CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 17573/S040

APPROVAL LETTER

FEB - 8 1999

NDA 17-573/S-040

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Attention: Joseph F. Lamendola, Ph.D., Vice President
US Regulatory Affairs

Dear Dr. Lamendola:

Please refer to your supplemental new drug application dated June 17, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vanceril 42 mcg (beclomethasone dipropionate) Inhalation Aerosol.

We acknowledge receipt of your submission dated November 3, 1998.

This supplemental new drug application provides for revisions to the labeling requested in our March 26, 1996 "inhaled steroid class labeling" letter, changes to the label for consistency with NDA 20-469 and a revision to the statement concerning CFCs in response to the May 3, 1996 Federal Register (61 FR 20096).

We have completed the review of this supplemental application, as amended, and it is approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Ms. Sandy Barnes, Project Manager, at (301) 827-1075.

Sincerely,

John K. Jenkins, M.D., F.C.C.P.
Director
Division of Pulmonary Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 17573/S040

APPROVABLE LETTER

NDA 17-573/S-020, S-025, S-032, S-033, S-035, S-037 and S-040

MAY 28 1997

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Attention: Joseph F. Lamendola, Ph.D.
Vice President, U.S. Regulatory Affairs

Dear Dr. Lamendola:

Please refer to your supplemental new drug applications dated March 24, 1982, September 13, 1984, August 21, 1986, June 25, 1987, February 16, 1988, November 9, 1989, and June 17, 1996 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vanceril 42 mcg (beclomethasone dipropionate) Inhalation Aerosol.

We acknowledge receipt of your submissions dated July 8, 1985 (S-020), and November 6, 1985 (S-025).

These supplemental applications provide for revisions to the labeling as follows:

S-020 - revisions to the labeling as requested in our approval letter for Vancenase (beclomethasone dipropionate) Nasal Inhaler dated September 24, 1981 and reformatting of the labeling as requested in the Federal Register Notice June 26, 1979;

S-025 - revisions to the DESCRIPTION, CLINICAL PHARMACOLOGY, INDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE REACTIONS, OVERDOSAGE, and DOSAGE AND ADMINISTRATION Sections of the package insert;

S-032 - the addition of a statement, to the PATIENT'S INSTRUCTIONS section of the package insert, amplifying the importance of replacing the dust cover;

S-033 - a revision to the WARNINGS section requested in our August 13, 1985 General Correspondence and a resubmission of the revisions from S-020 and S-025;

S-035 - the addition of a statement to the HOW SUPPLIED section and PATIENT'S INSTRUCTION FOR USE regarding storage conditions;

S-037 - the addition of the EPA CFC Warning and the addition of statements to the WARNING and PRECAUTIONS sections regarding chickenpox and measles exposure; and

S-040 - revisions to the labeling requested in our March 26, 1996 "inhaled steroid class labeling" letter, changes to the label for consistency with NDA 20-469 and a revision to the statement concerning CFCs in response to the May 3, 1996 Federal Register (61 FR 20096).

We have completed the review of these supplemental applications as submitted with draft labeling dated June 17, 1996, and supplement S-040 is approvable. Before supplement S-040 may be approved, however, it will be necessary for you to submit final printed labeling (FPL). The labeling should be revised as indicated by the enclosed marked-up draft labeling. To facilitate review of your submission, please provide highlighted or marked-up copies that show the changes that are being made.

Please submit 16 copies of the final printed labeling, ten of which are individually mounted on heavy-weight paper or similar material.

We note that supplemental application S-040 supersedes supplemental applications S-020, S-025, S-032, S-033, S-035 and S-037. Therefore these supplemental applications will be retained in our files.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of such action FDA may take action to withdraw the application.

We remind you of your commitment under NDA 20-486 to change the trademark for Vanceril Inhaler to Vanceril 42 mcg Inhalation Aerosol (beclomethasone dipropionate inhalation aerosol, 42 mcg) at the time of the next printing or by June 24, 1997, whichever occurs sooner.

Any changes to the carton or container necessitated by the attached revisions should be submitted with your response to this letter.

If you have any questions, please contact Ms. Sandra Barnes, Project Manager, at (301) 827-1075.

Sincerely yours,

John K. Jenkins, M.D.
Director
Division of Pulmonary Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure: Marked-up draft labeling

NDA 17-573

MAR 26 1996

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Attention: Richard N. Spivey, Pharm. D., Ph.D.
Senior Director, U.S. Regulatory Affairs

Dear Dr. Spivey:

Please refer to your new drug application for Vanceril® (beclomethasone diprionate) Inhaler submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act.

We have recently completed a review of the package inserts for inhaled corticosteroid products. The purpose of this review was to identify and institute changes for labeling of these products that would better standardize the labeling, as well as to up-date the information contained in the labeling for these agents to better reflect controlled data accumulated on these agents since their approval. We therefore are requesting that the following changes be made to the labeling for Vanceril® Inhaler.

1. The **DESCRIPTION** section should be updated as necessary to indicate the excipients that are present and, preferably, the concentration of each excipient.

2. The **CLINICAL PHARMACOLOGY** section should be revised to include the following:

   a. An updated discussion of any additional data from preclinical studies, generated since product approval, which have implications for the safety of the drug product; and

   b. an updated discussion of hypothalamic-pituitary-adrenal axis effects and other important safety information relating to clinically relevant doses derived from controlled clinical trials conducted by you, particularly regarding prolonged duration of use or use of higher dosages.

3. The following statement should replace the current **INDICATIONS** section in all products.

   a. *"[Name of drug] is indicated in the maintenance treatment of asthma as prophylactic therapy. [Name of drug] is also indicated for asthma patients who require systemic corticosteroid administration, where adding [name of drug] may reduce or eliminate the need for the systemic corticosteroids."*

   b. The sentence in comment 4.a. should be followed by wording below, formatted as a separate paragraph:

      "[Name of drug] is NOT indicated for the relief of acute bronchospasm."

4. The following statement should be deleted from the **WARNINGS** section of all products that contain it:

5. The following changes should be made in the **PRECAUTIONS** section.

   a. The following statement, included as class labeling, should be modified from:

      To:

      "The long-term local and systemic effects of [name of drug] in human subjects are still not fully known. In particular, the effects resulting from chronic use of [name of drug] on developmental or immunologic processes in the mouth, pharynx, trachea, and lung are unknown."

b. The current wording regarding the unknown effects of inhaled corticosteroids on pulmonary tuberculosis and other pulmonary and/or systemic infections should be deleted and the following sentence inserted in its place.

"Inhaled corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculosis infection of the respiratory tract; untreated systemic fungal, bacterial, parasitic or viral infections; or ocular herpes simplex."

6. The following comments refer to the **ADVERSE REACTION** section.

a. This section should be updated to reflect pharmacovigilance data obtained subsequent to drug approval from sources such as the published literature, spontaneous reporting and post-marketing surveillance. Specific adverse effects recommended for inclusion are:

(1) HPA axis effect, hypercorticism, adrenal insufficiency;

(2) growth inhibitory effects;

(3) cataracts, glaucoma; and

(4) hyperglycemia

b. Other adverse reactions not included in the above list should be added to the **ADVERSE REACTION** section if they are shown to be clinically significant in the use of the product.

7. The following changes should be made in the **DOSAGE AND ADMINISTRATION** section.

a. The current discussion in the class labeling on the use of inhaled corticosteroids in two patient populations (those not currently receiving and those receiving systemic corticosteroids) should be replaced with the following statements.

Patients Not Receiving Systemic Corticosteroids
Patients who require maintenance therapy of their asthma may benefit from treatment with [name of drug] at the doses recommended above. In patients who respond to [name of drug], improvement in pulmonary function is usually apparent within one to four weeks after the start of therapy. Once the desired effect is achieved, consideration should be given to tapering to the lowest effective dose.

Patients Maintained on Systemic Corticosteroids
Clinical studies have shown that [name of drug] may be effective in the management of asthmatics dependent or maintained on systemic corticosteroids and may permit replacement or significant reduction in the dosage of systemic corticosteroids.

The patient's asthma should be reasonably stable before treatment with [name of drug] is started. Initially, [name of drug] should be used concurrently with the patient's usual maintenance dose of systemic corticosteroid. After approximately one week, gradual withdrawal of the systemic corticosteroid is started by reducing the daily or alternate daily dose. Reductions may be made after an interval of one or two weeks, depending on the response of the patient. A slow rate of withdrawal is strongly recommended. Generally, these decrements should not exceed 2.5 mg of prednisone or its equivalent. During withdrawal, some patients may experience symptoms of systemic corticosteroid withdrawal; e.g. joint and/or muscular pain, lassitude and depression, despite maintenance or even improvement in pulmonary function. Such patients should be encouraged to continue with the inhaler but should be monitored for objective signs of adrenal insufficiency. If evidence of adrenal insufficiency occurs, the systemic corticosteroid doses should be increased temporarily and thereafter withdrawal should continue more slowly.

During periods of stress or a severe asthma attack, transfer patients may require supplementary treatment with systemic corticosteroids.

b. The following statement should be **inserted** into the **DOSAGE AND ADMINISTRATION** section, if not currently included in the labeling:

"Rinsing the mouth after inhalation is advised."

c. If included in the current labeling, the following statements should be **deleted**:

8. The following comment pertains to the **PATIENT INSERT** section.

The patient instructions for inhaler technique should include the word "***slowly***" in reference to the inhalation technique for optimal inhaler use, if not already included.

9. Labeling regarding "Pediatric Use" within the **INDICATIONS**, **PRECAUTIONS**, and **DOSAGE AND ADMINISTRATION** sections should be added to or revised as appropriate in accordance with the Pediatric Final Rule of December 13, 1994 [21 CFR 201.57(f)(9)(I)-(vii)].

Please submit draft labeling in the form of a supplement to this application. Please incorporate all previous revisions as reflected in the most recently approved package insert. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

If you have any questions, please contact, Ms. Gretchen Strange, Project Manager at (301) 827-1058.

Sincerely yours,

John K. Jenkins, M.D.
Director
Division of Pulmonary Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:NDA 17573/S040

ADMINISTRATIVE DOCUMENTS

PROJECT MANAGER LABELING REVIEW

JAN 2 6 1999

NDA 17-573/S-040

Applicant: Schering Corporation

Drug: Vanceril 42 mcg (beclomethasone dipropionate) Inhalation Aerosol

Date of submissions: November 3, 1998

This supplemental application provides for revisions to the labeling requested in our March 26, 1996 "inhaled steroid class labeling" letter, changes to the label for consistency with NDA 20-469 (including changing the name of the product from Vanceril Inhalation Aerosol to Vanceril 42 mcg Inhalation Aerosol), and a revision to the statement concerning CFCs in response to the May 3, 1996 Federal Register (61 FR 20096).

This submission contains final printed package inserts including patient's instructions for use, carton labels and container labels in response to our May 28, 1997 Approvable letter. The Approvable letter requested final printed labeling revised as indicated in marked-up draft labeling. In addition, the letter requested that the carton and container labels should be submitted if changes were necessary based on the revisions in the mark-up draft package insert.

The changes requested in the approvable letter were made to the package insert (including the patient's instructions for use) as requested, however, in addition, Schering requested the following revisions to the package insert.

1. The word "intramuscularly" was added to the end of the second paragraph of the Clinical Trials subsection of the CLINICAL PHARMACOLOGY Section.

2. A new paragraph regarding a report of oral candidiasis was added to the ADVERSE REACTION section for consistency with Vanceril 84 mcg Double Strength.

3. The second paragraph of the Patients Maintained on Systemic Corticosteroids subsection of the DOSAGE AND ADMINISTRATION section was removed as Schering believed it was a duplication of the last sentence of the previous paragraph.

4. The phrase "and is manufactured with dichlorodifluoromethane (CFC-12)" was added to the CFC warning.

The revisions to the carton and container labels are consistent the revised labeling and with the approved cartons and containers labels for NDA 20-486, Vancenase 84 mcg Double Strength.

Conclusions: With the concurrence of the medical officer and chemist on Schering's requested additional revisions, this supplemental application should be approved.

/S/

Sandy Barnes
Project Manager

cc: Orig NDA 17-573/S-040
Div File
HFD-570 S. Barnes
Initialed by

1/26/99

MAY 1 1997

CSO LABELING REVIEW

NDA: 17-573/S-020/S-025/S-032/S-033/S-035/S-037/S-040

Sponsor: Schering

Drug name: Vanceril Inhaler

Submissions dated:

S-020	24-Mar-82 (RW)
S-020 AL	8-Jul-85
S-025	13-Sep-84
S-025 AL	8-Jul-85
S-025 AL	6-Nov-85
S-032	21-Aug-86
S-033	25-Jun-87
S-035	16-Feb-88
S-037	9-Nov-89
S-040	17-Jun-96

INTRODUCTION:

The review of these labeling supplemental applications is particularly complicated due to the number of revisions and the submission of "changes being effected" supplements (S-035 and S-037) which do not incorporate the early proposed revisions, in addition, the 6-Nov-85 amendment to S-025 was submitted as "changes being effected."

SUMMARY (a detailed description of the contents of each supplemental application (with the exception of SPD-020), prepared by Gretchen Trout, can be found as Attachment 1):

S-020 - Provides for revisions to the package insert requested in the September 24, 1981 Approval letter for NDA 18-521 Vancenase (beclomethasone dipropionate) Nasal Inhaler. The changes requested were to the DESCRIPTION, CLINICAL PHARMACOLOGY, INDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE REACTIONS and ANIMAL PHARMACOLOGY AND TOXICOLOGY Sections of the package insert. In addition, Schering revised the format of the package insert to meet the Federal Register Notice June 26, 1979. The deficiencies were conveyed to the sponsor in a "Review Waiting Firm" (RW) letter on August 17, 1984.

The sponsor responded with an amendment on July 8, 1985 to both S-020 and S-025. See Summary of S-025 for details of the July 8, 1985 amendment.

S-025 - Provides for revision to the following sections of the package insert: DESCRIPTION, CLINICAL PHARMACOLOGY, INDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE REACTIONS, OVERDOSAGE, AND DOSAGE AND ADMINISTRATION.

The amendment dated July 8, 1985 incorporated the labeling changes from SPD-020 including revisions requested in our RW letters dated August 17, 1984 for SPD-20 and October 23, 1984 for SLR-025. This amendment was reviewed by both the medical officer and the chemist. The Chemist's review dated October 13, 1985 found the changes to the DESCRIPTION and HOW SUPPLIED section to be acceptable. The medical reviews dated October 1 and 15, 1985 found the amendment unacceptable. The recommendations were held pending the completion of a Pharmacology review and a consultation from HFD-150, The Division of Oncology and Pulmonary Drug Products.

The amendment dated November 6, 1985 is marked as a "Changes Being Effective" supplement and provided for the incorporation of a revision to the ADVERSE REACTION section requested in our letter dated October 23, 1984. The medical officer review dated November 22, 1985 concluded that the labeling was unacceptable since it did not include the changes requested in our August 13, 1985 (supplement request letter requesting a change to the ADVERSE REACTION section of the package insert) letter. This was not conveyed to the sponsor.

S-032 - Provides for the addition of a statement, to the PATIENT'S INSTRUCTIONS section of the package insert amplifying the importance of replacing the dust cover. An April 7, 1987 "Record of Telephone Conversation/Meeting" noted that this revision was unacceptable and recommended alternate wording.

S-033 - This supplemental application was a resubmission of the July 8, 1985 amendment to S-025. The sponsor also included a revision to the WARNINGS section requested in our August 13, 1985 General Correspondence. The added paragraph is considerably different from the requested revision, however, no review can be

found for this submission.

S-035 - This submission was submitted as "Changes being effected" and provides for the addition of a statement to the HOW SUPPLIED section and patient leaflet regarding storage conditions. A December 5, 1988 Chemistry review recommends approval with "our recommended wording for the first sentence in the Pharmacology section," this wording cannot be located.

S-037 - This submission was submitted as "Changes being effected" and provides for the addition of the EPA CFC Warning and the addition of statements to the WARNINGS and PRECAUTIONS sections regarding chickenpox and measles exposure. No review can be found for this submission.

S-040 - Provides for revisions to the labeling requested in our March 26, 1996 "inhaled steroid class labeling" letter, changes to the label for consistency with NDA 20-486, Vanceril 84 mcg Double Strength Inhalation Aerosol and a revision to the statement concerning CFCs in response to the May 3, 1996 Federal Register (61 FR 20096). This essentially changes all sections of the package insert with the exception of the HOW SUPPLIED Section.

I reviewed each of the outstanding labeling supplemental applications including any associated correspondence and have determined that all of the revisions including those requested by the FDA are represented in the latest supplemental application (S-040). Some of the wording originally requested has been modified; however, it is consistent with the other marketed products for this class of drugs.

When Schering submitted S-040 to NDA 17-573, NDA 20-486 for Vanceril 84 mcg Double Strength Inhalation Aerosol was still a pending application; therefore, I have revised the labeling submitted with S-040 to reflect the final labeling approved for NDA 20-486. The September 5, 1996, submission to NDA 20-486 included priming data for both the 42 mcg and 84 mcg products; therefore, I revised the priming information for NDA 17-573 as recommended in the Chemistry review dated December 10, 1996 for NDA 20-486.

RECOMMENDATIONS:

With the concurrence of the reviewers, Schering should be sent an approvable letter for S-040, requesting revised labeling as shown in the attached marked-up labeling. The approvable letter should also include the following requests:

1. We remind you of your commitment under NDA 20-486 to change the trademark for Vanceril Inhaler to Vanceril 42 mcg Inhalation Aerosol at the time of the next printing or by June 24, 1997, whichever occurs sooner.

2. Any changes to the carton or container necessitated by the attached revisions should be submitted with your response to this letter.

With the approval of S-040, the changes submitted in supplemental applications S-020, S-025, S-032, S-033, S-035 and S-037 have been superseded and the supplemental applications should be acknowledged and retained in the approvable letter for S-040.

/S/
Sandy Barnes
Project Manager

/S/
Concur Non concur
Richard Nicklas, M.D.
Medical Officer

/S/
Concur Non concur
Chong-Ho Kim, Ph. D.
Reviewing Chemist

/S/
Concur Non concur
Lawrence Sancilio, Ph.D.
Reviewing Pharmacologist

/S/
Concur Non concur
Bradley K. Gillespie, Pharm.D.
Reviewing Pharmacokineticist

cc:Orig NDA 17-573 4/25/97
Div File
HFD-570/Nicklas
HFD-570/Kim 4/23/97 5/1/97
HFD-570/Sancilio
HFD-570/S. Barnes/3-18-97

Attachment 1

S-025

Provides for revision to the ADVERSE REACTIONS section of the package insert. The current wording is as follows:

> Bronchospasm and rash have been reported rarely.

The proposed wording is as follows:

S-025 AL

This amendment provides for numerous revisions to the package insert. All of the revisions were made and are reflected in the printed label submitted along with S-033 with the following exceptions:

Schering proposed the addition of the following sentence in the DOSAGE AND ADMINISTRATION section of the package insert

This sentence was not added.

Also, in the CLINICAL PHARMACOLOGY section of the package insert, Schering proposed replacing "prednisolone" with "betamethasone". However in S-033 "dexamethasone" is the word used. And the following sentence is added:

> ...and in having a 16β-methyl instead of a 16-alpha methyl group.

S-025 BL

Provides for revision to the ADVERSE REACTIONS section of the package insert. The proposed wording supersedes the wording submitted in S-025. The new proposed

wording is as follows:

> Rare cases of immediate and delayed hypersensitivity reactions, including urticaria, angioedema, rash, and bronchospasm have been reported following the oral and intranasal inhalation of beclomethasone.

S-032

Provides for revision to the PATIENT'S INSTRUCTIONS section of the package insert. The company proposed adding the following wording:

> REPLACE THE CAP FOLLOWING USE. Should the cap be dislodged or lost, the inhaler mouthpiece should be inspected for the presence of foreign objects before each use.

S-033

Provides for revision to the WARNINGS section of the package insert. The following paragraph has been added:

> If recommended doses of inhaled beclomethasone are exceeded or if individuals are particularly sensitive or predisposed by virtue of recent systemic steroid therapy, symptoms of hypercorticism may occur, including very rare cases of mental disturbances, increased bruising, weight gain, and cushingoid features. If such changes occur, VANCERIL Oral Inhaler should be discontinued slowly consistent with accepted procedures for discontinuing oral steroid therapy.

(This paragraph was in the printed label submitted with S-033, but then was not in the printed label submitted with S-035)

S-035 Changes Being Effected

Provides for revision to the HOW SUPPLIED section of the package insert. The following sentence is to be added:

> Failure to use the product within this temperature range may result in improper dosing.

Provides for revision to the PATIENT LEAFLET with the addition of the following paragraph:

> Store between 2° and 30°C (36° and 86°F). Failure to use the product within

this temperature range may result in improper dosing. Shake well before using.

S-037 Changes Being Effected

Provides for revision to the body of the package insert. The following statement will appear after the HOW SUPPLIED section of the package insert:

> **Note**: The indented statement below is required by the Federal government's Clean Air Act for all products containing or manufactured with chlorofluorocarbons (CFCs).
>
> > **WARNING**: Contains dichlorodifluoromethane (CFC-11) and trichloromonofluoromethane (CFC-12), substances which harm public health and the environment by destroying ozone in the upper atmosphere.
>
> A notice similar to the above WARNING has been placed in the "Patient's Instructions for Use" portion of this package insert pursuant to EPA regulations.

Provides for revision to the PATIENT'S INSTRUCTIONS FOR USE section of the package insert. The following statement will be added:

> **Note**: The indented statement below is required by the Federal government's Clean Air Act for all products containing or manufactured with chlorofluorocarbons (CFCs).
>
> > This product contains dichlorodifluoromethane (CFC-11) and trichloromonofluoromethane (CFC-12), substances which harm public health and the environment by destroying ozone in the upper atmosphere.
>
> Your physician has determined that this product is likely to help your personal health. USE THIS PRODUCT AS DIRECTED, UNLESS INSTRUCTED TO DO OTHERWISE BY YOUR PHYSICIAN. If you have any questions about alternatives, consult with your physician.

Provides for revisions to the WARNINGS section of the package insert. The following paragraph has been added:

> Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in non-immune children or adults on corticosteroids. In such children or adults who have not had these diseases, particular care should be taken to avoid exposure. How the dose,

route and duration of corticosteroid administered affects the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known, if exposed to chickenpox, prophylaxis with varicella-zoster (VZIG) may be indicated. If exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information.) If chickenpox develops, treatment with antiviral agents may be considered.

Provides for revision to the PRECAUTIONS section of the package insert. The following paragraph has been added:

Information to Patients: Persons who are on immunosuppressant doses of corticosteroids should be warning to avoid exposure to chickenpox or measles. Patients should also be advised that if they are exposed, medical advice should be sought without delay.