



**TRANSMITTED BY FACSIMILE**

Mr. Donald E. Baker  
Senior Director, Regulatory Affairs  
Fujisawa Healthcare, Inc.  
3 Parkway Center North  
Deerfield, IL 60015

**RE: NDA #50-777**  
Protopic (tacrolimus) Ointment 0.03%, 0.1%  
MACMIS ID# 10491

Dear Mr. Baker:

This letter objects to Fujisawa Healthcare, Inc. (Fujisawa) dissemination of violative promotional materials for Protopic (tacrolimus) Ointment 0.03%, 0.1%. As part of its monitoring program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of a direct-to-consumer (DTC) television (TV) broadcast advertisement and DTC print advertisements for Protopic that are false or misleading in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. The DTC television broadcast advertisement ("Awakenings," 60 second spot, PCA88103) and DTC print advertisements (Adult - PT064, Caregiver - PT065), submitted under cover of Form FDA 2253, are violative for the reasons described below.

**Overstatement of Efficacy**

The DTC television broadcast advertisement and DTC print advertisements for Protopic Ointment feature models with smooth, even-colored skin, completely clear of lesions. These visual presentations imply that all patients treated with Protopic Ointment will experience 100% improvement (complete clearing) of their atopic dermatitis. However, this outcome is not representative of the typical response that a patient can expect with Protopic therapy. Specifically, the approved product labeling (PI) for Protopic Ointment includes data from clinical trials in which only 10% of adult patients treated with Protopic Ointment 0.03% or 0.1% experienced 100% improvement of atopic dermatitis. Therefore, the TV and print advertisements are misleading because they overstate the efficacy of Protopic Ointment.

**Broadening of Indication**

The TV advertisement begins by stating:

- "Millions of Americans suffer from eczema also known as atopic dermatitis. Now there's Protopic Ointment a steroid-free prescription treatment that soothes eczema anywhere on your body."

These claims suggest that Protopic Ointment is indicated as first line therapy to treat all types of atopic dermatitis. However, the PI states, "PROTOPIC Ointment, both 0.03% and 0.1% for adults, and only

0.03% for children aged 2 to 15 years, is indicated for short-term and intermittent long-term therapy in the treatment of patients with moderate to severe atopic dermatitis in whom the use of alternative, conventional therapies are deemed inadvisable because of potential risks, or in the treatment of patients who are not adequately responsive to or are intolerant of alternative, conventional therapies.” Therefore, the TV advertisement is misleading because it suggests that Protopic Ointment is approved for use in a broader patient population and a broader range of conditions than what has been demonstrated by substantial evidence.

We note that three frames later, the advertisement states, “Protopic Ointment can ease moderate to severe eczema for people who do not respond well or who may have side effects with other treatments. There is no cure for eczema, but Protopic can help manage it.” However, this disclosure is not sufficient to correct the initial misleading message that Protopic Ointment is indicated as first line therapy to treat all types of atopic dermatitis. Furthermore, this disclosure inadequately communicates Protopic’s approved indication is **limited** to the specific patient population mentioned (emphasis added).

Similarly, the DTC print advertisements are misleading because they do not adequately communicate the complete product indication. For example, the Adult and Caregiver DTC print advertisements present the following claims:

#### Caregiver Ad

- “Lucky kid. She’s the first generation to grow up with eczema *and* Protopic. It’s a steroid-free prescription medication to treat eczema in children two years and older.”

#### Adult Ad

- “Welcome touch. Soothe your eczema. Introducing Protopic, a prescription medicine for the treatment of your eczema. It can be used on the face, neck, and hands. Steroid-free. Clinically proven.”

The prominent presentation of these claims suggests that Protopic Ointment is indicated as first line therapy to treat all types of atopic dermatitis. We note that in small print, toward the bottom of the advertisement, you state “Protopic Ointment can be used for patients with moderate to severe eczema who do not respond well to or who may have side effects with traditional treatments.” However, as stated above, this disclosure is not sufficient to correct the prominent misleading message that Protopic Ointment is indicated as first line therapy to treat all types of atopic dermatitis, nor does it adequately communicate the approved indication. Furthermore, the claim that the child is “lucky” because “she’s the first generation to grow up with eczema *and* Protopic” is misleading because it implies that Protopic Ointment is superior to other products approved for atopic dermatitis, when such has not been demonstrated by substantial evidence. Moreover, this claim contributes to the misleading message that Protopic Ointment is indicated as first line therapy to treat all types of atopic dermatitis.

#### Minimization of Risk

In one segment of the TV advertisement, a female model moves her hand over her shoulder and the voiceover claims, “... soothes eczema anywhere on your body” and the supers “eczema” and “soothed” move across the screen. Similarly, the adult print advertisement presents the claim “soothe your eczema.” These claims of soothing eczema are misleading because they minimize the risk of

application site reactions that can occur with Protopic therapy. Specifically, the PI states, "The use of PROTOPIC Ointment may cause local symptoms such as skin burning (burning sensation, stinging, soreness) or pruritis." The PI also describes adult studies in which there was a 47% incidence of skin burning and 25% incidence of pruritis in patients treated with Protopic Ointment 0.1%.

**Requested Action**

Fujisawa should immediately discontinue these and all other promotional materials and activities for Protopic that contain the same or similar claims or presentations. We request that Fujisawa respond, in writing, with its intent to comply with the above. This response should list similarly violative materials with a description of the method for discontinuation and the discontinuation date. As discussed in our November 9, 2001, phone conversation DDMAC should receive your written response no later than November 30, 2001.

If you have any questions, please contact the undersigned by facsimile at 301-594-6771, or by written communication at the Division of Drug Marketing, Advertising and Communications, HFD-42, Room 17B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID# 10491 in addition to the NDA number.

Sincerely,

*{See appended electronic signature page}*

Rebecca Williams, Pharm.D.  
Regulatory Review Officer  
Division of Drug Marketing,  
Advertising, and Communications

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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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Rebecca Williams  
11/14/01 12:04:01 PM

# lucky kid

She's the first generation to grow up with eczema and Protopic.<sup>®</sup> It's a steroid-free prescription medication to treat eczema in children two years and older. It can even be used on the face, neck, and hands.

**Protopic**<sup>®</sup>  
(tacrolimus) Ointment  
0.03%



To learn more about Protopic,  
ask your doctor or call **1-888-436-8670**

*Protopic Ointment can be used for patients with moderate to severe eczema who do not respond well to or who may have side effects with traditional treatments. It can be used for short or repeated periods of treatment. Protopic is prescribed for adults in concentrations of 0.03% and 0.1% and for children, aged 2 to 15 years, in the 0.03% concentration only.*

*The most common side effects with Protopic were usually limited to stinging, burning, and itching upon application. The more severe and widespread the eczema, the greater the likelihood of these sensations. Skin irritations were short lasting, occurred early in treatment, and rarely required discontinuation of treatment. Avoid direct sunlight, tanning salons, and phototherapy. Wear loose-fitting clothing to protect skin from the sun. Do not cover the skin being treated with bandages, dressings, or wraps.*

*Only your healthcare professional can weigh the risks and benefits of a prescription medication and decide if this medication is the right one for you.*

*Please see important product information on the next page.*

**Fujisawa Healthcare, Inc.**

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## PATIENT INFORMATION ABOUT

# Protopic<sup>®</sup>

## (tacrolimus)

### Ointment

Read this important information before you start using PROTOPIC [pro-TOP-ik] Ointment and each time you refill your prescription. There may be new information. This summary is not meant to take the place of your doctor's advice.

#### What Is PROTOPIC?

PROTOPIC Ointment is a prescription medicine that is used to treat eczema (atopic dermatitis). It is for adults and children age 2 years and older. You can use PROTOPIC for short or intermittent long periods of treatment. Intermittent means starting and stopping repeatedly, as directed by your doctor. You can use it on all affected areas of your skin, including your face and neck.

#### Who should not use PROTOPIC?

##### Do not use PROTOPIC if you are

- breastfeeding
- allergic to PROTOPIC Ointment or any of its ingredients. The active ingredient is tacrolimus. Ask your doctor or pharmacist about the inactive ingredients.

Before you start using PROTOPIC, tell your doctor if you are:

- using any other prescription medicines, non-prescription (over-the-counter) medicines, or supplements
- receiving any form of light therapy (phototherapy, UVA or UVB) on your skin
- using any other type of skin product
- pregnant or planning to become pregnant

#### How Do I Use PROTOPIC?

Use PROTOPIC only to treat eczema that has been diagnosed by a doctor.

- Wash your hands before using PROTOPIC.
- Apply a thin layer of PROTOPIC to all skin areas that your doctor has diagnosed as eczema. Try to cover the affected areas completely. Most people find that a pea-sized amount squeezed from the tube covers an area about the size of a two-inch circle (approximately the size of a silver dollar).
- Apply the ointment twice a day, about 12 hours apart.
- Before applying PROTOPIC Ointment after a bath or shower, be sure your skin is completely dry.
- Do not cover the skin being treated with bandages, dressings or wraps. Unless otherwise instructed by your doctor, do not apply another type of skin product on top of PROTOPIC Ointment. However, you can wear normal clothing.
- Do not bathe, shower or swim right after applying PROTOPIC. This could wash off the ointment.
- If you are a caregiver applying PROTOPIC Ointment to a patient, or if you are a patient who is not treating your hands, wash your

PROTOPIC. This should remove any ointment left on the hands.

- Use PROTOPIC only on your skin. Do not swallow PROTOPIC.

Because 2 strengths of PROTOPIC are available for adult patients, your doctor will decide what strength of PROTOPIC Ointment is best for you.

Many people notice that their skin starts to improve after the first few weeks of treatment. Even though your skin looks and feels better, it is important to keep using PROTOPIC as instructed by your doctor.

If you do not notice an improvement in your eczema or if your eczema gets worse within the first few weeks of treatment, tell your doctor.

#### What Should I Avoid While Using PROTOPIC?

- Avoid sunlight and sun lamps, tanning beds, and treatment with UVA or UVB light. If you need to be outdoors after applying PROTOPIC, wear loose fitting clothing that protects the treated area from the sun. In addition, ask your doctor what other type of protection from the sun you should use.
- Check with your doctor or pharmacist before you
  - start taking any new medicines while using PROTOPIC.
  - Start using any other ointment, lotions, or creams on your skin.

#### What Are The Possible Side Effects of PROTOPIC?

The most common side effects of PROTOPIC are stinging, soreness, a burning feeling, or itching of the skin treated with PROTOPIC. These side effects are usually mild to moderate, are most common during the first few days of treatment, and typically lessen if your skin heals.

Less common side effects include acne, swollen or infected hair follicles, headache, increased sensitivity of the skin to hot or cold temperatures, or flu-like symptoms [common cold and congestion (stuffy nose)]. Some people may get skin tingling, upset stomach, herpes zoster (chicken pox or shingles), or muscle pain. While you are using PROTOPIC, drinking alcohol may cause the skin or face to become flushed or red and feel hot. Call your doctor if side effects continue or become a problem.

#### How Should I Store PROTOPIC?

Store PROTOPIC at room temperature (59° to 86°F). For instance, never leave PROTOPIC in your car in cold or hot weather. Make sure the cap on the tube is tightly closed. Keep PROTOPIC out of the reach of children.

#### General Advice about Prescription Medicines

Do not use PROTOPIC for a condition for which it was not prescribed. If you have any concerns about PROTOPIC, ask your doctor. Your doctor or pharmacist can give you information about PROTOPIC that was written for health care professionals. For more information, you can also visit the Fujisawa Internet site at [www.fujisawa.com](http://www.fujisawa.com) or call the PROTOPIC Help Line at 1-800-727-7003.

Fujisawa Healthcare, Inc.  
Deerfield, IL 60015  
[www.fujisawa.com](http://www.fujisawa.com)

45670  
Issued: December 2000

# welcome touch

Soothe your eczema. Introducing Protopic<sup>®</sup>,  
a prescription medicine for the treatment of your eczema.

It can even be used on the face, neck, and hands.

Steroid free. Clinically proven.

To learn more about Protopic,  
ask your doctor or call **1-888-436-8664**

**Protopic<sup>®</sup>**  
(tacrolimus) Ointment  
0.03% 0.1%



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*Only your healthcare professional can weigh the risks and benefits of a prescription medication and decide if this medication is the right one for you. Please see important product information on the next page.*

**Fujisawa Healthcare, Inc.**

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PATIENT INFORMATION ABOUT

# Protopic® (tacrolimus) Ointment

Read this important information before you start using PROTOPIC (pro-TOP-ik) Ointment and each time you refill your prescription. There may be new information. This summary is not meant to take the place of your doctor's advice.

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- breastfeeding
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Fujisawa Healthcare, Inc.  
Deerfield, IL 60015  
[www.fujisawa.com](http://www.fujisawa.com)

45670  
Issued: December 2000

**Audio:**



**Video:**

Cut to close-up of a woman's neck as she lifts her hair above her head.

**Audio:**



**Video:**

She turns her head as her hand continues across her shoulders.

**Audio:**



**Video:**

Cut to extreme close-up of her face.

**Narrator:**

Millions of Americans suffer from eczema...

**Audio:**



**Video:**

She reaches into water and brings it toward her face.

**Narrator:**

...also known as atopic dermatitis.

**Audio:**

**Narrator:**

Now there's Protopic  
Ointment...

5



**Video:**

Cut to a close-up of the  
woman's mouth. A drop falls  
from the corner of her mouth.

**Audio:**

**Narrator:**

...a steroid-free prescription  
treatment...

6



**Video:**

The close-up of the woman's  
mouth fades to white.

**CG:**

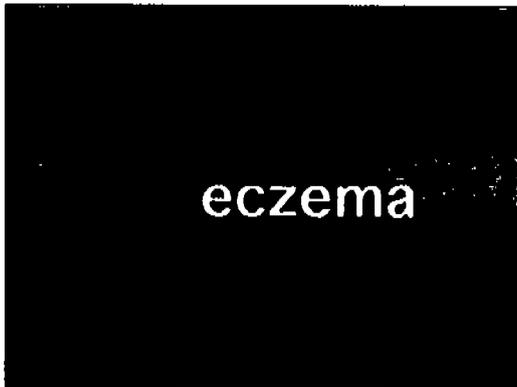
Protopic logo with generic  
appears.

**Audio:**

**Narrator:**

...that soothes eczema  
anywhere on your body.

7



**Video:**

Cut to the woman's wet  
shoulder

**CG:**

eczema appears, shrinks, and  
starts to fade.

**Audio:**

8



**Video:**

The camera continues across  
and down her back.

**CG:**

soothed builds to full strength.

**Audio:**

9



**Video:**

The camera pans across the woman's shoulder.

**CG:**

Protopic appears and starts to move to the lower right corner.

steroid free moves from right to left over Protopic.

**Audio:**

10



**Video:**

Her hand follows the flow of the water down her stomach.

**CG:**

1-866- builds in front of Protopic and moves toward the lower right corner.

**Audio:**

11



**Video:**

The camera continues to circle around and down her body.

**CG:**

1-866-Protopic

**Narrator:**

Protopic Ointment can ease...

**Audio:**

12



**Video:**

The camera continues to circle around and down her body. Her hand follows the water down her thigh.

**CG:**

1-866-Protopic

**Narrator:**

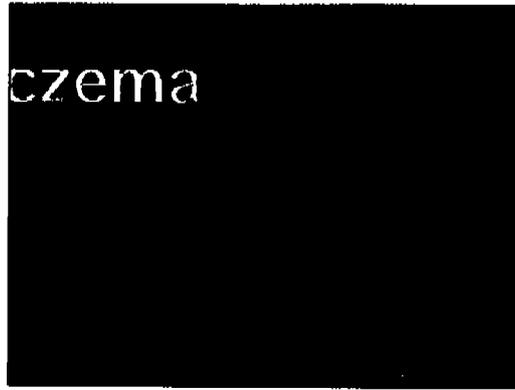
...moderate to severe eczema for people...

**Audio:**

**Narrator:**

...who do not respond well to or who may have side effects with other treatments. There is no cure for eczema, but Protopic can help manage it.

13



**Video:**

The camera continues to follow her hand down behind her knee.

**CG:**

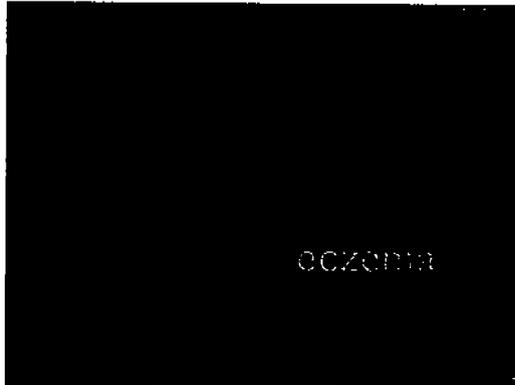
**eczema** appears, shrinks, and starts to fade.

**Audio:**

**Narrator:**

Many people see improvements after the first few weeks of treatment.

14



**Video:**

The camera revolves to the back of her calf. Her hands follow the flow of water down her lower leg to her ankle.

**CG:**

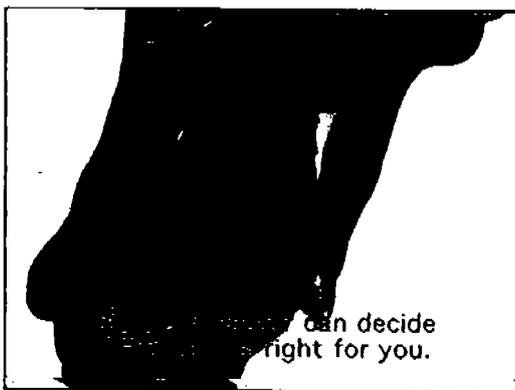
**eased** builds to full strength.

**Audio:**

**Narrator:**

The most common side effects of Protopic were usually...

15



**Video:**

Her hand continues to run over her foot as water cascades off her toes. Her hand runs over her heel and disappears out of frame.

**CG:**

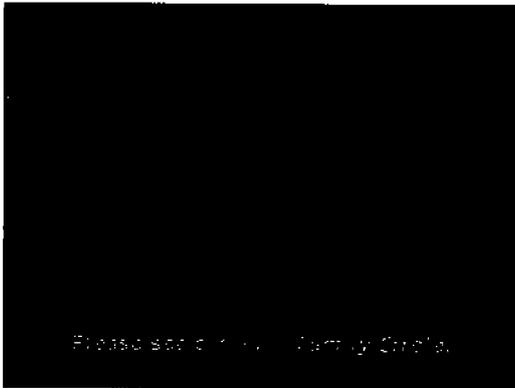
Only your doctor can decide if Protopic is right for you.

**Audio:**

**Narrator:**

...limited to stinging, burning, and itching.

16



**Video:**

Cut to close-up of the woman's profile.

**CG:**

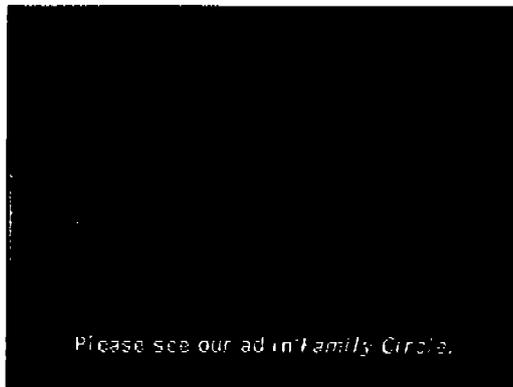
Please see our ad in Family Circle.

**Audio:**

**Narrator:**

These were usually mild to moderate...

17



**Video:**

The camera pans to the woman's face. She begins to smile.

**CG:**

Please see our ad in *Family Circle*.

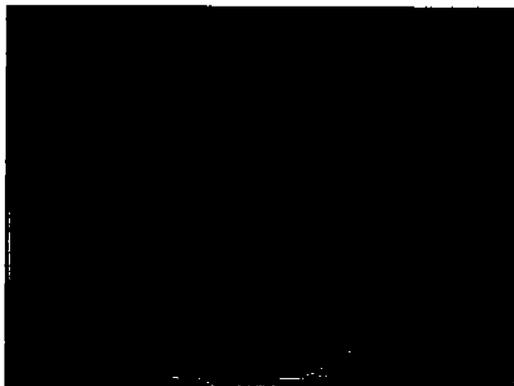
Publication name will change based on the month that the TV spot is airing.

**Audio:**

**Narrator:**

...occurred early in treatment...

18



**Video:**

**Audio:**

**Narrator:**

...and typically lessened as the skin healed.

19



**Video:**

**Audio:**

**Narrator:**

While using Protopic, protect your skin from sunlight and avoid sun lamps.

20



**Video:**

A man slowly embraces the woman in the towel.

**Audio:**

21



**Video:**

The man kisses the woman's neck.

**Audio:**

**Narrator:**

To learn more about Protopic, ask your doctor.

22



**Video:**

The woman leans into the man's shoulder.

**CG:**

To learn more, ask your doctor or call toll free 1-866-Protopic www.protopic.com

**Audio:**

**Narrator:**

To receive the free video, *Inside Eczema* call toll free 1-866-Protopic.

23



**Video:**

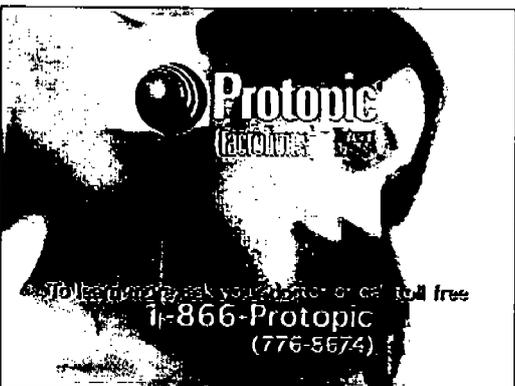
Pan over product shot of video.

**CG:**

To learn more, ask your doctor or call toll free 1-866-Protopic www.protopic.com

**Audio:**

24



**Video:**

Cut back to the man embracing the woman.

**CG:**

Protopic logo with generic. To learn more, ask your doctor or call toll free 1-866-Protopic (776-8674)