DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-929/S-012

AstraZeneca LP
1800 Concord Pike
PO Box 8355
Wilmington, DE 19803-8355

Attention: Mark DeSiato
Executive Director, Regulatory Affairs

Dear Mr. DeSiato:

Please refer to your supplemental new drug application dated April 28, 2008, received April 29, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for SYMBICORT (budesonide/formoterol) Inhalation Aerosol.

We acknowledge receipt of your submissions dated July 24, August 7, 20, and 25, November 26, and December 3, and 5, 2008 and January 9, 15, 22, and 23, and February 6, 19, 23, 24, and 26, 2009.

This supplemental new drug application provides for the use of SYMBICORT for the treatment of Chronic Obstructive Pulmonary Disease (COPD).

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

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling text for the package insert submitted February 26, 2009, and Medication Guide submitted February 19, 2009. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 21-929/S-012."

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable. We are waiving the pediatric study requirement for this supplement because the necessary studies are impossible or highly impracticable since the disease does not exist in children.

RISK EVALUATION AND MITIGATION STRATEGIES REQUIREMENTS

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the FDCA to authorize FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) for an approved drug if the 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)). This provision took effect on March 25, 2008.

Since SYMBICORT was approved July 2006, FDA has become aware of an increased incidence of lower respiratory tract infections in patients with COPD who take SYMBICORT. This information is from controlled clinical trials (one 6-month and one 12-month safety and efficacy trial) submitted with this supplemental new drug application. This information was not available when SYMBICORT was granted marketing authorization. Therefore, we consider this information to be "new safety information" as defined in FDAAA.

In accordance with section 505-1 of FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Your previously approved Medication Guide has been revised to include the new safety information. Pursuant to 21 CFR Part 208, FDA has determined that SYMBICORT poses a serious and significant public health concern requiring distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of SYMBICORT. FDA has determined that SYMBICORT is a product that has serious risks (relative to benefits) of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use SYMBICORT. FDA has also determined that Symbicort is a product for which patient labeling could help prevent serious adverse events. Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed SYMBICORT.

Your proposed REMS, submitted on January 15, 2009, and appended to this letter, is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS included in your January 15, 2009, submission.

Your assessment of the REMS should include:

a. An evaluation of patients' understanding of the serious risks of Symbicort.

Prominently identify submissions containing 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:

- **NDA 21-929 REMS ASSESSMENT**
- **NEW SUPPLEMENT FOR NDA 21-929**
  PROPOSED REMS MODIFICATION
  < other supplement identification > [if included]
  <REMS ASSESSMENT> [if included]

If you do not submit electronically, please send 5 copies of submissions containing REMS assessments or proposed modifications of the REMS.

PROMOTIONAL MATERIALS

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Pulmonary and Allergy Products and two copies of both the promotional materials and the package insert(s) directly 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.

LETTERS TO HEALTH CARE PROFESSIONALS

If you 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 an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
HFD-001, Suite 5100
5515 Security Lane
Rockville, MD 20852

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}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary and Allergy Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure: REMS, Package Insert, Medication Guide

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

/s/

Badrul Chowdhury

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