



Our STN: BL 103795/5149

Immunex Corporation  
Attention: Douglas Hunt  
Director, Regulatory Affairs  
Amgen, Incorporated  
One Amgen Center Drive  
Thousand Oaks, CA 91320-1799

Dear Mr. Hunt:

Your request to supplement your biologics license application (BLA) for Etanercept to include a new indication for the treatment of adult patients (18 years or older) with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy has been approved.

We acknowledge your written commitments as described in your letter of April 29, 2003, as outlined below:

**Postmarketing Studies subject to reporting requirements of 21 CFR 601.70.**

1. To conduct study protocol 20030211, a 48 week, 200 pediatric patient, multicenter placebo-controlled clinical trial, to determine the safety and efficacy of Etanercept in pediatric patients, 4 to 17 years of age, with chronic plaque psoriasis. The final study protocol will be submitted August 31, 2004, the study will be initiated by December, 31, 2004, patient accrual will be completed by December 31, 2005, the study will be completed by December 31, 2006 and the final study report with revised labeling if applicable, will be submitted by September 30, 2007. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "Required Pediatric Study Commitments."
2. To complete and submit data from study protocol 20030117, a multicenter study, to assess the efficacy and safety of Etanercept 50 mg twice weekly for periods beyond 12 weeks in adult psoriasis patients. The study will continue for a total duration of two years. The final study protocol was submitted to IND [REDACTED] on June 6, 2003. Patient accrual, 618 adult patients, was completed on July 29, 2003, the final patient visit for week 12 was completed by November 30, 2003, a 12 week clinical study report will be submitted by July 31, 2004, and the final study report will be submitted by August 31, 2006.

3. To conduct a prospective, multicenter, surveillance study of 2500 adult patients with chronic plaque psoriasis who will be treated with commercial Etanercept, but who have not been previously enrolled in an Etanercept study. The surveillance study will be performed to assess the incidence of serious adverse events including all malignancies and serious infections. All enrolled study subjects will be evaluated twice yearly for a period of at least five years. The final study protocol will be submitted by December 31, 2004, patient accrual will be completed by December 31, 2007, the study will be completed by December 31, 2012, and a final study report will be submitted by September 30, 2013.
4. To conduct a prospective, observational registry study of women with rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis and plaque psoriasis exposed to Etanercept during pregnancy or within two weeks prior to conception. This study will assess the outcomes in the offspring born to those women who were exposed to Etanercept during pregnancy relative to background risk in similar patients not exposed to Etanercept. These outcomes will include adverse effects such as major birth defects (congenital anomalies), minor birth defects, fetal size in relation to gestational age, birth weight, developmental milestones, malignancies, serious infections, premature delivery and pre-eclampsia, spontaneous abortions and still births and will be assessed in the first year after birth for infants prenatally exposed to Etanercept. A final protocol will be submitted by December 31, 2004 that will include the revised draft labeling with the inclusion of the pregnancy registry telephone number. The study will be initiated by March 31, 2005, patient accrual will be completed by March 31, 2010, the study will be completed by December 31, 2011, and the final study report will be submitted by September 30, 2012.

We request that you submit clinical protocols to your IND, with a cross-reference letter to BLA STN BL 103795. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to BLA STN BL 103795. Please use the following designators to label prominently all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- Postmarketing Study Protocol
- Postmarketing Study Final Report
- Postmarketing Study Correspondence
- Annual Report on Postmarketing Studies

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. The status report for each study should include:

- information to identify and describe the postmarketing commitment,
- the original schedule for the commitment,
- the status of the commitment (i.e. pending, ongoing, delayed, terminated, or submitted), and

- an explanation of the status including, for clinical studies, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our Web site (<http://www.fda.gov/cder/pmc/default.htm>). Please refer to the April 2001 Draft Guidance for Industry: Reports on the Status of Postmarketing Studies – Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997 (see <http://www.fda.gov/cber/gdlns/post040401.htm>) for further information.

Pursuant to 21 CFR 201.57(f)(2) patient labeling must be reprinted at the end of the package insert. We request that the text of information distributed to patients be printed in a minimum of 10-point font.

Please submit all final printed labeling at the time of use and include implementation information on FDA Form 356h. Please provide a PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels). In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with a cover letter requesting advisory comments to the Division of Drug Marketing, Advertising and Communication (HFD-42), Center for Drug Evaluation and Research, 5600 Fishers Lane/Room 8B45, Rockville, MD 20857. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by an FDA Form 2253.

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence to support that claim.

The regulatory responsibility for review and continuing oversight for this product transferred from the Center for Biologics Evaluation and Research to the Center for Drug Evaluation and Research effective June 30, 2003. For further information about the transfer, please see <http://www.fda.gov/cder/biologics/default.htm>. Until further notice, however, all correspondence, except as provided elsewhere in this letter, should continue to be addressed to:

CBER Document Control Center  
Attn: Office of Therapeutics Research and Review  
Suite 200N (HFM-99)  
1401 Rockville Pike  
Rockville, Maryland 20852-1448

This information will be included in your biologics license application file.

Sincerely,

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Marc Walton, M.D., Ph.D.  
Director  
Division of Therapeutic Biological Internal Medicine Products  
Office of Drug Evaluation VI  
Office of New Drugs  
Center for Drug Evaluation and Research

Enclosures: Package Insert  
Patient Package Insert