

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS’ REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor’s prescription only

LYSODREN 500 mg Tablets

The active ingredient and its amount:

Each tablet contains mitotane 500 mg.

Inactive and allergenic ingredients in the preparation - see Section 6 “Further Information”.

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, consult the doctor or pharmacist.

This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

The medicine is intended for the symptomatic treatment of advanced (unresectable, metastatic or relapsed) adrenal cortical carcinoma (ACC).

Therapeutic group: Antineoplastic agents.

2. BEFORE USING THE MEDICINE

ⓧ Do not use the medicine if:

- You are sensitive (allergic) to mitotane or to any of the other ingredients contained in the medicine (see section 6).
- You are breastfeeding. You must not breastfeed during treatment with Lysodren.
- You are being treated with medicines containing spironolactone (see “Drug interactions”).

ⓧ Special warnings regarding use of the medicine

Before treatment with this medicine, tell the doctor if:

- You have an injury (shock, severe trauma), an infection or illness while you are taking Lysodren. Tell the doctor immediately, who may decide to temporarily stop treatment.

- You have liver problems: Tell the doctor if you develop any of the following signs and symptoms indicating liver problems during Lysodren treatment: itching, yellow eyes or skin, dark urine, pain or discomfort in the right upper abdomen area. The doctor should do blood tests to check your liver function before and during treatment with Lysodren, and as clinically needed.

- You have severe kidney problems.

- You are using any of the medicines mentioned below (see “Drug interactions”).

- You have gynaecological problems such as bleeding and/or pelvic pain.

This medicine must not be handled by anyone other than the patient and his/her caregivers, and especially not by pregnant women. Caregivers must wear disposable gloves when handling the tablets.

The doctor may prescribe you some hormonal treatment (steroids) while you are taking Lysodren.

ⓧ Children and adolescents

There is very limited experience with patients in this age group.

ⓧ Drug interactions

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

Lysodren must not be used together with medicines containing spironolactone, which are usually used as diuretics for heart, liver or kidney diseases.

Lysodren may interfere with the action of several medicines. Therefore, you should tell the doctor if you are using medicines containing any of the following active ingredients:

- Warfarin or other anticoagulants (blood thinners), used to prevent blood clots.

- It may be necessary to change the dose of your anticoagulant.

- Anti-epileptics

- Rifabutin or rifampicin, used to treat tuberculosis

- Griseofulvin, used in the treatment of fungal infections

- Herbal preparations containing St. John’s wort (*Hypericum perforatum*)

- Sunitinib, etoposide: to treat cancer

ⓧ Use of the medicine with food and drink

Lysodren should preferably be taken during meals containing fat-rich food, such as: milk, chocolate, oil.

ⓧ Pregnancy, breastfeeding and fertility

Lysodren may harm the unborn child. Tell your doctor if you are pregnant or planning to become pregnant. If you could become pregnant, you must use effective contraception during treatment with Lysodren and even after stopping the treatment. Ask the doctor for advice.

You must not breastfeed while taking Lysodren, and even after stopping the treatment. Ask the doctor for advice.

ⓧ Driving and using machines

Lysodren has a significant influence on your ability to drive and use machines. Do not drive or use machines during or after the treatment as long as you suffer from any side effects that could affect your ability to drive or use machines, such as movement and coordination disorders, confusion, fatigue, vertigo or dizziness.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor’s instructions.

Check with the doctor or pharmacist if you are not sure about the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only.

The usual dosage is generally:

The usual starting dose for adults is 2 to 3 g (4 to 6 tablets) per day.

The doctor may start treatment at higher doses, such as 4 to 6 g (8 to 12 tablets).

In order to find the optimal dose for you, the doctor will regularly monitor the levels of Lysodren in your blood. The doctor may decide to stop treatment with Lysodren temporarily or to lower the dose if you experience certain side effects.

Use in children and adolescents

The starting daily dose of Lysodren is 1.5 to 3.5 g/m² body surface (this will be calculated by your doctor according to the weight and the size of the child).

Do not exceed the recommended dose.

You should swallow the tablets with a glass of water during meals containing fat-rich food. You can divide the total daily dose into two or three intakes.

You may split the tablet for immediate use to make it easier to swallow if needed. Swallow the halves of the tablet immediately after splitting.

If you took an overdose, 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 medicine with you.

If you forgot to take the medicine at the scheduled time, do not take a double dose. Take the next dose at the regular time.

Adhere to the treatment regimen as recommended by the doctor.

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

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

4. SIDE EFFECTS

As with any medicine, the use of Lysodren 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.

Tell the doctor immediately if you notice any of the following side effects:

- Adrenal insufficiency: fatigue, abdominal pain, nausea, vomiting, diarrhea, confusion
- Anemia: pallor of the skin, muscular fatigue, feeling breathless, vertigo mainly when standing up

- Liver damage: yellowing of the skin and eyes, itching, nausea, diarrhea, fatigue, dark colored urine

- Neurological disorders: movement and coordination disorders, abnormal sensations like pins and needles (tingling), memory loss, concentration difficulties, difficulty to talk, vertigo

These symptoms may indicate complications for which specific medications could be appropriate.

Side effects by frequency

Very common side effects - effects that occur in more than 1 in 10 users:

- Vomiting, nausea, diarrhea, abdominal pain

- Lack of appetite

- Abnormal sensations like pins and needles (tingling)

- Movement and coordination disorders, vertigo, confusion

- Feeling sleepy, fatigue, muscle weakness (muscle fatigue during exertion)

- Inflammation (swelling, heat, pain) of mucosa, skin rash

- Blood disorders (prolonged bleeding time)

- Increase of cholesterol, triglycerides (fats) and liver enzymes (in blood tests)

- Decrease in white blood cell count

- Breast overdevelopment in men

- Adrenal insufficiency

Common side effects - effects that occur in 1-10 users out of 100:

- Dizziness, headache

- Peripheral nervous system disorders (association of sensory disorders, muscular weakness and atrophy, decrease of tendon reflexes and vasomotor symptoms such as hot flushes, sweat, and sleep disorders)

- Mental impairment (such as memory loss, concentration difficulty)

- Movement disorder

- Decrease of red blood cells (anemia, with symptoms such as skin pallor and fatigue), decrease in blood platelets (may make you more prone to bruising and bleeding)

- Liver inflammation (hepatitis - auto-immune) (may cause yellowing of the skin and eyes, dark colored urine)

- Difficulty of coordinating muscles

Side effects with unknown frequency (effects whose frequency has not yet been determined):

- Fever

- General aching

- Flushing, high or low blood pressure, feeling of dizziness/vertigo when you suddenly stand up

- Increased production of saliva

- Eye disorders: visual impairment, blurred vision, double vision, distorted vision, complaint of glare

- Fungal infections

- Liver damage (may cause yellowing of the skin and eyes, dark colored urine)

- Decreased uric acid in blood tests

- Bladder inflammation with bleeding

- Presence of blood in the urine, presence of proteins in the urine

- Balance disorder

- Distorted sense of taste

- Impaired digestion

- Ovarian macrocysts (with symptoms such as pelvic pain, bleeding)

- Decreased androstenedione (precursor of sex hormones) in blood tests in females

- Decreased testosterone (sex hormone) in blood tests in females

- Sex hormone binding globulin (a protein that binds sex hormones) increased in blood tests

- Decreased free testosterone (sex hormone) in blood tests in males

- Hypogonadism in males (with symptoms such as breast overdevelopment, libido decreased, erectile dysfunction, fertility disorders)

In children and adolescents, thyroid gland problems, neuro-psychological problems, growth retardation and one case of encephalopathy have been observed.

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

Reporting of side effects

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il/>

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine should be kept 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.) that appears on the carton package and on the bottle.

- **There are no special storage conditions. It is recommended to store at room temperature. Store in the original packaging. For use up to one year from the day of opening.**

- Any leftover product or waste should be disposed of in accordance with local rules for medicines that are toxic to cells (cytotoxic medicines).

- Do not throw the medicine away via wastewater or household waste. Consult the pharmacist about how to dispose of medicine that is not in use. These measures will help protect the environment.

6. FURTHER INFORMATION

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

microcrystalline cellulose, maize starch, macrogol 3350, silica colloidal anhydrous.

What the medicine looks like and what are the contents of the package

Lysodren are white, convex, round tablets, scored on one side, and embossed on the other side with BL over L1.

Lysodren is available in plastic bottles containing 100 tablets.

License holder and address: CTS Ltd., 4 Haharash St., Hod Hasharon 45240.

Manufacturer name and address: HRA Pharma Rare Diseases, France.
200 avenue de Paris 92320 Chatillon, France

This leaflet was revised in 05/2021 according to Ministry of Health guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 166-52-35626-00