



BLA 208471/S-010

## SUPPLEMENT APPROVAL

Sanofi-aventis U.S. LLC  
Attention: Chetan Somaiya  
Global Regulatory Lead  
55 Corporate Drive  
Bridgewater, NJ 08807

Dear Chetan Somaiya:

Please refer to your supplemental biologics license application (sBLA) received January 24, 2025, and your amendments, submitted under section 351(a) of the Public Health Service Act for Adlyxin (lixisenatide) injection.

This Prior Approval sBLA provides for updates to Subsection 6.3 Postmarketing Experience of the Prescribing Information (PI) to include two additional terms: 'alopecia' and 'dysesthesia' as requested in our December 11, 2024, Supplement Request letter.

Additional revisions were made to the PI and Medication Guide (MG) to align with recently approved changes in other products in the glucagon-like peptide-1 receptor agonist class, including but not limited to:

- In Section 1 Indications and Usage, the following Limitations of Use were removed:
  - Has not been studied in patients with chronic pancreatitis or a history of unexplained pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
  - Has not been studied in patients with gastroparesis and is not recommend in patients with gastroparesis.
  - Should not be used in patients with type 1 diabetes mellitus.
- In Section 5 Warnings and Precautions, Subsection 5.6 Severe Gastrointestinal Adverse Reactions was added.
- In Section 8 Use in Specific Populations, Subsection 8.7 Gastroparesis was removed.
- Additional edits made throughout the PI and MG to modernize with current labeling guidances, clarify language, and improve readability and organization of information.

## **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.

## **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,<sup>1</sup> that is identical to the enclosed labeling (text for the PI, Instructions for Use, and MG) and include the labeling changes proposed in any pending “Changes Being Effected” (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*.<sup>2</sup>

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 Effected” (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 the claimed indication 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.

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> 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>.

## **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*.<sup>3</sup>

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 601.12(f)(4)]. Form FDA 2253 is available at FDA.gov.<sup>4</sup> Information and Instructions for completing the form can be found at FDA.gov.<sup>5</sup>

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety-related information [21 CFR 601.12(f)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 601.12(f)(4).

## **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).

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.

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<sup>3</sup> For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

<sup>4</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>5</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

If you have any questions, contact Marisa Petruccelli, Safety Regulatory Project Manager, at (240) 402-6147.

Sincerely,

*{See appended electronic signature page}*

Monika Houstoun, Pharm.D., M.P.H.  
Deputy Director for Safety  
Division of Diabetes, Lipid Disorders, and Obesity  
Office of Cardiology, Hematology, Endocrinology,  
and Nephrology  
Office of New Drugs  
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use 100mcg/mL pen (version previously approved on July 30, 2021)
  - Instructions for Use Starter Pack (version previously approved on July 30, 2021)

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**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.**  
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/s/  
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MONIKA A HOUSTOUN  
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