DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 20-692/S-035

SUPPLEMENT APPROVAL

GlaxoSmithKline
P. O. Box 13398
Five Moore Drive
Research Triangle Park, NC 27709-3398

Attention: Kevin C. Fitzgerald, R.Ph.
Director, Regulatory Affairs

Dear Mr. Fitzgerald:

Please refer to your Supplemental New Drug Application (sNDA) dated March 19, 2010, received March 19, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Serevent Diskus (salmeterol xinafoate inhalation powder).

We acknowledge receipt of your amendments dated May 18, July 30, and September 17, 2010.

This Prior Approval supplemental new drug application provides for a REMS (risk evaluation and mitigation strategy) for Serevent Diskus (salmeterol xinafoate inhalation powder).

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

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FDCA authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS), if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a)]. The details of the REMS requirements were outlined in our REMS notification letter dated February 18, 2010.

Since Serevent Diskus (salmeterol xinafoate inhalation powder) was approved on September 19, 1997, we have become aware of serious asthma outcomes (asthma related death, intubations, and hospitalizations) with the use of the class of long acting beta agonist (LABA), of which Serevent Diskus (salmeterol xinafoate inhalation powder) is a member. Our information was obtained from the Salmeterol Multi-Center Asthma Research Trial (SMART) and the clinical trial data presented as a meta-analysis at the December 10-11, 2008, joint meeting of the Pulmonary Allergy Drugs, Drug Safety and Risk Management, and Pediatric Advisory Committees, and the discussion at the joint Advisory Committee meeting, which raised concerns regarding the use of LABA without concomitant asthma controller therapy, particularly in pediatric and adolescent patients. We consider this information to be "new safety information" as defined in section 505-1(b)(3) of the FDCA.

Your proposed REMS, submitted on September 17, 2010, and appended to this letter, is approved. The REMS consists of a Medication Guide, communication plan, and a timetable for submission of assessments of the REMS. The Medication Guide for Serevent Diskus was approved on June 25, 2010.

The REMS assessment plan should include but may not be limited to:

a. An evaluation of patients' understanding about the risks associated with the use of Servent Diskus, including the increased risk of asthma-related deaths.
b. An analysis of physicians' understanding about the increased risk of asthma-related deaths and the safe use of LABAs.
c. A description of specific measures that would be taken to increase awareness if the assessment of healthcare prescribers indicates that prescriber awareness is not adequate.
d. A narrative summary with analysis of all reported asthma-related deaths during the reporting period.
e. Drug use patterns (reasons for use, patient demographics, length of therapy, prescribing medical specialties)
f. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
g. An assessment of concomitant therapy with other asthma controller medications (e.g., inhaled corticosteroids, montelukast, etc.).
h. With regard to the communication plan:
    a. The date of launch of the communication plan (DHCP letter, website, and communication to professional societies)

b. The number of recipients of the DCHP letter distribution
c. Date(s) of distribution of the DHCP letter
d. A copy of all documents included in each distribution
e. The professional societies to which you communicated
f. The information that the professional societies disseminated to its members and the timing for the dissemination

i. Based on the information reported, an assessment of and conclusion of whether the REMS is meeting its goal and whether modifications to the REMS are needed.

Assessments of an approved REMS must include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

If you currently distribute or plan to distribute an authorized generic product under this NDA, you will also need to submit a REMS, REMS supporting document, and any required appended documents for that authorized generic, to this NDA. In other words, you must submit a complete proposed REMS that relates only to the authorized generic product. Review and approval of the REMS is required before you may market your product.

Prominently identify the submission containing the REMS assessments or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 20-692 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 20-692
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)

FOR NDA 20-692
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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
Division of Drug Marketing, Advertising, and Communications
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.(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 Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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, call Eunice Chung, Regulatory Project Manager, at (301) 796-4006.

Sincerely,

{See appended electronic signature page}

Sally Seymour, M.D.
Deputy Director for Safety
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE(S):
REMS

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

/s/

SALLY M SEYMOUR
11/18/2010