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SUPPLEMENT APPROVAL

Janssen Research and Development, LLC
Attention: Salvatore Morello
Director, Global Regulatory Liaison
Welsh & McKean Roads, P.O. Box 776
Spring House, PA 19477

Dear Mr. Morello:

Please refer to your Supplemental Biologics License Application (sBLA), dated and received July 16, 2012, submitted under section 351(a) of the Public Health Service Act for Simponi (golimumab).

We acknowledge receipt of your amendments dated October 11, 2012, October 22, 2012, October 31, 2012, November 13, 2012, November 19, 2012, November 19, 2012, December 06, 2012, December 07, 2012, December 07, 2012, December 14, 2012, December 19, 2012, December 20, 2012, January 23, 2013, January 25, 2013, January 31, 2013, February 13, 2013, February 19, 2013, February 26, 2013, March 13, 2013, April 02, 2013, April 05, 2013, April 09, 2013, April 18, 2013, April 25, 2013, April 29, 2013, April 29, 2013, April 30, 2013, May 03, 2013, May 06, 2013, May 10, 2013 and May 14, 2013.

This Prior Approval supplemental biologics application proposes the addition of a new indication:

Simponi (golimumab) is indicated in adult patients with moderately to severely active ulcerative colitis who have demonstrated corticosteroid dependence or who have had an inadequate response to or failed to tolerate oral aminosalicylates, oral corticosteroids, azathioprine, or 6-mercaptopurine for:

- inducing and maintaining clinical response
- improving endoscopic appearance of the mucosa during induction
- inducing clinical remission
- achieving and sustaining clinical remission in induction responders.

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, 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, text for the patient package insert, Medication Guide) and include the labeling changes proposed in any pending “Changes Being Effected” (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 Effected” (CBE) 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.

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your April 30, 2013, submission containing final printed carton and container labels.

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 an orphan designation was granted for your pediatric indication, you are exempt from this requirement.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

Since Simponi (golimumab) was approved on April 24, 2009, we have become aware of additional cases of Hepatosplenic T-cell Lymphoma (HSTCL), a rare form of malignancy, in patients with inflammatory bowel disease (IBD) receiving tumor necrosis factor (TNF) blockers. Simponi (golimumab) is a member of the TNF blocker class. In addition, during review of this application, we became aware of the potential for immunogenicity to impact the pharmacokinetics, efficacy and safety of Simponi (golimumab), and of serious adverse events, including opportunistic infections and malignancies, in patients receiving higher doses of TNF blockers. We consider this information to be “new safety information” as defined in section 505-1(b)(3) of the FDCA.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify unexpected serious risks in patients receiving Simponi (golimumab) for inflammatory bowel disease of Hepatosplenic T-cell Lymphoma (HSTCL), development of immunogenicity, or serious adverse events, including opportunistic infections and malignancies.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

PMR #1 A study to bank samples from inflammatory bowel disease patients treated with Simponi (golimumab) for future evaluation to identify genetic mutations and other biomarkers that may predispose them to developing Hepatosplenic T-Cell Lymphoma (HSTCL).

The timetable you submitted on April 25, 2013, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 02/2014
Study Completion: 02/2020
Final Report Submission: 02/2021

PMR #2 A study to reanalyze banked immunogenicity serum samples from ulcerative colitis trials of Simponi (golimumab), C0524T16, C0524T17 and C0524T18, to determine the presence of anti-drug antibodies (ADA) using an improved ADA assay format with reduced sensitivity to product interference.

The timetable you submitted on April 25, 2013, states that you will complete this study according to the following schedule:

Final Report Submission: 04/2014

PMR #3 A prospective, multi-center, long-term, observational study of ulcerative colitis patients treated with Simponi (golimumab) in a routine clinical setting, to assess the long-term safety of Simponi (golimumab). The study's primary outcome should be the incidence of lymphoma. Design the study around a testable hypothesis to rule out a clinically meaningful increase in lymphoma above an estimated background risk in a suitable comparator. Secondary endpoints should be pre-specified and may include the incidence of other malignancies. Select and justify the choice of appropriate comparator population(s) and corresponding background rate(s) relative to Simponi-exposed patients. Provide sample sizes and effect sizes that can be ruled out under various enrollment target scenarios and loss to follow-up assumptions. Patients should be enrolled over an initial 5-year period and then followed for a period of at least 10 years from the time of enrollment. Progress updates of patient accrual and a demographic summary should be provided in your annual reports. Safety data should be provided in periodic safety reports.

The timetable you submitted on April 25, 2013, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 05/2014

Study Completion: 05/2029

Final Report Submission: 05/2030

Submit the protocols to your IND 100181 with a cross-reference letter to this BLA. Submit all final reports to your BLA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: "Required Postmarketing Protocol Under 505(o)", "Required Postmarketing Final Report Under 505(o)", "Required Postmarketing Correspondence Under 505(o)".

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 601.70 requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 601.70 to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 601.70.

We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

**POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS
UNDER SECTION 506B**

We remind you of your postmarketing commitments:

PMC #4 Conduct a study to evaluate the pharmacokinetics of Simponi (golimumab) in pediatric patients 5 to 17 years of age with moderately to severely active ulcerative colitis. Pharmacokinetic measurements should be conducted for exposure-response analysis and compared to adult patients with ulcerative colitis treated with Simponi (golimumab). Also, collect serum samples for immunogenicity testing and conduct analyses of the impact of immunogenicity on the pharmacokinetics of Simponi (golimumab).

The timetable you submitted on May 14, 2013, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 09/2013
Study Completion: 12/2015
Final Report Submission: 05/2016

PMC #5 Conduct a study to evaluate the effectiveness and safety of Simponi (golimumab) in pediatric patients 5 to 17 years of age with moderately to severely active ulcerative colitis. The study should be designed to establish that the dose regimen(s) of Simponi (golimumab) identified in PMC#4 is(are) effective and safe for induction treatment, as well as for continued treatment after induction. Pharmacokinetic measurements should be conducted for exposure-response analysis. Collect serum samples for immunogenicity testing and conduct analyses of the impact of immunogenicity on pharmacokinetics, efficacy and safety.

The timetable you submitted on May 14, 2013, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 01/2017
Study Completion: 12/2021
Final Report Submission: 05/2022

Submit clinical protocols to your IND 100181 for this product. Submit 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

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(s) 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(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. 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

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, call Kevin Bugin, Regulatory Project Manager, at (301) 796-2302.

Sincerely,

{See appended electronic signature page}

Andrew E. Mulberg, M.D., F.A.A.P., C.P.I.
Deputy Director
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE(S):

Content of Labeling
Carton and Container Labeling