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RESEARCH**

APPLICATION NUMBER:

21-891

APPROVABLE LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-891

Schering-Plough HealthCare Products
Attention: Mary Williams
Associate Director, Regulatory Affairs
556 Morris Avenue
Summit, NJ 07901-1330

Dear Ms. Williams:

Please refer to your new drug application (NDA) dated August 2, 2005, received August 3, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Children's Claritin (loratadine) chewable tablets 5 mg.

We acknowledge receipt of your submissions dated December 20, 2005, and January 27, February 3 and 24, March 3 (2 submissions), 14, and 30, and May 3 and 18, 2006.

We have completed our review of this application, as amended, and it is approvable. Before the application may be approved, however, it will be necessary for you to submit the information described below.

According to the Division of Scientific Investigations (DSI) audit of your bioequivalence study (CL2003-02), data from certain test subjects must be excluded from the bioequivalence determination.

To address this issue, we recommend the following:

1. Re-analysis of bioequivalence data: Exclude subjects 4-6 (3 subjects) from the loratadine data and subjects 1-3, 13-15 and 22-24 (9 subjects) from the desloratadine data in the bioequivalence analysis and then repeat the analysis before submitting an amendment to the NDA.
2. Repeat assay of samples: If the bioequivalence re-analysis described above does not show that your product is bioequivalent to Claritin® tablet and you have sufficient samples for the above mentioned subjects, you should do a repeat assay of the samples for these subjects and send the report of the re-analysis of the bioequivalence data as an amendment to the NDA. You should also send the analytical report to DSI to show that the issues in the Form 483 have been adequately addressed.

In addition, it will be necessary for you to submit the 5- and 10-count carton, 2-count sachet, and the bi-fold card and bi-fold card tray draft labeling for our review revised as follows:

1. Because the red flag "Allergy" is not considered part of the proprietary name for this drug product, relocate the term "Allergy" to appear immediately below the established name on the principal display panel.
2. For accurate and complete labeling, revise the established name of this drug product to read as follows: "~~_____~~"

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

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all non-clinical 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.

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. 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.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, call Elaine Abraham, Regulatory Project Manager, at (301) 796-0843.

Sincerely,

{See appended electronic signature page}

Andrea Leonard-Segal, M.D.
Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Andrea Segal

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