



NDA 21416/S-011

**SUPPLEMENT APPROVAL**

GlaxoSmithKline LLC  
Attention: Linda Rebar  
Director, Global Regulatory Affairs  
2301 Renaissance Blvd  
PO Box 61540, RN0420  
King of Prussia, PA 19406-2772

Dear Ms. Rebar:

Please refer to your Supplemental New Drug Application (sNDA) dated August 15, 2012, submitted under section 505(b)/pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Rythmol SR (propafenone HCl) Extended-Release Capsules, 225, 325, and 425 mg.

This "Prior Approval" supplemental new drug application provides for labeling revised as follows:

1. Under HIGHLIGHTS/RECENT MAJOR CHANGES, the additions related to Brugada Syndrome to the Contraindications and Warnings and Precautions sections have been noted.
2. Under CONTRAINDICATIONS, in both HIGHLIGHTS and FULL PRESCRIBING INFORMATION, "Known Brugada Syndrome" has been added.
3. Under HIGHLIGHTS/WARNINGS AND PRECAUTIONS, the following text has been added:

RYTHMOL SR may unmask Brugada or Brugada-like Syndrome. Evaluate patients via ECG after initiation of therapy. (4, 5.2)

4. Under WARNINGS AND PRECAUTIONS, the following has been added as section 5.2:

**Unmasking Brugada Syndrome**

Brugada Syndrome may be unmasked after exposure to RYTHMOL SR. Perform an ECG after initiation of RYTHMOL SR and discontinue the drug if changes are suggestive of Brugada Syndrome [*see Contraindications (4)*].

5. Minor formatting changes have been made throughout.

We have completed our review of this supplemental application. 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, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug

registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling, with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(1)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion (OPDP)  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

### **REPORTING REQUIREMENTS**

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, please call Russell Fortney, Regulatory Project Manager, at (301) 796-1068.

Sincerely,

*{See appended electronic signature page}*

Mary Ross Southworth, Pharm.D.  
Deputy Director for Safety  
Division of Cardiovascular and Renal Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

ENCLOSURE: Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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MARY R SOUTHWORTH  
02/14/2013