

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 20.998/s-009

APPROVAL LETTER



NDA 20-998/S-009

G.D. Searle L.L.C.
Attention: Eva Essig, Ph.D.
Associate Director, Global Regulatory Affairs
4901 Searle Parkway
Skokie, IL 60077

Dear Dr. Essig:

Please refer to your supplemental new drug application dated June 12, 2000, received June 14, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for CelebrexTM (celecoxib capsules) Capsules, 100 mg and 200 mg.

We acknowledge receipt of your submissions dated February 04; March 21; April 08, 17, and 23; May 01, 09, and 17, 2002. Your submission of December 20, 2001 constituted a complete response to our April 12, 2001 action letter.

This supplemental new drug application provides for changes to the **Warnings, Precautions, Adverse Events, and Clinical Studies** sections of the labeling based on a large gastrointestinal outcome study for Celebrex.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert).

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). 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. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-998/S-009." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.
We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Barbara Gould, Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}

Lawrence Goldkind, M.D.
Deputy Division Director
Division of Anti-Inflammatory, Analgesic and Ophthalmic
Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

**APPEARS THIS WAY
ON ORIGINAL**

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 20-998-S/009

APPROVABLE LETTER

NDA 20-998/S-009

G.D. Searle
Attention: Eva Essig, Ph.D.
Associate Director, Worldwide Regulatory Affairs
4901 Skokie Parkway
Skokie, Illinois 60077

Dear Dr. Essig:

Please refer to your supplemental new drug application dated April 12, 2001, received April 13, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Celebrex (celecoxib capsules) Capsules, 100 mg and 200 mg.

We acknowledge receipt of your submissions dated April 16, 25, and 26; May 1, 14 and 29; June 6, 2001. Your submission of April 12, 2001 constituted a complete response to our April 12, 2001 action letter.

This supplemental new drug application provides for changes to the **Warnings and Clinical Studies** sections of the labeling based on a large gastrointestinal outcome study for Celebrex.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit draft labeling revised as indicated in the enclosed/marked-up draft.

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Under 21 CFR 314.50(d)(5)(vi)(b), we request that you update your NDA by submitting all safety information you now have regarding your new drug. The safety update should include data from all nonclinical and clinical studies of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.

2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
 - Present new safety data from the studies for the proposed indication using the same format as the original NDA submission.
 - Present tabulations of the new safety data combined with the original NDA data.
 - Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.
 - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.
3. Present a retabulation of the reasons for premature study discontinuation by incorporating the drop-outs from the newly completed studies. Describe any new trends or patterns identified.
4. Provide case report forms and narrative summaries for each patient who died during a clinical study or who did not complete a study because of an adverse event. In addition, provide narrative summaries for serious adverse events.
5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.
6. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.
7. Provide English translations of current approved foreign labeling not previously submitted.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal meeting or telephone conference with this division to discuss what further steps need to be taken before the application may be approved.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with these changes prior to approval of this supplemental application.

If you have any questions, call Yoon J. Kong, Pharm.D., Regulatory Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}

Jonca C. Bull, M.D.
Acting Director
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

**APPEARS THIS WAY
ON ORIGINAL**