

BLA 021839/S-031

SUPPLEMENT APPROVAL

Ipsen Biopharmaceuticals, Inc.
Attention: Kirsten Overoye-Chan
Senior Director Global Regulatory Affairs
One Main Street
7th Floor
Cambridge, MA 02142

Dear Kirsten Overoye-Chan:

Please refer to your supplemental biologics license application (sBLA), dated and received, May 17, 2023, and your amendments, submitted under section 351(a) of the Public Health Service Act for Increlex (mecasermin) injection.

This Prior Approval supplemental biologics license application provides for the following:

- Updates to Section 2.1 (Dosage) to align with the current information in the Increlex Company Core Data Sheet (CCDS) v3.0
- Updates to Section 5.1 Hypoglycemia with “Severe hypoglycemia leading to hypoglycemic seizures has been observed with INCRELEX treatment [see *Adverse Reactions (6.1)*]” as a summary of the most severe manifestation of hypoglycemia observed during the clinical trials experience
- Updates to Section 6.1 (Clinical Trial Experience), recategorizing the adverse reaction of “cardiac murmur” from the Systems Organ Class (SOC) Cardiac Disorders to the SOC Investigations, per the final clinical study report (CSR) of pivotal Study 1419¹
- Sections 8.6 and 8.7 were deleted from the PI due to the lack of information
- Editorial changes were made to the Prescribing Information based on published Labeling Guidances and Regulations.

¹ Study 1419: A study of long-term recombinant human insulin-like growth factor-1 (rhIGF-1) treatment of children with short stature due to severe primary IGF-1 deficiency.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

WAIVER OF HIGHLIGHTS ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at FDA.gov,² that is identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert, and Instructions for Use) and include the labeling changes proposed in any pending “Changes Being Effectuated” (CBE) supplements.

Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.³

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending “Changes Being Effectuated” (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in Microsoft Word format that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for

² <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

³ We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your supplemental application, you are exempt from this requirement.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs*.⁴

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.⁵ Information and Instructions for completing the form can be found at FDA.gov.⁶

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Meghna M. Jairath, Pharm.D., Senior Regulatory Project Manager, at (301) 796-4267.

Sincerely,

{See appended electronic signature page}

Naomi Lowy, MD
Deputy Director
Division of General Endocrinology
Office of Cardiology, Hematology,
Endocrinology, and Nephrology
Office of New Drugs
Center for Drug Evaluation and Research

⁴ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁶ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Patient Package Insert (version approved October 20, 2023)
 - Instructions for Use (version approved October 20, 2023)

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/

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