Patient package insert according to Pharmacists' Regulations (Preparations) – 1986
This medicine can be sold with a physician's prescription only

Protopic® 0.03% ointment

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 the medicine".

Read this entire leaflet carefully before using the 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 for you. Do not pass it on to others. It may harm them, even if you think that their medical condition is the same as yours.

1. What is the medicine intended for?

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 a macrolide antibiotic (e.g. azithromycin, clarithromycin, erythromycin).

Special warnings regarding the use of the medicine

Before the treatment with Protopic, tell the doctor if:

- You suffer from **liver failure**.
- You suffer from **malignant skin tumours** or if you suffer from a **weakened immune system** (immuno-compromised) whatever the cause.
- You suffer from an **inherited skin barrier disease**, such as Netherton's syndrome, or lamellar ichthyosis (extensive scaling of the skin due to thickening of the outer layer of the skin) or if you suffer from **erythroderma** (inflamed, red and scaly skin).
- You suffer from a cutaneous 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 with **Protopic**, consult the doctor.

- You suffer from **infected lesions**. Do not apply the ointment to infected lesions.
- You notice a **change in the appearance of your skin**.

Additional warnings:
- Based on the results of long-term studies and experience, a link between **Protopic** ointment treatment and the development of malignancies has not been confirmed, but definitive conclusions cannot be drawn.
- 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, sunscreen). In addition, consult the doctor regarding additional sun protection measures.
- If you are being treated with **Protopic** and are due to undergo light therapy, inform the doctor, as simultaneous treatment with Protopic and light therapy is not recommended.
- If the doctor instructs you to continue treatment twice a week to keep the atopic dermatitis cleared, continue medical follow-up at a frequency of at least every 12 months even if there is no apparent change in your condition. In children, after completing 12 months of maintenance treatment with the medicine, discontinue treatment with the ointment and assess whether it is necessary to continue treatment.
- It is recommended to use **Protopic** ointment at the lowest possible dosage and frequency, and for the shortest possible duration necessary. This decision should be based on your doctor's assessment of how your eczema responds to **Protopic** ointment.

Children
- **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 treatment with **Protopic** on the developing immune system in children, especially the young, is not known.

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

- Moisturising creams and lotions can be used during treatment with **Protopic**, but these products should not be used within two hours of applying **Protopic**.

- There is no information regarding the use of **Protopic** while using other skin preparations or while taking oral corticosteroids (e.g. cortisone) or medicines which affect the immune system.

Use of Protopic and alcohol consumption
Drinking alcohol during treatment with the medicine may cause the skin or face to become flushed or red and feel hot.

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you may be pregnant or are planning to become pregnant, consult a doctor or pharmacist before using this medicine.

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 the medicine

The medicine contains butylhydroxytoluene (E321) which may cause local skin reactions (e.g. contact dermatitis) or irritation to the eye and mucus membranes.

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 about the dosage and the manner of treatment with the medicine.
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.
- Avoid applying the ointment inside the nose, mouth or eyes. If the ointment contacts any of 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 the application, 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 goes 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 in adults (16 years of age and older). The doctor will decide which strength is best for you.

Usually, **Protopic 0.1%** treatment starts twice a day, morning and 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 all affected regions of the skin until the eczema goes away. Improvement can be observed 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 cleared or almost cleared (**Protopic 0.03%** is appropriate for children and adults and **Protopic 0.1%** for adults). Apply **Protopic** once a day twice a week 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 review 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 to compensate.

Continue with the treatment as recommended by the doctor, even if there is an improvement in your health. Do not stop treatment with the medicine 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 occur in more than 1 in 10 users):
- burning sensation and itching

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

Common side effects (effects that occur 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 (regardless the 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 occur in 1-10 out of 1,000 users):
- acne

Following twice-weekly treatment, application site infections have been reported in adults and children. Impetigo (a superficial bacterial infection that causes blisters or sores on the skin) has been reported in children.
There are reports of Rosacea (facial redness), rosacea-like dermatitis, flat brown spots on the skin (Lentigo), oedema at the application site and herpes eye infections.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect 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" found on the homepage of the Ministry of Health website (www.health.gov.il) directing to the online form for reporting side effects or via the 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.
- **Storage conditions**: Store below 25°C.
- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, the 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 containing white to light yellow ointment.
Approved package sizes: 30 and 60 grams per package.
Not all package sizes may be marketed.

Manufacturer name and address:

LEO Pharma A/S, Ballerup, Denmark.

Revised in September 2023 according to MOH guidelines.

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

127-71-30667-00

Registration holder: Dexcel LTD
1 Dexcel St., Or Akiva 3060000, Israel