



NDA 021929/S-019

SUPPLEMENT APPROVAL

AstraZeneca LP
1800 Concord Pike
P. O. Box 8355
Wilmington, DE 19803-8355

Attention: Matthew E. Arnold
Associate Director, Regulatory Affairs

Dear Mr. Arnold:

Please refer to your Supplemental New Drug Application (sNDA) dated and received March 19, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Symbicort (budesonide and formoterol) Inhalation Aerosol 80 mcg/4.5 mcg, and 160 mcg/4.5 mcg.

We acknowledge receipt of your amendments dated November 19, 2010, and January 14, 2011, and your risk evaluation and mitigation strategy (REMS) assessment dated November 19, 2010.

This Prior Approval supplemental new drug application provides for a proposed modification to the approved REMS for Symbicort (budesonide and formoterol) Inhalation Aerosol.

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.

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 Medication Guide), 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).

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

The REMS for Symbicort (budesonide and formoterol) Inhalation Aerosol was originally approved on February 27, 2009. The REMS consisted of a Medication Guide and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of a revised Medication Guide, the addition of a Communication Plan to alert health care providers about the risk of serious asthma outcomes (asthma related deaths, intubations, and hospitalizations), and a revised timetable for submission of assessments of the REMS.

Your proposed modified REMS, submitted on January 14, 2011, and appended to this letter, is approved.

The revised REMS assessment plan should include, but is not limited to, the following:

1. An evaluation of patients' understanding of the serious risks of Symbicort including the increased risk of asthma-related deaths.
2. An analysis of prescribers' understanding of the increased risk of asthma-related deaths and the safe use of long acting beta₂-adrenergic agonists (LABAs).
3. 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.
4. A narrative summary with analysis of all reported asthma-related deaths during the reporting period.
5. Drug use patterns (reasons for use, patient demographics, length of therapy, prescribing medical specialties)
6. With regard to the communication plan:
 - a. The date of launch of the communication plan
 - b. The number of recipients of the Dear Health Care Provider (DHCP) 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 that you communicated to

- f. The information that the professional societies disseminated to its members and the timing for the dissemination
7. Based on the information reported, an assessment of and conclusion regarding whether the REMS is meeting its goal and whether modifications to the REMS are needed.

We remind you that assessments of an approved REMS must also 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.

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 must submit a complete proposed REMS that relates only to the authorized generic product. Submit a proposed REMS, REMS supporting document, and any required appended documents as a prior approval supplement. Approval of the proposed REMS is required before you may market your authorized generic product.

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

NDA 021929 REMS ASSESSMENT

**NEW SUPPLEMENT FOR NDA 021929
PROPOSED REMS MODIFICATION
REMS ASSESSMENT**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 021929
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 314.81(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 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 Colette Jackson, Regulatory Project Manager, at (301) 796-1230.

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

ENCLOSURES:
Medication Guide
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
02/16/2011