



NDA 21-366/S-011

AstraZeneca Pharmaceuticals LP
US Agent for IPR Pharmaceuticals, Inc.
Attention: Patricia A. DeFeo, MS
Director, Regulatory Affairs
1800 Concord Pike, P. O. Box 8355
Wilmington, DE 19803-8355

Dear Ms. DeFeo:

Please refer to your supplemental new drug application dated February 1, 2007, received February 2, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Crestor (rosuvastatin calcium) Tablets.

We acknowledge receipt of your submission dated July 18 (email), 2007.

This supplemental new drug application provides for labeling changes in the following sections:

To the **CLINICAL PHARMACOLOGY**, *Drug-Drug Interactions*, a new subsection has been added to read:

Lopinavir/Ritonavir: Coadministration of CRESTOR and a combination product of two protease inhibitors (400 mg lopinavir / 100 mg ritonavir) in healthy volunteers was associated with an approximately 2-fold and 5-fold increase in rosuvastatin steady-state $AUC_{(0-24)}$ and C_{max} respectively. This increase is considered to be clinically significant. Interactions between CRESTOR and other protease inhibitors have not been examined. (See PRECAUTIONS, Drug Interactions, WARNINGS, Myopathy/Rhabdomyolysis, and DOSAGE AND ADMINISTRATION.)

To the **WARNINGS**, *Myopathy/Rhabdomyolysis* subsection, to the paragraph that begins with "Consequently" the following change was made to the first sentence of number four to read:

4. The risk of myopathy during treatment with rosuvastatin may be increased with concurrent administration of other lipid-lowering therapies, cyclosporine, or lopinavir/ritonavir (see CLINICAL PHARMACOLOGY, Drug Interactions, PRECAUTIONS, Drug Interactions, and DOSAGE AND ADMINISTRATION).

To the **PRECAUTIONS**, Drug Interactions, a new subsection, has been added to read:

Lopinavir/Ritonavir: Coadministration of CRESTOR and a combination product of two protease inhibitors (400 mg lopinavir / 100 mg ritonavir) in healthy volunteers was associated with an approximately 2-fold and 5-fold increase in rosuvastatin steady-state $AUC_{(0-24)}$ and C_{max} respectively. These increases should be considered when initiating and titrating CRESTOR in patients with HIV taking lopinavir/ritonavir (see DOSAGE AND ADMINISTRATION).

To the **ADVERSE REACTIONS**, Postmarketing Experience subsection, “memory loss” was added.

To the **DOSAGE AND ADMINISTRATION**, “Dosage in Patients Taking Cyclosporine” subsection has been changed to read:

Dosage in Patients Taking Cyclosporine or Combination of Lopinavir and Ritonavir
In patients taking cyclosporine, therapy should be limited to CRESTOR 5 mg once daily (see WARNINGS, Myopathy/Rhabdomyolysis, and PRECAUTIONS, Drug Interactions). In patients with HIV taking a combination of lopinavir and ritonavir, the dose of CRESTOR should be limited to 10 mg once daily (see WARNINGS, Myopathy/Rhabdomyolysis, and PRECAUTIONS, Drug Interactions).

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html> that is identical to the enclosed labeling (text for the package insert) submitted July 18, 2007, by email. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, “SPL for approved NDA 21-366/S-011.”

PROMOTIONAL MATERIALS

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send three copies of both 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
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Margaret Simoneau, M.S., R.Ph., Regulatory Project Manager, at (301) 796-1295.

Sincerely,

{See appended electronic signature page}

Mary Parks, M.D.
Director
Division of Metabolism and Endocrinology
Products (DMEP)
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

**This is a representation of an electronic record that was signed electronically and
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/s/

Eric Colman
7/23/2007 11:23:29 AM
Eric Colman for Mary Parks