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APPLICATION NUMBER:

21-430

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-430
NDA 20-785/S-031

Celgene Corporation
86 Morris Avenue
Summit, NJ 07901

Attention: Megan Parsi
Director, Regulatory Affairs

Dear Ms. Parsi:

Please refer to your new drug application (NDA) dated December 22, 2003, received December 23, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Thalomid® (thalidomide) capsules, 50 mg, 100 mg, and 200 mg.

We acknowledge receipt of your submissions dated May 13, 2005; August 17, 2005; October 13 and 25, 2005. The May 13, 2005 submission constituted a complete response to our October 22, 2004 action letter.

We also acknowledge receipt of your submission dated November 1, 2005, which was not reviewed for our November 10, 2005 action letter.

We acknowledge receipt of your submission dated November 23, 2005, received November 25, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Thalomid® (thalidomide) capsules 50 mg, 100 mg, and 200 mg. The November 23, 2005 submission constitutes a complete response to our November 10, 2005 action letter.

We further acknowledge receipt of your submissions dated November 17 and December 7, 2005; February 2 and 17, 2006; and March 14 and 16, 2006; May 10, May 11, May 15, May 16 and May 19, 2006.

Finally, we acknowledge your December 5, 2005 submission to NDA 20-785/S-031 which includes comparable labeling revisions to the parent NDA. This submission constitutes a complete response to the November 23, 2005 action letter.

New drug application 21-430 provides for the use of Thalomid® (thalidomide) capsules, 50 mg, 100 mg, and 200 mg for the treatment of patients with newly diagnosed multiple myeloma.

We have completed our review of these applications, as amended. They are approved under the provisions of accelerated approval regulations (21 CFR 314.510 and 314.520), effective on the date of this letter, for use as recommended in the agreed upon labeling text and required patient labeling.

Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

The final printed labeling (FPL) must be identical to the enclosed labeling text and required patient labeling. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate these individual submissions "**FPL for approved NDA 21-430 and NDA 20-785/S-031.**" Approval of these submissions by FDA is not required before the labeling is used.

Products approved under the accelerated approval regulations 21 CFR 314.510 require further studies to verify and describe their clinical benefit. We remind you of your post marketing study commitments specified in your submission dated May 11, 2006. These commitments, along with any completion dates agreed upon, are listed below.

- A. Submit the clinical study report for THAL-MM-003, A Randomized Phase III Trial of Thalidomide Plus Dexamethasone Versus Dexamethasone in Newly Diagnosed Multiple Myeloma, as noted below:

Protocol Submission:	July 11, 2002 (Submitted as SPA to IND 49,481, Serial #070)
Study Start:	March 13, 2003
Final Report Submission:	July 2007

- B. Conduct an epidemiologic study (An Epidemiology Study of Venous Thrombotic Events in Thalidomide Treated Multiple Myeloma Patients) to address the questions detailed below:

Safety questions

1. What is the failure rate for each of the different types of thromboembolic prophylaxis (e.g., antiplatelet or anticoagulant therapy) for MM patients treated with a thalidomide-containing regimen?
2. What is the failure rate for each type of DVT treatment (dose-adjusted heparin, low molecular weight heparin, coumadin) for those patients with MM and a DVT who continue to receive ongoing treatment with thalidomide?
3. What is the failure rate for each type of post-DVT thromboembolic prophylaxis for those patients with MM and a DVT who continue to receive ongoing treatment with thalidomide?

This prospective epidemiologic study will enroll select patients identified in the S.T.E.P.S. program, and collect the necessary additional data on these patients to further evaluate occurrences of thrombosis and anticoagulant use. The final details of the design will be as agreed between the Agency and Celgene. The dates for submission of the protocol, study start date and final report submission are indicated below:

Protocol Submission: October 2006
Study Start: March 2007
Final Report Submission: March 2010

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final study reports to NDA 20-785. For administrative purposes, all submissions relating to this postmarketing study commitment must be clearly designated "Subpart H-Postmarketing Study Commitment." In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. 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, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

Immediately submit all promotional materials (both promotional labeling and advertisements) to be used within the first 120 days after approval. Send one copy to the Division of Drug Oncology Products and two copies of the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81). With the approval of administrative NDA 21-430, this NDA number will be retired. All 15-day alert reports, periodic (including quarterly) adverse drug experience reports, field alerts, annual reports, supplements, and other submissions should be addressed to the original NDA 20-785 for this drug product, not to this NDA. In the future, no submissions should be made to NDA 21-430, except for the final printed labeling requested above.

If you have any questions, call Carl Huntley, Regulatory Project Manager, at (301) 796-1372.

Sincerely,
{See appended electronic signature page}

Renata Albrecht, M.D.
Division Director
Division of Special Pathogen
and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Robert L. Justice, M.D.
Acting Division Director
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Enclosure: Labeling