

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

761090Orig1s000

Trade Name: TAKHZYRO

*Generic or
Established:* lanadelumab-flyo

Sponsor: Dyax Corporation

Approval Date: August 23, 2018

Indication: For prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients 12 years and older.

CENTER FOR DRUG EVALUATION AND RESEARCH

761090Orig1s000

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	X
Other Action Letters	
Labeling	X
REMS	
Officer/Employee List	X
Multidiscipline Review(s) <ul style="list-style-type: none">• Summary Review• Office Director• Cross Discipline Team Leader• Clinical• Non-Clinical• Statistical• Clinical Pharmacology	X
Product Quality Review(s)	X
Clinical Microbiology / Virology Review(s)	
Other Reviews	X
Risk Assessment and Risk Mitigation Review(s)	X
Proprietary Name Review(s)	X
Administrative/Correspondence Document(s)	X

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

761090Orig1s000

APPROVAL LETTER



BLA 761090

BLA APPROVAL

Dyax Corporation
300 Shire Way
Lexington, MA 02421

Attention: Ms. Joyel C. Morris
Associate Director, Global Regulatory Affairs

Dear Ms. Morris:

Please refer to your Biologics License Application (BLA) dated and received December 26, 2017, submitted under section 351(a) of the Public Health Service Act for TAKHZYRO (lanadelumab-flyo) .

LICENSING

We have approved your BLA for TAKHZYRO (lanadelumab-flyo) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, TAKHZYRO under your existing Department of Health and Human Services U.S. License No. 1789. TAKHZYRO is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients 12 years and older.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture lanadelumab drug substance at Rentschler Biopharma SE, Erwin-Rentschler-Str. 21, 88471, Laupheim, Germany. The formulated drug product will be manufactured and filled at Cook Pharmica LLC, 1300 South Patterson Drive, Bloomington, IN 47403. Packaging, labeling, and storage of the drug product will be conducted at (b) (4). You may label your product with the proprietary name, TAKHZYRO, and market it in a 300 mg/2 mL dosage in a 5 mL single-dose vial.

DATING PERIOD

The dating period for your drug product, TAKHZYRO, shall be 24 months from the date of manufacture when stored at 5 °C± 3°C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4) °C.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of TAKHZYRO to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2.

We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot. Any changes in the manufacturing, testing, packaging, or labeling of TAKHZYRO, or in the manufacturing facilities, will require the submission of information to your biologics license application for our review and written approval, consistent with 21 CFR 601.12.

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 text.

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 [21 601.14(b)] in structured product labeling (SPL) format, as described at

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

Content of labeling must be identical to the enclosed labeling (text for the package insert and text for the patient package insert). Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels **and/or** carton and immediate container labels submitted on June 1 and 29, 2018, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved BLA 761090.**” Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for lanadelumab was not referred to an FDA advisory committee because evaluation of the application did not raise significant safety or efficacy issues in the HAE population and therefore outside expertise was not necessary.

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

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

POSTMARKETING COMMITMENTS SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

3466-1 Submit the results of the ongoing Study DX-2930-04 with lanadelumab in patients 12 years of age and older with Type I or II hereditary angioedema (HAE) to provide long term efficacy and safety assessments, including clinical laboratory tests and immunogenicity, HAE attack data, and occurrence of adverse events including hypersensitivity, injection site reactions, LFT elevations, hospitalizations, and deaths.

The timetable you submitted on July 11, 2018, states that you will conduct this study according to the following schedule:

Final Report Submission: 05/2020

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

3466-2: Conduct a low endotoxin recovery (LER) study using an appropriate container (e.g., no endotoxin absorption or interference) to hold (b) (4) spiked with either RSE or CSE (5-10 EU/mL) at (b) (4) °C for (b) (4). Samples should be tested using the kinetic turbidimetric LAL assay daily during the hold time, and recoveries should be calculated using the nominal spike values or the LRW spiked control at time 0.

The timetable you submitted on July 11, 2018, states that you will conduct this study according to the following schedule:

Final Report Submission: 09/2018

Submit clinical protocols to your IND 116647 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled “**Postmarketing Commitment Protocol**,”

“Postmarketing Commitment Final Report,” or “Postmarketing Commitment Correspondence.”

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>. Information and Instructions for completing the form can be found at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (21 CFR 600.80). You should submit postmarketing adverse experience reports to:

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements for licensed biological products (21 CFR 600.81).

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA-3486 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4206
Silver Spring, MD 20903

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at <http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm>.

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biologics qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, call Colette Jackson, Senior Regulatory Health Project Manager, at (301) 796-1230.

Sincerely,

{See appended electronic signature page}

Mary T. Thanh Hai, MD
Acting Director
Office of Drug Evaluation II
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

Content of Labeling
Carton and Container Labeling

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/

MARY T THANH HAI
08/23/2018