DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202429/S-005

SUPPLEMENT APPROVAL

Hoffmann La Roche, Inc.
Attention: Irene Figari
Regulatory Program Management
Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080-4990

Dear Ms. Figari:

Please refer to your Supplemental New Drug Application (sNDA) dated August 8, 2013, received August 9, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zelboraf (vemurafenib) tablets, 240 mg.

We acknowledge receipt of your amendments dated September 30, 2013, January 27, 2014, and February 5, 2014.

This Changes Being Effected supplemental new drug application provides for the following revisions to the label: the addition of DRESS Syndrome in WARNINGS AND PRECAUTIONS, Hypersensitivity Reactions; and in ADVERSE REACTIONS, Postmarketing Experience; the addition of progression of pre-existing chronic myelomonocytic leukemia with NRAS mutation ADVERSE REACTIONS, Postmarketing Experience; and the addition of dosing instructions in case of vomiting in DOSAGE AND ADMINISTRATION, Recommended Dose.

In addition, as permitted under 21 CFR 314.70(c)(6)(iii)(E) this supplement provides for a change to the "How Should I Take Zelboraf" section of the Medication Guide to include dosing instructions in case of vomiting.

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 and Medication Guide 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 and the 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 includes 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 this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

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 Norma Griffin, Senior Regulatory Health Project Manager, at (301) 796-4255.

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
02/06/2014