DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 203388/S-010

**SUPPLEMENT APPROVAL**

Genentech, Inc.
Attention: Jennifer Yang
Regulatory Program Management
1 DNA Way
South San Francisco, CA 94080-4990

Dear Ms. Yang:

Please refer to your Supplemental New Drug Application (sNDA) dated May 6, 2016, received May 6, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ERIVEDGE (vismodegib) capsules, 150 mg.

We also refer to our approval letter dated November 2, 2016, which contained the following error: the vertical lines denoting recent major changes [per 21 CFR 201.57(d)(9)], in Sections 5.1, 5.2 and 5.4 in the USPI, were omitted in the label attached to the letter.

This replacement approval letter incorporates the correction of the error. The effective approval date will remain November 2, 2016, the date of the original approval letter.

This Prior Approval supplemental new drug application provides for the following updates to the package insert:

- To revise the Warnings and Precautions, Embryo-Fetal Toxicity subsection; and the Use in Specific Populations, Females and Males of Reproductive Potential, Contraception subsection to advise females of reproductive potential to use effective contraception during Erivedge therapy and for 24 months, instead of 7 months, after the final dose.
- To revise the Warnings and Precautions, Blood Donation subsection to advise patients not to donate blood or blood products while receiving ERIVEDGE and for 24 months, instead of 7 months, after the final dose.
- To add a new subsection, Premature Fusion of the Epiphyses to Warnings and Precautions; to update the Use in Special Populations, Pediatric Use subsection; and to update the Patient Counseling section to include information regarding premature fusion of the epiphyses in pediatric patients.
- To update the Adverse Reactions, Laboratory Abnormalities and Postmarketing Experience subsections to include information regarding CPK elevation and Musculoskeletal and connective tissue disorders.

- To revise the Use in Specific Populations, Lactation subsection to advise a nursing woman that breastfeeding is not recommended during therapy with Erivedge and for 24 months, instead of 7 months, after the final dose.
- To revise the Nonclinical Toxicology, Carcinogenesis, Mutagenesis, Impairment of Fertility subsection to include information from a dedicated 26-week rat fertility study.

In addition, the Medication Guide was updated to reflect updates made in the package insert.

## APPROVAL & LABELING

We have completed our review of this supplemental 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 the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), 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, Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, 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, 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 none of these criteria apply to your application, you are exempt from this requirement.

**PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

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

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf ).

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. 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.

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 information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above, by fax to 301-847-8444, or electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf ).

**REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Claire Myers, Ph.D., Regulatory Project Manager, at (240) 402-6612.

Sincerely,

*{See appended electronic signature page}*

Jeffery Summers, M.D.
Deputy Director for Safety
Division of Oncology Products 2
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE: Content of Labeling

---

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

---

/s/

---

JEFFERY L SUMMERS
11/02/2016