

BLA 761121

**BLA ACCELERATED APPROVAL**

Genentech, Inc.  
Attention: Megan Salt  
Regulatory Program Management  
1 DNA Way  
South San Francisco, CA 94080

Dear Ms. Salt:

Please refer to your biologics license application (BLA) dated and received December 19, 2018, and your amendments, submitted under section 351(a) of the Public Health Service Act for POLIVY (polatuzumab vedotin-piiq) for injection.

**LICENSING**

We have approved your BLA for POLIVY (polatuzumab vedotin-piiq) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, POLIVY under your existing Department of Health and Human Services U.S. License No. 1048. POLIVY is indicated in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified, after at least two prior therapies.

**MANUFACTURING LOCATIONS**

Under this license, you are approved to manufacture (b) (4) polatuzumab vedotin-piiq drug substance at (b) (4). The final formulated product will be manufactured, filled, and packaged at (b) (4) and labeled and packaged at (b) (4) or at Genentech, Inc., Hillsboro, OR, USA. You may label your product with the proprietary name POLIVY and will market it in single-use vials, 140 mg per vial, for injection.

**DATING PERIOD**

The dating period for POLIVY shall be 24 months from the date of manufacture when stored at 2 – 8 °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. (b) (4)

Results of ongoing stability should be submitted throughout the dating period, as they become available, including the results of stability studies from the first three production lots.

We have approved the stability protocols in your license application for the purpose of extending the expiration dating periods of your [REDACTED] <sup>(b) (4)</sup>, drug substance, and drug product under 21 CFR 601.12.

### **FDA LOT RELEASE**

You are not currently required to submit samples of future lots of POLIVY 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 POLIVY, 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 AND 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> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information). 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.

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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>.

## **CARTON AND CONTAINER LABELING**

Submit final printed carton and container labeling that are identical to the carton and container labeling submitted on June 5, 2019, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (April 2018, Revision 5)*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved BLA 761121.**” Approval of this submission by FDA is not required before the labeling is used.

## **ADVISORY COMMITTEE**

Your application for POLIVY was not referred to an FDA advisory committee because evaluation of the data did not raise significant safety or efficacy issues in the intended population.

## **ACCELERATED APPROVAL REQUIREMENTS**

Products approved under the accelerated approval regulations, 21 CFR 601.41, require further adequate and well-controlled clinical trials to verify and describe clinical benefit. You are required to conduct such clinical trials with due diligence. If postmarketing clinical trials fail to verify clinical benefit or are not conducted with due diligence, we may, following a hearing in accordance with 21 CFR 601.43(b), withdraw this approval. We remind you of your postmarketing requirements specified in your submission dated June 4, 2019. These requirements, along with required completion dates, are listed below. Verification of clinical benefit through either PMR 3630-1 or PMR 3630-2 would be adequate to fulfill the accelerated approval requirement.

PMR 3630-1 Complete Study GO39942, a randomized, double-blind, placebo-controlled trial that evaluates polatuzumab vedotin-piiq in combination with R-CHP (rituximab, cyclophosphamide, doxorubicin, prednisone) versus R-CHOP in patients with previously untreated diffuse large B-cell lymphoma. The primary endpoint would be progression-free survival. Key secondary endpoints would include complete remission rate per independent review committee and overall survival.

Final Protocol Submission:	11/2018
Trial Completion:	06/2021
Final Report Submission:	12/2021

PMR 3630-2 Complete Study MO40598, a randomized clinical trial that evaluates polatuzumab vedotin-piiq in combination with rituximab, gemcitabine, and oxaliplatin (R-GemOx) versus R-GemOx alone in patients with relapsed or refractory large B-cell lymphoma. The primary endpoint would be overall survival. Key secondary endpoints would include progression-free survival and complete remission rate.

Final Protocol Submission:	09/2019
Trial Completion:	12/2023
Final Report Submission:	06/2024

A final submitted protocol is one that the FDA has reviewed and commented upon, and you have revised as needed to meet the goal of the study or clinical trial.

Submit clinical protocols to your IND 109409 for this product, with a cross-reference letter to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each requirement in your annual report 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.

Submit final reports to this BLA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated “**Subpart E Postmarketing Requirement(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(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 NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B**

We remind you of your postmarketing commitments:

PMC 3630-3 Develop and validate a sensitive assay to evaluate the neutralizing capacity of anti-polatuzumab vedotin-piiq antibodies (ADA) in confirmed ADA-positive patient samples. The assay should be designed to be capable of detecting neutralizing ADA in the presence of polatuzumab vedotin-piiq levels that are expected to be present in patient samples at the time of ADA sample collection. The final report should include the assay validation report and assay standard operating procedure.

The timetable you submitted on June 4, 2019, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	07/2020
Final Report Submission:	10/2020

A final submitted protocol is one that the FDA has reviewed and commented upon, and you have revised as needed to meet the goal of the study or clinical trial.

Submit clinical protocols to your IND 109409 for this product, with a cross-reference letter to this BLA. 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**

Under 21 CFR 601.45, you are required to submit, during the application pre-approval review period, all promotional materials, including promotional labeling and advertisements, that you intend to use in the first 120 days following marketing approval (i.e., your launch campaign). If you have not already met this requirement, you must immediately contact the Office of Prescription Drug Promotion (OPDP) at (301) 796-1200. Please ask to speak to a regulatory project manager or the appropriate reviewer to discuss this issue.

As further required by 21 CFR 601.45, submit all promotional materials that you intend to use after the 120 days following marketing approval (i.e., your post-launch materials)

**U.S. Food and Drug Administration**  
Silver Spring, MD 20993  
[www.fda.gov](http://www.fda.gov)

at least 30 days before the intended time of initial dissemination of labeling or initial publication of the advertisement. We ask that each submission include a detailed cover letter together with three copies each of the promotional materials, annotated references, and approved Prescribing Information, Medication Guide, and Patient Package Insert (as applicable).

Send each submission directly to:

OPDP Regulatory Project Manager  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotions (OPDP)  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Alternatively, you may submit promotional materials for accelerated approval products electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry.<sup>3</sup>

## **REPORTING REQUIREMENTS**

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

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

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<sup>3</sup> When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

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 4207  
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 FDA.gov.<sup>4</sup>

### **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 Wanda Nguyen, PharmD, Regulatory Project Manager, at 301-796-2808.

Sincerely,

*{See appended electronic signature page}*

Richard Pazdur, MD  
Acting Director  
Office of Hematology and Oncology Products  
Center for Drug Evaluation and Research

#### ENCLOSURE:

- Content of Labeling
  - Prescribing Information

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<sup>4</sup> <http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm>

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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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RICHARD PAZDUR  
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