

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**NDA 22-206**

**APPROVAL LETTER**



NDA 22-206

**NDA APPROVAL**

Watson Laboratories, Inc.  
Attention: Paul Long, R.Ph., M.B.A.  
Associate Director, Regulatory Affairs  
577 Chipeta Way  
Salt Lake City, UT 84108

Dear Mr. Long:

Please refer to your new drug application (NDA) dated December 12, 2007, received December 13, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for RAPAFLO<sup>®</sup> (silodosin) Capsules, 4mg and 8mg.

We acknowledge receipt of your submissions dated December 12, 2007, February 5, 2007, February 6, 2008, March 11, 2008, April 4, 2008, May 2, 2008, June 3, 2008, July 10, 2008, August 18, 2008, August 25, 2008, September 10, 2008, September 15 and September 29, 2008.

This new drug application provides for the use of RAPAFLO<sup>®</sup> (silodosin) Capsules, 4mg and 8mg, for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).

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 content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format submitted on September 29, 2008.

Your application for Rapaflo<sup>®</sup> was not referred to an FDA advisory committee because your product is a member of the class of alpha-1-adrenergic receptor antagonist products, including previously approved products, and your product did not pose unique concerns beyond those applicable to other members of this class.

Effective as of this letter date, we request that you submit the following information for RAPAFLO<sup>™</sup> (silodosin):

1. All reports (US and foreign) of serious hepatic adverse events, both labeled and not labeled, as 15-day Alert Reports.
2. Comprehensive follow-up of all reported cases associated with hepatic adverse events listed in #1 above. The information should be obtained using the active query concept (defined below), as stated in the proposed rule on Safety Reporting Requirements for Human Drug and Biological Products [published in the Federal Register of March 14, 2003 (68 FR 12406)]. Follow-up information could be attained from medical records, laboratory results, supporting documents, hospital discharge summaries, and/or other

sources that would sufficiently clarify relevant details of patient treatment, differential diagnosis and the course of clinical events, including any complications of liver injury.

3. Active query is defined as direct verbal contact (i.e., in person or by telephone or other interactive means such as a videoconference) by a qualified health care professional representing Watson, with the initial reporter of a hepatic adverse drug experience. Active query entails, at a minimum, a focused line of questioning designed to capture clinically relevant information associated with RAPAFLOR<sup>TM</sup> (silodosin) and the hepatic adverse drug experience, including, but not limited to, information such as baseline data, patient history, physical exam, diagnostic results, and supportive lab results.
4. Quarterly summaries of hepatic events (see above).

### **CARTON AND IMMEDIATE CONTAINER LABELS**

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)*.

Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 22-206.**” Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

### **PEDIATRIC RESEARCH EQUITY ACT (PREA)**

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) 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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see [www.fda.gov/cder/ddmac](http://www.fda.gov/cder/ddmac).

### **REPORTING REQUIREMENTS**

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

### **MEDWATCH-TO-MANUFACTURER PROGRAM**

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at [www.fda.gov/medwatch/report/mmp.htm](http://www.fda.gov/medwatch/report/mmp.htm).

If you have any questions, call Olga Salis, Regulatory Project Manager, at (301) 796-0837.

Sincerely,

*{See appended electronic signature page}*

Daniel Shames, M.D.  
Deputy Director  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Enclosure (PI and Immediate Container and Carton Labels)

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

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Daniel A. Shames  
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