

January 23, 2006

Dear Healthcare Provider,

Astellas Pharma US, Inc. would like to inform you of important labeling changes for the class of topical calcineurin inhibitors (TCIs), including Protopic® (tacrolimus) Ointment. Protopic Ointment, both 0.03% and 0.1% for adults and only 0.03% for children aged 2 to 15 years, is indicated as *second-line therapy* for the short-term and non-continuous chronic treatment of moderate to severe atopic dermatitis in non-immunocompromised adults and children who have failed to respond adequately to other topical prescription treatments for atopic dermatitis or when those treatments are not advisable. **Protopic Ointment is not indicated for children younger than 2 years of age.**

The important labeling changes include the addition of a warning section with a boxed warning. Furthermore, a Medication Guide has been added to provide instructions and information to patients regarding the proper use of this medication.

The new WARNINGS section follows:

<p style="text-align: center;">WARNING</p> <p>Long-term Safety of Topical Calcineurin Inhibitors Has Not Been Established</p> <p>Although a causal relationship has not been established, rare cases of malignancy (e.g., skin and lymphoma) have been reported in patients treated with topical calcineurin inhibitors, including PROTOPIC Ointment.</p> <p>Therefore:</p> <ul style="list-style-type: none">• Continuous long-term use of topical calcineurin inhibitors, including PROTOPIC Ointment, in any age group should be avoided, and application limited to areas of involvement with atopic dermatitis.• PROTOPIC Ointment is not indicated for use in children less than 2 years of age. Only 0.03% PROTOPIC Ointment is indicated for use in children 2-15 years of age.
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Prolonged systemic use of calcineurin inhibitors for sustained immunosuppression in animal studies and transplant patients following systemic administration has been associated with an increased risk of infections, lymphomas, and skin malignancies. These risks are associated with the intensity and duration of immunosuppression.

Based on the information above and the mechanism of action, there is a concern about potential risk with the use of topical calcineurin inhibitors, including PROTOPIC Ointment. While a causal relationship has not been established, rare cases of skin malignancy and lymphoma have been reported in patients treated with topical calcineurin inhibitors, including PROTOPIC Ointment. Therefore:

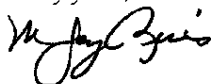
- PROTOPIC Ointment should not be used in immunocompromised adults and children.
- If signs and symptoms of atopic dermatitis do not improve within 6 weeks, patients should be re-examined by their healthcare provider and their diagnosis be confirmed (see PRECAUTIONS: General).
- The safety of PROTOPIC Ointment has not been established beyond one year of non-continuous use.

Modifications have also been made to other sections of the labeling for Protopic Ointment. We recommend you carefully review the revised labeling in its entirety. You will find them incorporated in the attached Prescribing Information and Medication Guide.

Astellas Pharma US, Inc. is committed to providing you with the most current information for Protopic Ointment so that you and your patients can make informed treatment decisions. It is important that you forward any adverse event information associated with the use of Protopic Ointment to Astellas Pharma US, Inc. at 1-800-727-7003. You can also report the information directly to the FDA via the MedWatch system at 1-800-332-1088, by fax at 1-800-332-0178, or the Internet at www.fda.gov/medwatch.

If you have additional questions, please contact us at 1-800-727-7003 or e-mail us at medicalinformation@us.astellas.com.

Sincerely yours,



M. Joyce Rico, MD
Vice President, Medical Sciences

See full Prescribing Information and Medication Guide attached.

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