DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 018917/S-025

SUPPLEMENT APPROVAL

Promius Pharma, LLC
Attention: Kumara Sekar, Ph.D.
Senior Director, Global Regulatory Affairs and Compliance
200 Somerset Corporate Boulevard
7th Floor
Bridgewater, NJ 08807

Dear Dr. Sekar:

Please refer to your Supplemental New Drug Application (sNDA) dated November 9, 2010, received November 22, 2010, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Sectral (acebutolol hydrochloride) 200 mg and 400 mg Tablets.

This Changes Being Effected supplemental new drug application provides for changes to the **WARNINGS** section of the label.

The following changes were made:

1. Under **WARNINGS**, the first paragraph was changed from:

> **WARNINGS**
> **Anesthesia and Major Surgery**
> The necessity, or desirability, of withdrawal of β-blocking therapy prior to major surgery is controversial. β-adrenergic receptor blockade impairs the ability of the heart to respond to β-adrenergically mediated reflex stimuli. While this might be of benefit in preventing arrhythmic response, the risk of excessive myocardial depression during general anesthesia may be enhanced and difficulty in restarting and maintaining the heart beat has been reported with betablockers. If treatment is continued, particular care should be taken when using anesthetic agents which depress the myocardium, such as ether, cyclopropane, and trichlorethylene, and it is prudent to use the lowest possible dose of Sectral. Sectral, like other β-blockers, is a competitive inhibitor of β-receptor agonists, and its effect on the heart can be reversed by cautious administration of such agents (*e.g.,* dobutamine or isoproterenol-see **OVERDOSAGE**). Manifestations of excessive vagal tone (*e.g.,* profound bradycardia, hypotension) may be corrected with atropine 1 to 3 mg IV in divided doses.
>
> To:

WARNINGS, Major Surgery
Chronically administered beta-blocking therapy should not be routinely withdrawn prior to major surgery; however, the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

We have completed our review of this supplemental application and 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 (text for the package insert), 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 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(l)(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).

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

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:

Michael Monteleone
Regulatory Project Manager
(301) 796-1952

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE:
Agreed-Upon Labeling

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

/s/

MARY R SOUTHWORTH
03/03/2011