



sBLA 103792/5313 and 5318

**SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING
COMMITMENTS**

Genentech, Inc.
Attention: Dhushy Thambipillai
Regulatory Program Management
1 DNA Way, MS 241B
South San Francisco, CA 94080-4990

Dear Ms. Thambipillai:

Please refer to your Supplemental Biologics License Applications (sBLA) 103792/5313 dated December 17, 2013, received December 19, 2013, and sBLA 103792/5318 dated March 17, 2014, received March 18, 2014, submitted under section 351(a) of the Public Health Service Act for Herceptin[®] (trastuzumab).

We acknowledge receipt of your amendments dated April 4, 21, and 30, 2014.

The Prior Approval Supplemental (PAS) biologics application sBLA 103792/5313 provides for the 8-year median duration follow-up results from the planned full analysis of the efficacy and safety of 1-year and 2-year Herceptin[®] treatment (8 mg/kg i.v. loading dose, 6 mg/kg i.v. every three weeks) versus observation and as a comparison of 1-year versus 2-years of Herceptin[®] treatment in fulfillment of PMC 1 and PMC 2 associated with sBLA 103792/5175. This PAS also provides for label revisions with safety findings from Study BO16348 (HERA) and a recommendation to not extend adjuvant treatment beyond 1-year which was added to the Dosage and Administration Section with supporting information provided in the Warnings and Precautions and Adverse Reaction sections.

The Changes Being Effected (CBE) supplemental biologics application sBLA 103792/5318 provides for the deletion of information that was erroneously carried over from the final study report for the joint Analysis of NSABP B-31 and NCCTG N9831 under Figure 5 in the label approved with Efficacy Supplement sBLA 103792/5311 on March 7, 2014.

APPROVAL & LABELING

We have completed our review of these supplemental applications. They are 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 CFR 601.14(b)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling text for the package insert and include the labeling changes proposed in any pending “Changes Being Effectuated” (CBE) supplements. 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.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this BLA, including pending Changes Being Effectuated supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in MS Word format that includes the changes approved in this supplemental application.

FULFILLMENT OF POSTMARKETING COMMITMENTS

We have received your submission dated December 17, 2013, containing the final reports for the following postmarketing commitments listed in the January 18, 2008, approval letter for sBLA 103792/5175.

- PMC 1 To provide a final clinical study report (CSR) of the safety and efficacy of 2-years of trastuzumab treatment in Study BO16348 (HERA) in order to provide a final analysis of cardiac toxicity based on serial ejection fraction monitoring, characterizing the cumulative incidence, severity, duration, and reversibility. The final study report will include the primary datasets and programs for generation of analyses; analyses will include, but not be limited to the analyses described in the statistical analysis plan. The final CSR will be submitted by December 31, 2013. If the results from the 2-year trastuzumab arm are released by the IDMC at the interim analysis, then the final CSR will be submitted by December 31, 2009.

- PMC 2 To provide updated safety information of the observation and 1-year trastuzumab arms in Study BO16348 (HERA). Interim cardiac safety updates (narratives of new primary or secondary cardiac events) will be provided on an annual basis beginning in December 2008 and continuing until the time of the final CSR, which will be submitted by December 31, 2013. If the results from the 2-year trastuzumab arm are release by the IDMC at the interim analysis, then the CSR will be submitted by December 31, 2009.

We have reviewed your submission and conclude that the above commitments are fulfilled.

We remind you that there are postmarketing requirements and postmarketing commitments that are still open.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, contact Amy Tilley, Regulatory Project Manager, at 301-796-3994 or amy.tilley@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Amna Ibrahim, M.D.
Acting Director
Division of Oncology Products 1
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/

AMNA IBRAHIM
06/30/2014