



NDA 22-007/S-005

**SUPPLEMENT APPROVAL**

Dey Pharma, L.P.  
2751 Napa Valley Corporate Drive  
Napa, CA 94558

Attention: Wayne Talton  
Vice President, Regulatory Affairs

Dear Mr. Talton:

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 Perforomist (formoterol fumarate) Inhalation Solution.

We acknowledge receipt of your amendments dated May 17, and October 28, 2010, and January 7, 2011.

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

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 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 Perforomist (formoterol fumarate) Inhalation Solution was approved on May 11, 2007, 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 Perforomist (formoterol fumarate) Inhalation Solution 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 considered this information to be “new safety information” as defined in section 505-1(b) of the FDCA.

Your proposed REMS, submitted on January 7, 2011, 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 Perforomist (formoterol fumarate) Inhalation Solution was approved on June 2, 2010.

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

1. An evaluation of the patients’ understanding of the serious risks associated with Perforomist (formoterol fumarate) Inhalation Solution including the increased risk of asthma-related deaths.
2. An analysis of the prescriber understanding of the increased risk of asthma-related deaths and the safe use of LABAs.
3. A description of specific measures that would be taken to increase awareness if the assessment of the prescribers indicates that the prescribers’ awareness is not adequate.
4. A narrative summary with analysis of all reported asthma-related deaths during the reporting period.
5. Drug use patterns such as reasons for use, patient demographics, length of therapy, prescribing medical specialties.
6. 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.
7. An assessment of the communication plan. With regard to the communication plan, Dey Pharma 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 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 their members and the timing of the dissemination

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.

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 022007 REMS ASSESSMENT**

**NEW SUPPLEMENT FOR NDA 022007  
PROPOSED REMS MODIFICATION  
REMS ASSESSMENT  
NEW SUPPLEMENT (NEW INDICATION FOR USE)  
FOR NDA 022007  
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 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

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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  
02/01/2011