BLA 103795/5123_ORIG_AP_PKG

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER(S)
103795/5123

Trade Name: Enbrel

Generic Name(s): (etanercept)

Sponsor: Immunex Corporation
Agent:

Approval Date: July 24, 2003

Indication: Provides for treatment of ankylosing spondylitis

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APPLICATION NUMBER:

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STN: 103795/5123

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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

103795/5123

Approval Letter(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20852

Our STN: BL 103795/5123

JUL 24 2003

Immunex Corporation
Attention: Douglas Hunt
Director, Regulatory Affairs
One Amgen Center Drive
Mail Stop 24-2-C
Thousand Oaks, CA 91320

Dear Mr. Hunt:

Your request to supplement your biologics license application for Etanercept to include a new indication for reducing signs and symptoms in patients with active ankylosing spondylitis has been approved.

We acknowledge your written commitments to conduct postmarketing studies as described in your letter of July 23, 2003 as outlined below:

Postmarketing Studies subject to reporting requirements of 21 CFR 601.70.

1. To follow 290 ankylosing spondylitis patients, of which 60 had restrictive chest expansion (defined as 2 cm or less at baseline), currently enrolled in open label extension studies (16.0040 and EU 312) for two years. Descriptive data on the incidence of inflammatory bowel disease, exacerbations of pre-existing inflammatory bowel disease and serious adverse events including serious infections will be collected. Analyses will be performed to clarify whether the event rate for serious pulmonary infections in patients with restricted chest expansion differs from that observed in patients who do not have a reduction in chest expansion. The final protocol for study 16.0040 will be submitted by September 30, 2003, and implemented at all study sites by December 31, 2003, the studies will be completed by July 31, 2004, the combined study report will be completed by December 31, 2004 and the final study report will be submitted by January 31, 2005. If one of the studies is not going to be conducted under IND, please submit the protocol to your biologics license application (BLA), STN 103795.

Postmarketing Studies not subject to reporting requirements of 21 CFR 601.70.

2. Immunex will reduce the number of references in the Etanercept package insert to no more than ten. A revised package insert containing 10 or fewer references will be submitted as an amendment to your BLA supplement, STN BL 103795/5102 by August 8, 2003.

We request that you submit clinical protocols to your IND, with a cross-reference letter to this biologics license application (BLA), STN BL 103795/5123. Submit all study final reports to your BLA STN BL 103795/5123. 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://fda.gov/cder/pmc/default.htm). Please refer to the April 2001 Draft Guidance for Industry (April 2001): 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 an FDA Form 2253 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Branch, HFM-602, 1401 Rockville Pike, Rockville, MD 20852-1448. 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 submitted data to support such claims to us and had them approved.

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/cber/transfer/transfer.htm and http://www.fda.gov/OHRMS/DOCKETS/98fr/03-16242.html. 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,

(b)(6)

Patricia Keegan, M.D.
Acting Director
Division of Clinical Trials Design and Analysis
Office of Therapeutics Research and Review
Center for Drug Evaluation and Research

Enclosures: Final Draft Package Insert
Final Draft Patient Information Insert

(b)(6)

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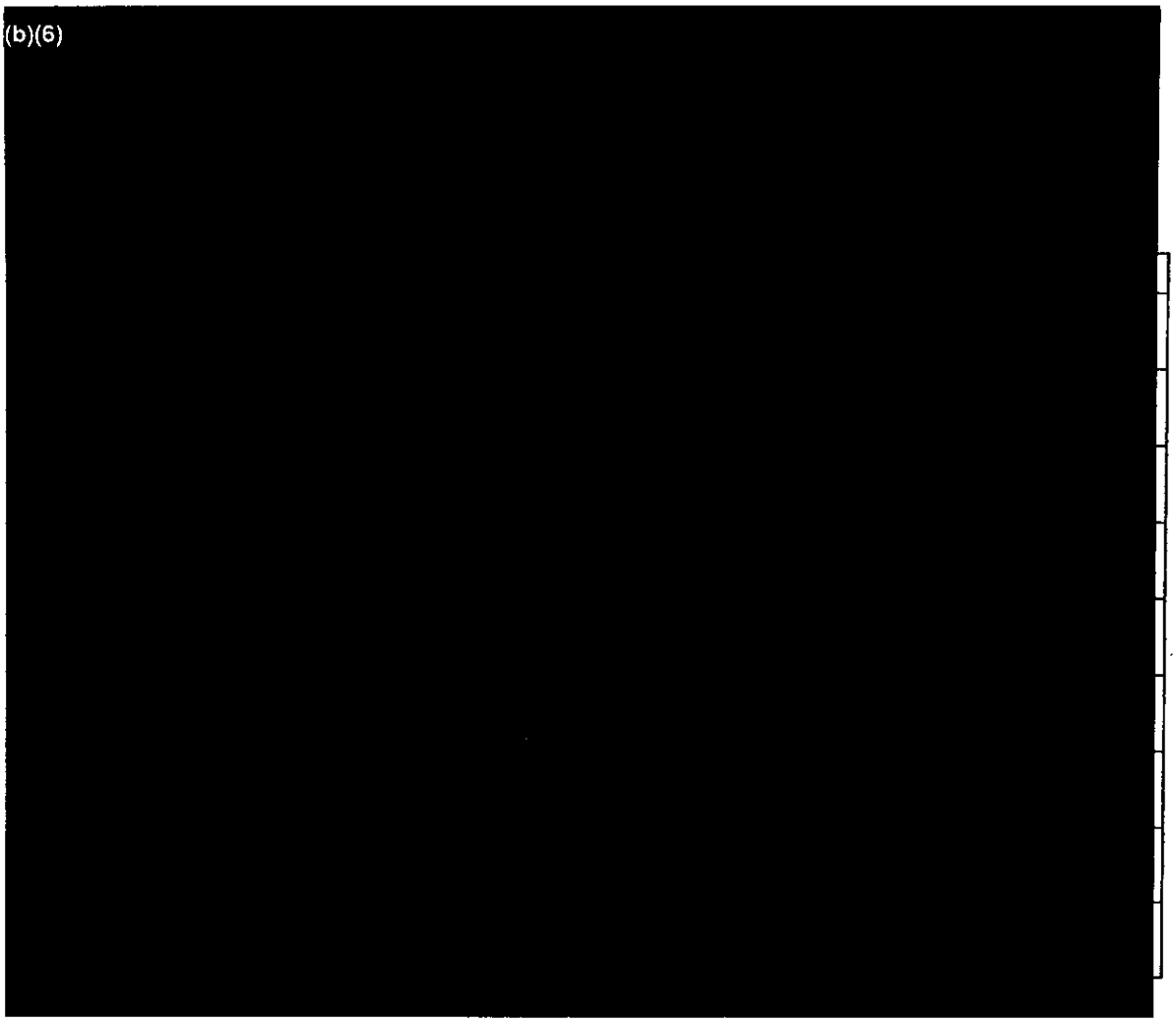
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