DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22518/S-002
NDA 22518/S-004

SUPPLEMENT APPROVAL
REMS ASSESSMENT ACKNOWLEDGEMENT
RELEASE REMS ELEMENT

Schering-Plough Corporation
2000 Galoping Hill Road
Kenilworth, NJ 07033-0530

Attention: Michael Belman
Director & Liaison, Global Regulatory Affairs

Dear Mr. Belman:

Please refer to your Supplemental New Drug Applications (sNDA) dated June 22, 2011, received June 22, 2011, and July 22, 2001, received July 22, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Dulera (mometasone furoate and formoterol fumarate) Inhalation Aerosol.

We acknowledge receipt of your amendments dated July 8, and August 5, 2011.

We also acknowledge receipt of your risk evaluation and mitigation strategy (REMS) assessment dated June 22, 2011. After consultation between the Office of Surveillance and Epidemiology and the office of New Drugs, we found the REMS assessment to be adequate. However, we have the following comment regarding your prescriber survey:

1. On your next prescriber survey , include a question to specifically assess prescriber knowledge of the following prescribing information:
   - DULERA should not be used in patients whose asthma is adequately controlled on low or medium dose inhaled corticosteroids.

Supplemental new drug application (S-002) proposes to eliminate the requirement of the Medication Guide as an element of the approved Dulera (mometasone furoate and formoterol fumarate) Inhalation Aerosol REMS.

Supplemental new drug application (S-004) proposes to add the term “anaphylactic reaction” to the Post-Marketing Experience (6.2) section of the Package Insert.

We have completed our review of these supplemental applications, as amended. They are 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 package insert, text for the patient package insert, 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 Dulera (mometasone furoate and formoterol fumarate) Inhalation Aerosol was originally approved on June 22, 2010. The REMS consists of a Medication Guide, a communication plan, and a timetable for submission of assessments of the REMS.

Your proposed modification to the REMS consists of eliminating the requirement for the Medication Guide as an element of the REMS.

We have determined that maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21 CFR 208.1. Therefore, it is no longer necessary to include the Medication Guide as an

element of the approved REMS to ensure that the benefits of the Dulera (mometasone furoate and formoterol fumarate) Inhalation Aerosol outweigh the risks.

Therefore, we agree with your proposal, and a Medication Guide is no longer required as part of the REMS for Dulera (mometasone furoate and formoterol fumarate) Inhalation Aerosol.

We remind you that the Medication Guide will continue to be part of the approved labeling for Dulera (mometasone furoate and formoterol fumarate) Inhalation Aerosol. in accordance with 21 CFR 208.

The timetable for submission of assessments of the REMS will remain the same as that approved on June 22, 2010.

The revised 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 death 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 (reasons for use, patient demographics, length of therapy, prescribing medical specialties)
5. 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 that you communicated to
    f. The information that the professional societies disseminated to its members and the timing for the dissemination
    g. 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)(3) 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 22518 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 22518
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 22518
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:
Content of Labeling
REMS

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

/s/

LADAN G JAFARI
08/18/2011

SALLY M SEYMOUR
08/18/2011