Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Flutarol
Cream

Active ingredient
1 gram of cream contains fluorouracil 50 mg

Inactive ingredients and allergens: see section 2 'Important information about some of this medicine's ingredients' and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your 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 it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

Flutarol Cream is used to treat skin conditions such as actinic keratosis and superficial skin cancer (basal cell carcinoma, BCC).

Therapeutic group: Anticancer medicines.

.2 Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient fluorouracil or to any of the other ingredients in this medicine (see section 6 'Additional information').
- You are pregnant, think you may be pregnant or are breastfeeding.
- You are using medicines known as antiviral nucleosides (e.g. brivudine, sorivudine).These medicines are usually used to treat chickenpox or shingles.

Special warnings about using this medicine
Before using Flutarol, tell your doctor if:
- You have no activity or deficiency of the enzyme DPD (dihydropyrimidine dehydrogenase (DPD) (partial or complete DPD deficiency).

Special caution is required during treatment with Flutarol in the following cases:
- When using the medicine, do not smoke or get close to open flames - there is a risk of severe burns. Fabrics (e.g., clothing, bedding, dressings, etc.) that come in contact with this medicine burn more easily and constitute a serious fire hazard. Washing clothing and bedding may reduce medicine build-up, but not totally remove it.
- Avoid contact of the medicine with the eyes or mouth, especially when the medicine is intended for the area of eyelids, nose or lips (see section 3 'How to use this medicine').
- Do not use this medicine on open wounds. This may lead to increased absorption of the medicine in the blood, which very rarely may cause side effects.
- Do not use this medicine on ulcerated or inflamed skin. This may lead to increased absorption of the medicine in the blood, which very rarely may cause side effects.
- While using **Flutarol**, avoid direct exposure to sunlight, or sunlamps and sunbeds as much as possible, as these increase the activity of **Flutarol** and may increase skin reactions.
- Exposure to UV radiation (e.g., natural sunlight, tanning salon) should be avoided.
- A closed bandage or an adhesive bandage may increase the inflammatory reaction of the

skin.

Children and adolescents
This medicine is not intended for children and adolescents under 18 years of age.

Drug interactions
If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Particularly if you are treated with:
- Antiviral medicines for treatment of diseases such as chickenpox or shingles - brivudine, sorivudine, or if you have taken these medicines during the last 4 weeks. These medicines may increase the activity of this medicine, thus increasing the chance of side effects (see section 4 'Side effects').

Pregnancy, breastfeeding, and fertility
Pregnancy:
Do not use **Flutarol** and contact your doctor if you are pregnant or think you might be pregnant.

Females of childbearing potential must use an effective contraception method during treatment and for 7 months after treatment with **Flutarol**. Male patients (or their female partners of childbearing potential) must use an effective contraception method during treatment and for 4 months after treatment with **Flutarol**.
If you become pregnant during treatment, inform your doctor immediately and seek genetic counseling.

Breastfeeding:
Do not use **Flutarol** and contact your doctor if you are breastfeeding. If use during breastfeeding is absolutely necessary, breastfeeding must be discontinued.

Fertility:
The use of **Flutarol** may impair female and male fertility. Use of the medicine is not recommended for men attempting to father a child.

Driving and using machines
It is unlikely that the medicine will have any effect on your ability to drive or operate machines.

Important information about some of this medicine's ingredients
Flutarol contains ingredients which may cause side effects:
- **Stearyl alcohol** which may cause skin irritation (e.g. contact dermatitis).
- **Propylene glycol** which may cause skin irritation. This medicine contains 115 mg propylene glycol per 1 g of cream, which is equivalent to 11.5% w/w. Since the medicine contains this ingredient, do not use it on open wounds, large body area or damaged skin (such as burns) without consulting with your doctor or pharmacist.
- **Methyl paraben and propyl paraben** which may cause allergic reactions (sometimes delayed).

3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to use this medicine.

How to apply
- For external use only.
- Apply **Flutarol** to skin only and avoid medicine contact with the eyes and mouth.
- Apply a thin layer of the cream to the affected area as instructed by your doctor.

- It is very important that you do not apply an amount larger than that recommended by your doctor and do not apply the cream to open wounds. This may lead to some of the medicine being absorbed into the bloodstream, which very rarely may cause side effects.

Only your doctor will determine your dose and how you should use this medicine. **The recommended dosage** is usually:

- Apply a thin layer of Flutarol to the affected area 1-2 times a day for at least three to four weeks.
- Wash your hands thoroughly after applying **Flutarol** (except situations in which the hands are the treated area).
- Your doctor will tell you if you need to bandage the treated area.
- The maximal area of the region treated at each time is 23 X 23 cm (approximately the size of a plate). Larger areas will be treated in separate parts each time.

Do not exceed the recommended dose.

If you have accidentally swallowed some cream, consult your doctor or pharmacist immediately, or go directly to a hospital emergency room and bring the medicine package with you.

If the cream has accidentally entered into your eyes, mouth or nose, or if someone else has used it, wash the cream off with water and immediately contact your doctor or pharmacist, or go to a hospital emergency room and bring the medicine package with you.

If you forget to apply the medicine at the required time, apply the cream as soon as you remember. If it is nearly time to apply the next dose, skip the missed dose and continue with the next dose as part of the routine treatment. Do not apply a double dose to make up for the forgotten dose. Apply the next dose at the regular time and consult your doctor.

Adhere to the treatment as recommended by your doctor.

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. <u>Side effects</u>

Like with all medicines, using **Flutarol** may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

<u>Important information about treatment with **Flutarol**</u>
Flutarol destroys cancerous and precancerous cells, while having little effect on normal cells.

When you use **Flutarol**, it is likely that the area of skin that you are treating will become red. This may be followed by inflammation/swelling, possibly some discomfort, skin peeling and eventually healing. This is the expected normal response to treatment, indicating that **Flutarol** is working.

Sometimes the response is more severe. If your skin becomes much worse, if you experience pain, or if you are worried, contact your doctor. Your doctor may prescribe another cream to relieve the discomfort.

After stopping treatment, you may find that your skin takes one to two months to heal completely.

Flutarol will also treat skin abnormalities that were previously not visible to the naked eye, and these abnormalities may become red and inflamed.

Contact your doctor immediately if you experience any of the following side effects:
- Abdominal pain or other abdominal problems such as cramps, diarrhea or vomiting.
- Swelling or soreness of the mouth and tongue.
- Fever or feeling generally unwell.

These side effects occur if you use too much of the cream or if you apply the cream to open wounds.

Additional side effects
Very rare side effects – affect less than 1 in 10,000 users:
- Side effects related to the skin and subcutaneous tissue: itching, redness, burning sensation, severe peeling, severe swelling or inflammation, ulceration, blistering, irritation, pain, red wheals on the skin (hives) and rash. In general, these effects are a severe response to treatment and usually occur in the areas of the skin where the cream has been applied. Exposure to sunlight may increase the intensity of the reaction.
- Rash on areas other than where the cream was applied.
- Hair loss.

Side effects of unknown frequency (the frequency of these effects has not been established yet):
- Painful and/or watering eyes
- Taste disturbance
- Headache, dizziness, nausea
- Bleeding at the treatment area.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the external package and tube. The expiry date refers to the last day of that month.
- Do not throw away any medicine via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Storage conditions:
- Store at a temperature below 25°C.
- Use within 8 weeks of opening.

6. Additional information

In addition to the active ingredient, this medicine also contains:
White petrolatum, stearyl alcohol, propylene glycol, polysorbate 60, methylparaben, propylparaben, purified water

What the medicine looks like and contents of the pack:

Flutarol is a white, smooth cream. It is marketed in tubes of 20 g and 40 g.

Not all pack sizes may be marketed.

Registration holder's name and address: Taro Pharmaceutical Industries Ltd. 14 Hakitor St., Haifa Bay 2624761

Revised in June 2023 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 172-39-37365-99