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

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

PICATO 0.05%, Gel for external use for the skin of the body and extremities

The gel contains the active substance:
Ingenol mebutate 500 microgram/gram (0.05%)

For list of excipients - please see section 6 "Additional information".

Read this entire leaflet carefully before you start taking this medicine. This leaflet contains concise information about the medicine. If you have any further questions, refer to the physician or pharmacist.

This medicine has been prescribed for your illness. Do not pass it on to others. It may harm them, even if you think that their illness is similar.

1. What is the medicine used for?

Picato is intended for topical treatment (external on the skin) of actinic keratosis in adults, also called solar keratosis. Actinic keratosis are rough areas of skin caused by too much exposure to the sun during lifetime. Picato 0.05% is intended for the treatment of actinic keratosis of the skin on the body, arms, hands and legs.

Therapeutic group: antibiotics and chemotherapeutic agents for dermatological use, other chemotherapeutic agents.

2. Before using the medicine

Do not use the medicine if:

- You are hypersensitive (allergic) to the active ingredient (ingenol mebutate) or to any of the other ingredients of this medicine (see section 6 "Additional information").
- Do not use in children under 18 years of age.

Special warnings regarding the use of this medicine

Consult a doctor or pharmacist before using Picato.

- Do not get Picato in your eyes. Wash your hands thoroughly after you have applied the gel. Wash your hands again if you happen to touch the area where you applied the gel. Take care not to transfer gel from the treatment area into your eyes. In the event of accidental contact, remove the gel by rinsing with plenty of water and seek medical assistance as soon as possible.
- Do not swallow this medicine. Drink plenty of water if you accidentally swallow this medicine and seek medical assistance.
- Make sure that your skin has healed from any other treatment or surgery before using Picato. Do not apply Picato on open-wounds or damaged skin.
- Do not apply this medicine internally, to the area near the eyes, to the inside of the nostrils, the inside of the ear or on the lips.
- Avoid sunlight exposure as much as possible (including sunlamps and tanning beds).
- Be vigilant for any new scaly red patches, open sores, elevated or warty growths within the treatment area. Should any occur, talk to your doctor immediately.
- This medicine is intended to treat one area of 25 cm^2 for two days.
- Do not apply more gel than the doctor has advised.
- You should expect to get local skin reactions, such as reddening and swelling, after treatment with this medicine (see section 4 "side effects"). Refer to your physician if these local skin reactions get severe.

If you are taking, have recently taken or planning to take any other medicines, including non-prescription drugs and nutrition supplements, tell the doctor or pharmacist.

Tell the doctor before starting the treatment, if you have previously used Picato or other similar medicines.

Pregnancy and breastfeeding

Consult the doctor before using this medicine if you are pregnant or breastfeeding, if you think you may be pregnant or are planning a pregnancy. You should avoid the use of Picato if you are pregnant.
If you are breastfeeding, avoid physical contact between the infant and the treated area for 6 hours after application of this medicine.

Children and adolescents

Actinic keratosis does not occur in children, and this medicine must not be used in children and adolescents under 18 years of age (see section 2 "Do not use the medicine if").

Driving and use of machinery

This medicine does not have any effect on your ability to drive or to use machines.

3. How to use this medicine?

Always use according to doctor's instructions. Check with the doctor or pharmacist if you are not sure.

If you have been prescribed two different strengths for treatment of two different areas, you should make sure that you use the prescribed strength on the correct area. Do not apply Picato 0.05% on the face or scalp as this could lead to intense local skin responses.

The dosage and administration will be determined by the doctor only.
The usual recommended dosage is:

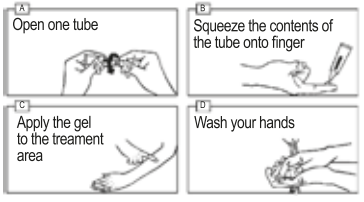
- For the treatment of actinic keratosis on the body, arms, hands and legs is one tube of Picato 0.05% (containing 235 micrograms of ingenol mebutate) once a day for 2 days in a row.

Do not exceed the recommended dose.

- For external use only.

Instructions for use:

- Open a new tube each time you use Picato. Remove the cap from the tube just before use.
- Squeeze the gel from the tube onto a fingertip.
- Apply the content of one tube to one area of 25 cm^2 (e.g. 5 cm x 5 cm).
- Gently rub the gel onto the treatment area.
- Allow the area to dry for 15 minutes. Avoid touching the treatment area for 6 hours after applying the medicine.
- Wash your hands with soap and water immediately after applying the gel, and also in between administrations if prescribed two different strengths for two different areas. If you are treating your hands you should only wash the fingertip which you used for applying the gel.
- Do not apply Picato immediately after taking a shower or less than two hours before bedtime.
- Do not wash the areas where you applied the gel for at least 6 hours after you apply it.
- Do not touch the treatment area yourself or allow anyone or any pets to touch the treatment area for a period of 6 hours after applying the gel.
- Do not cover the treated area with air or water tight bandages after you have applied Picato.
- The full effect of Picato can be evaluated approximately 8 weeks after treatment.



If you use Picato for treatment of the neck

If more than half of the treatment area is located in the *upper* part of the neck:
– Use Picato 0.015% (for the skin of the face and scalp)
If more than half of the treatment area is located in the *lower* part of the neck:
– Use Picato 0.05% (for the skin of the trunk and extremities)

If you use more Picato than you should

Wash the area with soap and water. Please contact the doctor if you experience severe skin reactions.
If a child has accidentally swallowed the medicine, refer immediately to the doctor or to a hospital emergency room and bring the package of the medicine with you.

If you forget to use Picato, consult the doctor.
Persist with the treatment as recommended by the doctor.

Even if there is an improvement in your health, do not stop taking this medicine without consulting the doctor.

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 any further questions regarding the use of this medicine, consult the doctor or pharmacist.

4. Side effects

Like all medicines, the use of Picato can cause side effects in some users. Do not be alarmed while reading the list of side effects, you may not suffer from any of them.

Seek medical attention right away if you experience an allergic reaction that may include swelling of the mouth, tongue or throat when using this medicine. This side effect is uncommon.

After using this medicine, the skin where you apply it is likely to get red, peel and have scabs. These side effects most often occur within one day after applying this medicine, and may get worse for up to one week after you have stopped using this medicine. These effects will usually get better within 4 weeks from when you started the treatment.

Infection of the skin in the treatment area can occur (has been reported as a common side effect, which may appear in 1-10 out of 100 users, when treating the face and scalp).

Swelling of the application site is very common (has been reported in more than 1 in 10 users). Application site swelling on the face or scalp may gravitate to the eye area.

If the symptoms described above intensify beyond the first week after you have stopped using this medicine, or if there is discharge of pus, you might have an infection and should consult a doctor.

The most frequently occurring side effects when treating the face and scalp:
Very common side effects (effects that appear in more than 1 in 10 users):
On the treatment area:
– Some of the outer layer of your skin may wear away (erosion)
– Blisters
– Peeling of the skin
– Scabs
– Redness due to widening of the small blood vessels (erythema)
– Pain (including application site burning)

The most frequently occurring side effects when treating the trunk and extremities:
Very common side effects (effects that appear in more than 1 in 10 users):
On the treatment area:
– Some of the outer layer of your skin may wear away (erosion)
– Blisters
– Peeling of the skin
– Scabs
– Redness due to widening of the small blood vessels (erythema)

Other possible side effects when treating the face and scalp:
Common side effects (effects that appear in 1-10 out of 100 users):
On the treatment area: Itching (pruritus), Irritation

Other side effects:
– Swelling of the area around the eyes (periorbital oedema)
– Swelling (edema) of the eyelid
– Headache

Uncommon side effects (effects that appear in 1-10 out of 1,000 users):
On the treatment area:
– Tingling or numbness (paraesthesia)
– Open sores (ulcers)
– Discharge (secretion) of fluid
– Change in skin color (pigmentation change)

Other side effects:
– Eye pain
– Injury or irritation to the surface of the eye (cornea, conjunctiva) following accidental exposure

Rare side effects (effects that appear in 1-10 out of 10,000 users):
On the treatment area:
– Scarring

Other possible side effects when treating the trunk and extremities:
Common side effects (effects that appear in 1-10 out of 100 users):
On the treatment area:
– Itching (pruritus)
– Irritation
– Pain (including application site burning)

Uncommon side effects (effects that appear in 1-10 out of 1,000 users):
On the treatment area:
– Tingling or numbness (paraesthesia)
– Open sores (ulcers)
– Change in skin color (pigmentation change)
– Warmth

Other side effects:
– Injury or irritation to the surface of the eye (cornea, conjunctiva) following accidental exposure

Rare side effects (effects that appear in 1-10 out of 10,000 users):
On the treatment area:
– Scarring

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

Side effects can be reported to the Ministry of Health by clicking on the link "דיווח על תופעת 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://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

5. How to store the medicine?

- Avoid poisoning! This medicine and all other medicines, must be stored in a safe 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. date) stated on the package. The expiry date refers to the last day of that month.
- For single use only. Do not re-use the tube once opened.
- Do not throw away any medicines via household waste. Consult the pharmacist regarding unused medicine wastage, in order to help protect the environment.
- **Storage conditions:** Store in a refrigerator (2°C - 8°C)

6. Additional information

In addition to the active ingredient, this medicine also contains:

Isopropyl alcohol, hydroxyethylcellulose, benzyl alcohol, citric acid monohydrate, sodium citrate, purified water.

What does the medicine look like and what does the package contain?

A clear and colorless gel.

Each package contains 2 tubes, each tube contains 235 micrograms of ingenol mebutate in 0.47 gram of gel.

Manufacturer: LEO Laboratories Ltd., Dublin, Ireland

This leaflet was checked and approved by the Ministry of Health on 08/2017

Drug registration number at the national medicines registry of the Ministry of Health:
151-38-33889-00

Picato 0.05% PIL PB1017-07

Registration holder: Dexcel® Ltd.
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