



BLA 761074

BLA APPROVAL

Mylan GmbH
Attention: Barbara Miltzer
Director, Regulatory Science, Biologics
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504

Dear Ms. Miltzer:

Please refer to your Biologics License Application (BLA) dated November 3, 2016, received November 3, 2016, and your amendments, submitted under section 351(k) of the Public Health Service Act for Ogivri (trastuzumab-dkst) 420 mg/vial for injection, multi-dose vial.

We acknowledge receipt of your major amendment dated July 28, 2017, which extended the goal date by three months.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2062 to Mylan GmbH, Zurich, Switzerland, under the provisions of section 351(k) of the Public Health Service Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product Ogivri (trastuzumab-dkst). Ogivri is indicated for the treatment of HER2-overexpressing breast cancer and the treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Ogivri (trastuzumab-dkst) at (b) (4). The (b) (4) Bacteriostatic Water for Injection (BWFI), USP (containing 1.1% benzyl alcohol) will be manufactured, filled, labeled and packaged at Biocon Limited (FEI: 3003981475) in Bangalore, Karnataka, India. You may label your product with the proprietary name, Ogivri, and will market it in 420 mg/vial for injection, multi-dose vial.

DATING PERIOD

The dating period for Ogivri shall be 48 months from the date of manufacture when stored at 2-8° C. The dating period for BWFI, USP (containing 1.1% benzyl alcohol) shall be 18 months from the date of manufacture when stored at (b) (4)° 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.

The expiration date for the packaged product, Ogivri plus BWFI, USP (containing 1.1% benzyl alcohol) shall be dependent on the shortest expiration date of any component.

We have approved the stability protocols in your license application for the purpose of extending the expiration dating period of your drug substance and BWFI, USP (containing 1.1% benzyl alcohol) under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Ogivri (trastuzumab-dkst) and each kit component 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 Ogivri (trastuzumab-dkst), 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). 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, 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 761074.**” Approval of this submission by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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.

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable. Breast cancer and gastric cancer occur, for the most part in the adult population. The incidence of these cancer types in pediatric patients is extremely rare and as such, clinical pediatric studies are impossible or highly impracticable.

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

We remind you of your postmarketing commitment:

- 3309-1 Perform a method validation study to confirm the suitability of the FcγRIIIa-V₁₅₈ surface plasmon resonance (SPR) binding assay for use as a potency assay for drug substance and drug product lot release and stability testing.

The timetable you submitted on November 28, 2017, states that you will conduct this study according to the following schedule:

Final Report Submission: 06/2018

Submit 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, and any changes in plans since the last annual report. 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

If you have any questions, call Charlene Wheeler, MSHS, Senior Regulatory Project Manager, at (301) 796-1141.

Sincerely,

{See appended electronic signature page}

Julia Beaver, MD
Director
Division of Oncology Products 1
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURES:

Content of Labeling
Carton and Container Labeling

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

/s/

JULIA A BEAVER
12/01/2017