



NDA 020831/S-22

**SUPPLEMENT APPROVAL**

Novartis Pharmaceuticals Corporation  
One Health Plaza  
East Hanover, NJ 07936-1080

Attention: Yifeng Jia, Ph.D.  
Drug Regulatory Manager

Dear Dr. Jia:

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 Foradil Aerolizer (formoterol fumarate inhalation powder).

We acknowledge receipt of your amendments dated June 11, and 17, and September 27, 2010, and February 11, March 2, April 6 and April 15, 2011.

This Prior Approval supplemental new drug application provides for a proposed risk evaluation and mitigation strategy (REMS) for Foradil Aerolizer (formoterol fumarate 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.

**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 determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a)].

Since Foradil Aerolizer (formoterol fumarate inhalation powder) was approved on February 16, 2001, we have become aware of serious asthma outcomes (asthma-related death, intubations, and hospitalizations) with the use of the class of long acting beta agonists (LABAs), of which Foradil Aerolizer (formoterol fumarate 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 LABAs without concomitant asthma controller therapy, particularly in pediatric and adolescent

patients. We considered this information to be “new safety information” as defined in section 505-1(b) of the FDCA.

In our letter dated February 18, 2010, we notified you that a REMS was required for Foradil Aerolizer (formoterol fumarate inhalation powder) to ensure that the benefits of the drug outweigh the risks described above. We indicated that your REMS must include a Medication Guide, communication plan, and timetable for submission of assessments of the REMS.

We also refer to our communication dated March 21, 2011, where we informed you that we have determined that is not necessary for the Medication Guide to be part of a REMS to ensure that the benefits of Foradil Aerolizer (formoterol fumarate inhalation powder) outweigh its risks. We believe that the Medication Guide is necessary for patients’ safe and effective use of Foradil Aerolizer (formoterol fumarate inhalation powder), and it will be part of the approved labeling and subject to the requirements under 21 CFR 208.

Your proposed REMS, submitted on April 6, 2011, and appended to this letter, is approved.

The REMS consists of a communication plan and a timetable for submission of assessments of the REMS.

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

1. An analysis of prescribers’ understanding of the increased risk of asthma-related deaths and the safe use of LABAs.
2. 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.
3. A narrative summary with analysis of all reported asthma-related deaths during the reporting period.
4. Drug use patterns such as reasons for use, patient demographics, length of therapy, prescribing medical specialties.
5. 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.
6. An assessment of concomitant therapy with other asthma controller medications (e.g., inhaled corticosteroids, montelukast, etc.).
7. An assessment of the communication plan. With regard to the communication plan, Novartis will report to the Agency the following:
  - 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 that you communicated to
  - f. The information that the professional societies disseminated to its members and the timing for the dissemination
8. 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 020831 REMS ASSESSMENT**

**NEW SUPPLEMENT FOR NDA 020831  
PROPOSED REMS MODIFICATION  
REMS ASSESSMENT**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)  
FOR NDA 020831  
REMS ASSESSMENT  
PROPOSED REMS MODIFICATION (if included)**

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

**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

ENCLOSURES:  
REMS  
REMS Materials

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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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SALLY M SEYMOUR  
05/18/2011