Cover Letter- Request for Review of Suffixes for Proper Name. Gaithersburg (MD): Leadiant Biosciences; 2018 MAR 14. Available from: \\cdsesub1\evsprod\bla761092\0009\m1\us\12-cover-letter\cover-letter-14mar2018.pdf

[c] Request for Review of Suffixes for Proper Name- Evaluation Report. (b) (4) 2018 MAR 14. Available from: \\cdsesub1\evsprod\bla761092\0009\m1\us\112-other-corr\request-review-suffix-proper-name-report.pdf

[d] See Section VI which describes that any suffixes should be devoid of meaning in Guidance for Industry: Nonproprietary Naming of Biological Products. 2017. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf

We determined that the proposed suffix -lvlr, is not too similar to any other products' suffix designation, does not look similar to the names of other currently marketed products, that the suffix is devoid of meaning, does not include any abbreviations that could be misinterpreted, and does not make any misrepresentations with respect to safety or efficacy of this product.

3 COMMUNICATION OF DMEPA'S ANALYSIS

These findings were shared with OPDP. Per an email correspondence dated June 5, 2018, OPDP did not identify any concerns that would render this proposed suffix unacceptable. DMEPA also communicated our findings to the Division of Transplant and Ophthalmology (DTOP) via e-mail on June 5, 2018.

4 CONCLUSION

We find Leadiant Biosciences's proposed suffix -lvlr acceptable and recommend the nonproprietary name be revised throughout the draft labels and labeling to elapegademase-lvlr.

4.1 RECOMMENDATIONS FOR LEADIANT BIOSCIENCES

We find the nonproprietary name, elapegademase-lvlr, conditionally acceptable for your proposed product. Should your 351(a) BLA be approved during this review cycle, elapegademase-lvlr will be the proper name designated in the license and you should revise your proposed labels and labeling accordingly. However, please be advised that if your application receives a complete response, the acceptability of your proposed suffix will be re-evaluated when you respond to the deficiencies. If we find your suffix unacceptable upon our re-evaluation, we would inform you of our finding.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

NASIM N ROOSTA
06/07/2018

DANIELLE M HARRIS
06/07/2018