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

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

Ledaga®

The active ingredient:
Each gram of gel contains:
Chlormethine (as hydrochloride) 160 mcg

For the list of the additional ingredients, please see section 6.

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 for the treatment of 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 Intended for?

Local treatment for patients with stage IA and IB mycosis fungoides-type cutaneous T-cell lymphoma who have received previous skin treatment.

Therapeutic group: Nitrogen mustard analog.

2. Before Using this Medicine:

Do not use the medicine if:
You are hypersensitive (allergic) to the active ingredient (chlormethine) or to any of the additional ingredients in the medicine (for a list of the additional ingredients, see section 6). Tell your doctor if you have ever had an allergic reaction to chlormethine.

Special warnings regarding the use of this medicine

Soft tissue or eye injury:

- If the gel comes into contact with the eyes it may cause eye pain, burning, swelling, redness, inflammation, sensitivity to light and blurred vision. The gel may even cause permanent damage to the eyes, including blindness. If the gel gets in the eyes, rinse the eyes right away for at least 15 minutes with a large amount of water, saline or an eye wash solution, **and seek medical help immediately (including an Ophthalmologist examination).**
- If the gel comes into contact with mucous membranes such as the mouth or the nose it may cause pain, redness and ulcers, which may be severe. Rinse the affected area right away for at least 15 minutes with a large amount of water, **and seek medical help immediately.**
- Skin inflammation (Dermatitis) is the most common side effect and may be severe. The risk of skin inflammation increases if **Ledaga** is applied to the face, genital area, anus, or skin folds. **Refer to your doctor** if you develop skin reactions such as: redness, swelling, inflammation, itching, blisters, ulcers or secondary skin infections. If these symptoms appear, consult your doctor regarding the amount of medicine that should be applied.

- Increased risk of certain types of skin cancer (non-melanoma skin cancer): Certain types of skin cancer may develop on areas treated with **Ledaga** and areas that are not treated with **Ledaga**. Your doctor will check your skin in order to identify the possibility of skin cancer development during and after your treatment with **Ledaga**. **Refer to your doctor** if you notice any new skin lesions.
- **Secondary exposure to Ledaga:** People other than the patient receiving the treatment must avoid direct contact with this medicine. This kind of contact can lead to skin inflammations, injury to mucous membranes (such as the mouth and the nose), and certain types of cancer. When applying the medicine, one must wear disposable nitrile gloves and wash the hands with soap and water after removing the gloves. If during application one comes into contact with the medicine, the affected area must be washed with soap and water immediately for at least 15 minutes, clothing that came into contact with the medicine must be removed, **and medical attention must be sought immediately if the gel gets in the eyes, mouth or nose.**
- **Ledaga** is a cytotoxic drug therefore the instructions for use of the medicine should be followed carefully.

See also section 3 "How to Use the Medicine" and section 4 "Side Effects".

Tell your doctor or pharmacist if you are taking, or have recently taken, any other medicines including non-prescription drugs and nutritional supplements.

Pregnancy and Breastfeeding:

If you are pregnant or planning to become pregnant, consult a doctor before using the medicine. **Ledaga** could harm an unborn baby. Do not become pregnant while using **Ledaga**. Refer to a doctor immediately if you have become pregnant while using **Ledaga**.

During treatment with **Ledaga** women of childbearing age should use contraceptive means such as a condom (for men) and/or spermicide. During treatment with **Ledaga**, men with female partners should use barrier methods of birth control such as a condom for men and/or spermicide.

If you are breastfeeding or planning to breastfeed, consult a doctor before using the medicine. It is not known if **Ledaga** passes into breast milk. The doctor will help you decide whether to breastfeed or use **Ledaga**. Do not breastfeed and use the medicine simultaneously.

Children: it is not known whether **Ledaga** is safe and effective for treatment of children.

Smoking:

Ledaga is inflammable.

Therefore, do not smoke in its vicinity. Do not light a cigarette or expose yourself to fire until the medicine is completely dry.

Driving and operating machinery:

This medicine is not expected to have any effect on your ability to drive or operate machinery.

Important information about some of the medicine's ingredients:
The medicine contains butylated hydroxytoluene which may cause local skin reactions (such as contact dermatitis), or irritation of the eyes and mucous tissues.
The medicine contains propylene glycol which may cause irritation to the skin.

3. How to Use this Medicine

- Always use according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure.
- This medicine is indicated for use on the skin.

The dosage and administration will be determined by your doctor only.
Usual recommended dosage:
Apply a thin layer of **Ledaga** to completely dry skin once daily. Apply at least 4 hours before or 30 minutes after showering or washing.
Stop treatment with this medicine if skin ulcers (of any grade), blisters, or skin inflammation (i.e., significant skin redness with edema) appear.
Upon improvement, treatment can be restarted at a reduced frequency, every three days. If the treatment has not caused the above-mentioned effects for at least one week the frequency of application can be increased to every other day for at least one week and then back to a dose of once daily.

Do not exceed the recommended dose.

- **For use on the skin only.** Do not apply **Ledaga** to the eyes, mouth, nose or near them.
- **Ledaga is inflammable.** Keep away from fire and avoid smoking until the gel has dried.

Instructions for use:
- Caregivers must use disposable nitrile gloves when using **Ledaga.**
- Wash hands with soap and water after applying **Ledaga** (even after using gloves).
- Caregivers who accidently come into contact with the medicine must wash the affected area with soap and water immediately for at least 15 minutes and remove clothing that came into contact with the medicine.
- After use, carefully throw the used nitrile gloves into the trash.
- Use right away, or within 30 minutes, after taking the medicine out of the refrigerator.
- Return the medicine to the refrigerator immediately after use.
- Apply a thin layer of **Ledaga** to completely dry skin once daily at least 4 hours before or 30 minutes after showering or washing.
- After applying **Ledaga,** let the treated areas dry for 5-10 minutes before covering them with clothing.
- Moisturizers may be applied to the treated areas two hours before or two hours after applying **Ledaga**.
- Do not use air or water-tight bandages on areas of the skin treated with **Ledaga**.

Tests and follow-up:

The doctor will check your skin in order to identify the possibility of skin cancer development during and after treatment with **Ledaga.**

If you have accidentally used a larger dosage or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you.

If you forget to take this medicine at the set time, do not take a double dose. Take the next dose at the usual time and consult a doctor.

Continue with the treatment as recommended by your doctor.
Even if your medical condition improves, do not stop treatment with the medicine without consulting a 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 additional questions about using the medicine, consult your doctor or pharmacist.

4. Side Effects

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

Seek medical help immediately:

- If the gel comes into contact with the eyes it may cause eye pain, burning, inflammation, sensitivity to light and blurred vision. It may even cause permanent damage to the eyes, including blindness. If the gel gets in the eyes, rinse the eyes right away for at least 15 minutes with a large amount of water, saline or an eye wash solution, **and seek medical help immediately (including an Ophthalmologist examination).**
- If the gel comes into contact with mucous membranes (such as the mouth or the nose) it may cause pain, redness and ulcers, which may be severe. Rinse the affected area right away for at least 15 minutes with a large amount of water, **and seek medical help immediately.**
- Skin inflammation (Dermatitis) is the most common side effect and may be severe. The risk of skin inflammation increases if **Ledaga** is applied to the face, genital area, anus, or skin folds. Refer to your doctor if you develop skin reactions such as: redness, swelling, inflammation, itching, blisters, ulcers or secondary skin infections. If these symptoms appear, consult your doctor regarding the amount of medicine that should be applied.
- Increased risk of certain types of skin cancer (non-melanoma skin cancer): Certain types of skin cancer may develop on areas treated with **Ledaga** and areas that are not treated with **Ledaga**. Your doctor will check your skin in order to identify the possibility of skin cancer development during and after your treatment with **Ledaga**. Refer to your doctor if you notice any new skin lesions.
- **Secondary exposure to Ledaga:** People other than the patient receiving the treatment must avoid direct contact with this medicine. This kind of contact can lead to skin inflammation, injury to mucous membranes (such as the mouth and the nose), and certain types of cancer. Caregivers who accidentally come into contact

with the medicine must wash the affected area with soap and water right away for at least 15 minutes, remove affected clothing **and seek medical help immediately if the gel gets in the eyes, mouth or nose.**

Additional Side Effects:
The most common side effects are: redness, swelling, itching, skin ulcers or blisters, skin infections and inflammations and darkening of areas of the skin.
Ledaga may cause fertility problems in men and women and may affect your ability to become pregnant. Consult your doctor, if this matter is of concern to you.

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

Side effects can be reported to the Ministry of Health via the link "Report Side Effects of Drug Treatment" found on the home page of the Ministry of Health's website (www.health.gov.il), which refers 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 kept in a safe place out of the reach of children and/or infants, to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by your 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.
- **Storage conditions:**
  Manufacturer and warehouse: Store in a freezer (-15°C to -25°C)
  In pharmacy and at home: Store in a refrigerator (2°C - 8°C) in a spot that is separate and away from food stored in the refrigerator. Avoid contact between the medicine and food while it is being stored in the refrigerator.
- Use the gel within 60 days from the time the medicine is transferred from the freezer to the refrigerator and no later than the expiry date appearing on the package.
- With clean hands, place the product back in its original packaging and return it to the refrigerator immediately after use.
- Consult your doctor or pharmacist before using a product that was out of the refrigerator for more than one hour a day.
- After 60 days, carefuly throw the rest of the medicine. Medicine that is not in use, empty tubes, and used disposable nitrile gloves should be thrown into the trash.

6. Additional Information:

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

Diethylene glycol monoethyl ether, propylene glycol, isopropyl alcohol, glycerin, lactic acid racemic, hydroxypropylcellulose, sodium chloride, DL-menthol, edetate disodium dihydrate, butylated hydroxytoluene.

What the medicine looks like and contents of the package:

Ledaga is a clear and transparent gel. **Ledaga** comes in a tube of 60 grams.

Registration holder and address: Rafa Laboratories Ltd., P.O. Box 405, Jerusalem 9100301

Manufacturer and address: Helsin Birex Pharmaceuticals Ltd., Dublin, Ireland.

Drug registration number at the national registry of the Ministry of Health:
157 12 34556 00

Updated in November 2020
044001-H