Patient package insert according to Pharmacists' Regulations (Preparations) – 1986

This medicine can be sold with a physician's prescription only

Protopic® 0.03% Ointment

Composition:
1 gram of ointment contains:
Tacrolimus (as monohydrate) 0.3 mg

Inactive ingredients and allergens in the medicine – see section 6 "Additional information" and in section 2 "Important information about some of the ingredients of this medicine"**.**
Read this entire leaflet carefully before using this medicine. This leaflet contains concise information about the medicine. If you have any further questions, ask the doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if you think that their medical condition is the same as yours.

This medicine is not intended for use in children under 2 years of age.

1. What is the medicine intended for?

The treatment of moderate to severe skin asthma (atopic dermatitis) in adults or children 2 years of age and older who are not adequately responsive to or are intolerant of conventional therapies.

For the prevention of flaring of moderate to severe skin asthma (atopic dermatitis) and prolongation of the flare-free remission periods in patients suffering from a high frequency of flaring of the disease (4 or more times per year), who were responsive to primary treatment of tacrolimus ointment twice a day for 6 weeks (sores cleared, almost cleared or there was moderate relief).

Therapeutic group:
Immunomodulating agent - a substance that alters the abnormal immune system response and relieves itching and skin inflammation.

2. Before using the medicine

Do not use the medicine if:
You are hypersensitive (allergic) to the active ingredient (tacrolimus), or to any of the other ingredients this medicine contains (see section 6) or to antibiotics from the macrolide group (e.g. azithromycin, clarithromycin, erythromycin).

Special warnings regarding the use of the medicine
Before the treatment tell the doctor if:
- You suffer from impaired liver function.
- You suffer from malignant skin tumors.
- You suffer from a weak immune system.
- You suffer from an inherited skin disease such as Netherton's syndrome or lamellar ichthyosis (extensive scaling of the skin as a result of thickening of the outer layer of the skin).
- You suffer from erythroderma (inflamed, red and scaly skin).
- You suffer from Graft Versus Host Disease (an immune reaction of the skin – a common complication in patients who have undergone a bone marrow transplant).
- You suffer from swollen lymph nodes at initiation of treatment. If the lymph nodes become swollen during the treatment, consult the doctor.
- You suffer from infected lesions. Do not apply the ointment to infected lesions.
- You notice any change in the appearance of your skin.

Additional warnings:
Protopic 0.03% is not approved for use in children under two years of age. Therefore, it should not be used in this age group. Consult a doctor.
The effect of **Protopic** on the developing immune system in children, especially the young, is not known.
The safety of using this medicine for a prolonged period is not known. A very small number of patients using **Protopic** developed tumors (for example skin or lymph tumors), however a link to **Protopic** treatment has not been proven.
Avoid prolonged exposure to the sun or artificial sunlight such as tanning beds. If you spend time outdoors after applying **Protopic,** be sure to have proper protection (long and loose fitting clothing, sunscreens). In addition, consult your doctor regarding sun protection measures.
If you are being treated with **Protopic** and are due to undergo light therapy, inform your doctor as simultaneous treatment with **Protopic** and light therapy is not recommended.
If the doctor instructs you to continue treatment twice a week after atopic dermatitis has cleared, continue medical follow-up at a frequency of at least once a year even if there is no apparent change in your condition.
In children, after completing 12 months of prophylactic treatment with the medicine, discontinue treatment with the ointment and assess whether continued treatment is necessary.

Drug interactions
If you are taking or have recently taken any other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Medicines not to be used together with Protopic
- After applying **Protopic**, do not use moisturising creams and lotions for two hours.
- There is no information regarding the use of other topical skin preparations or oral corticosteroids (e.g. cortisone) or medicines which affect the immune system while using **Protopic.**

Use of Protopic with alcohol
Drinking wines or alcoholic beverages during treatment with the medicine may cause flushing, redness or a sensation of heat on the skin or face.

Pregnancy and breastfeeding
Do not use the medicine during pregnancy and breastfeeding.
Consult the doctor or pharmacist before taking any medicine.

Use in children
This medicine is not approved for use in children under two years of age.

Driving and using machines
No impairment of the ability to drive or operate machines is expected when using this medicine.

Important information about some of the ingredients of this medicine
The medicine contains butyl hydroxytoluene (E321) which may cause local skin reactions (e.g. contact dermatitis), or eye and mucus tissue irritation.

3. How to use the medicine?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure.
The dosage is in accordance with the doctor's instructions only.
Use the medicine at set times as determined by the attending doctor.
The dosage and method of administration will be determined by the doctor only. The usual method of administration is as follows:

General
- Apply a thin layer of **Protopic** on the affected areas of the skin.
- **Protopic** may be applied on most parts of the body, including the face and neck, in the creases of the elbows and knees.
- Do not apply the ointment inside the nose, mouth or eyes. If the ointment comes into contact with these areas it should be thoroughly wiped off and/or rinsed off with water.
- Do not cover or wrap the skin being treated with bandages or wraps.
- Wash your hands after applying unless your hands are also being treated.
- Before applying **Protopic** after a shower, be sure your skin is completely dry.

Children (two years of age and older)
Apply **Protopic** 0.03% twice a day, morning and evening, for a period of up to three weeks. Afterwards, apply once a day to on each affected region on the skin until the eczema has gone away.
Adults (16 years of age and older)
There are two strengths of **Protopic** (**Protopic** 0.03% and **Protopic** 0.1% ointment) and they are available for use for adults 16 years of age and older. The doctor will decide which strength is best for you.
Usually, treatment is started with **Protopic** 0.1% twice a day, once in the morning and once in the evening, until the eczema has cleared. Depending on the response of the eczema to the treatment, the doctor will decide if the frequency of application can be reduced or if you should switch to the lower strength, namely **Protopic** 0.03%.

Treat each affected region of the skin until the eczema has gone away. Improvement can be seen within one week of treatment. If there is no improvement after two weeks, consult the doctor about other treatments.

The doctor may instruct you to continue applying **Protopic** twice weekly after atopic dermatitis has fully or almost cleared (**Protopic** 0.03% is appropriate for children and adults and **Protopic** 0.1% for adults). Apply **Protopic** once a day, twice weekly, to areas of the body affected by atopic dermatitis. Be sure to leave a 2-3 day interval without using **Protopic**, between applications.
If the symptoms reappear use **Protopic** twice daily, as detailed above, and refer to the doctor to reassess the treatment.

Do not exceed the recommended dose.

Do not swallow! The medicine is intended for external use only.

In case of accidental swallowing or if a child has accidentally swallowed the medicine, immediately refer to a doctor or proceed to a hospital emergency room and bring the package of the medicine. Do not try to induce vomiting.

If you forgot to apply the ointment at the scheduled time continue treatment as usual, but do not apply a double dose as compensation.

Continue with the treatment as recommended by the doctor, even if there is an improvement in your health. Do not stop treatment without consulting the doctor or pharmacist.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have further questions on the use of this medicine, consult the doctor or pharmacist.

4. Side effects

Like any medicine, the use of **Protopic** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Very common side effects (effects that appear in more than 1 in 10 users)
- burning sensation and itching

These effects are usually mild to moderate and pass within one week of initiating **Protopic** treatment.

Common side effects (effects that appear in 1-10 out of 100 users)
- redness
- feeling of warmth
- pain
- increased skin sensitivity (especially to hot and cold)
- skin tingling
- rash
- local skin infection without a clear cause including but not limited to: inflamed or infected hair follicles, cold sores, viral infections caused by the herpes virus
- facial flushing or skin irritation after drinking alcohol

Uncommon side effects (effects that appear in 1-10 out of 1,000 users)
- acne

Following twice weekly application, development of infections of the application site has been reported in adults and children. Impetigo (a localized bacterial infection that causes blisters or sores on the skin) has been reported in children.
There are reports of facial skin inflammation (rosacea), rosacea-like dermatitis, flat brown spots on the skin (lentigo), oedema at the ointment application site and eye infections caused by the herpes simplex virus.

A very small number of patients who have used **Protopic** have reported malignant tumors (for example lymphoma, including skin lymphoma or other skin tumors). A link between them and **Protopic** treatment has not been proven based on the data available so far.

If a side effect appears, if one of the side effects worsens or if you suffer from a side effect which is not mentioned in this leaflet, consult the doctor.

Side effects can be reported to the Ministry of Health via the link "דיווח על תופעות לוואי עקב טיפול תרופתי" that can be found on the home page of the Ministry of Health website (www.health.gov.il) directing to the online form of adverse events reporting or via the following link: https://sideeffects.health.gov.il

5. How to store the medicine?

Avoid poisoning! This medicine and any other medicine must be stored in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (EXP) stated on the package. The expiry date refers to the last day of that month.
Store below 25°C.
The product can be used for up to 3 months after first opening of the tube.

6. Additional information

In addition to the active ingredient, this medicine also contains:
White soft paraffin, liquid paraffin, propylene carbonate, white beeswax, hard paraffin, butylhydroxytoluene (E321), all-rac-α-tocopherol.

What the medicine looks like and what the package contains:
Tubes of 30 or 60 grams that contain white to light yellow ointment.
Not all package sizes may be marketed.

Manufacturer and address:
LEO Pharma A/S, Ballerup, Denmark.

Revised in June 2021 according to MOH guidelines.

Drug registration number at the national drug registry of the Ministry of Health: 127.71.30667

Protopic Ointment 0.03 PIL PB1021-10

Registration holder: Dexcel® Ltd.
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