

Package leaflet: Information for the user

Lysodren 500 mg tablets

Mitotane

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

Always keep with you the Lysodren Patient Card included at the end of this leaflet.

What is in this leaflet:

1. What Lysodren is and what it is used for
2. What you need to know before you take Lysodren
3. How to take Lysodren
4. Possible side effects
5. How to store Lysodren
6. Contents of the pack and other information

1. What Lysodren is and what it is used for

Lysodren is an antitumoral medicine.

This medicine is used for the treatment of symptoms of advanced non operable, metastatic or recurrent malignant tumours of the adrenal glands.

2. What you need to know before you take Lysodren

Do not take Lysodren

- if you are allergic to mitotane or any of the other ingredients of this medicine (listed in section 6).
- if you are breast-feeding. You must not breast-feed while taking Lysodren.
- if you are being treated with medicines containing spironolactone (see "Other medicines and Lysodren").

Warnings and precautions

Talk to your doctor or pharmacist before taking Lysodren.

You should tell your doctor if any of the following applies to you:

- if you have an injury (shock, severe trauma), an infection or if you have any illness while you are taking Lysodren. Tell your doctor immediately, who may decide to temporarily stop treatment.
- if you have liver problems: Tell your doctor if you develop any of the following signs and symptoms of liver problems during Lysodren treatment: itching, yellow eyes or skin, dark urine, and pain or discomfort in the right upper stomach area. Your doctor should do blood tests to check your liver function before and during treatment with Lysodren, and as clinically indicated.
- if you have severe kidney problems
- if you are using any medicines mentioned below (see "Other medicines and Lysodren")

- if you have gynaecological problems such as bleeding and/ or pelvic pain.
This medicine should not be handled by persons other than the patient and his/her caregivers, and especially not by pregnant women. Caregivers should wear disposable gloves when handling the tablets.

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

Always keep with you the Lysodren Patient Card included at the end of this leaflet.

Other medicines and Lysodren

Please tell your doctor or pharmacist if you are using or have recently used any other medicines, including medicines obtained without a prescription.

You must not use Lysodren with medicines containing spironolactone, often used as a diuretic for heart, liver or kidney diseases.

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

- warfarin or other anticoagulants (blood thinners), used to prevent blood clots. The dose of your anticoagulant may need adjustment.
- antiepileptics
- 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: to treat cancer

Lysodren with food and drink

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

Pregnancy, breast-feeding and fertility

Lysodren may harm the foetus. If you are pregnant or planning to become pregnant, tell your doctor. If you may become pregnant, you should use an effective contraception during treatment with Lysodren and even after stopping it. Ask your doctor for advice.

You must not breast-feed while taking Lysodren and even after stopping it. Ask your doctor for advice.

Driving and using machines

Lysodren has a major influence on your ability to drive and use machines. Ask your doctor for advice.

3. How to take Lysodren

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Dose and schedule

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

Your 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, your doctor will monitor regularly the levels of Lysodren in your blood. Your 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). The experience in patients in this age group is very limited.

Method of administration

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

If you take more Lysodren than you should

Tell your doctor immediately if you have taken accidentally more Lysodren than you should or if a child has accidentally swallowed some.

If you forget to take Lysodren

If you accidentally miss a dose, just take the next dose as scheduled. Do not take a double dose to make up for the forgotten one.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, Lysodren can cause side effects, although not everybody gets them.

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

- Adrenal insufficiency: fatigue, abdominal pain, nausea, vomiting, diarrhoea, confusion
- Anaemia: cutaneous pallor, muscular fatigability, feeling breathless, vertigo especially when standing up
- Liver damage: yellowing of the skin and eyes, itching, nausea, diarrhoea, fatigue, dark coloured urine
- Neurological disorders: movement and coordination disorders, abnormal sensations like pins and needles, memory loss, concentration difficulty, difficulty to talk, vertigo

These symptoms may reveal complications for which specific medication could be appropriate.

Side effects may occur with certain frequencies, which are defined as follows:

- very common: may affect more than 1 in 10 people
- common: may affect up to 1 in 10 people
- not known: frequency cannot be estimated from the available data

Very common side effects

- vomiting, nausea (feeling sick), diarrhoea, belly pain
- lack of appetite
- abnormal sensations like pins and needles
- movement and coordination disorders, vertigo, confusion
- feeling sleepy, fatigue, muscle weakness (fatigue of muscle during effort)
- inflammation (swelling, heat, pain) of mucosa, skin rash
- blood disorders (bleeding time prolonged)
- increase of cholesterol, triglycerides (fats) and liver enzymes (in blood tests)
- decrease in white blood cells count
- breast overdevelopment in men
- adrenal insufficiency

Common side effects

- dizziness, headache
- peripheral nervous system disorders (association of sensory disorders, muscular weakness and atrophy, decrease of tendon reflex 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 (anaemia, with symptoms such as skin pallor and fatigue), decrease in blood platelets (may make you more prone to bruising and bleeding)
- hepatitis (auto-immune) (may cause yellowing of the skin and eyes, dark coloured urine)
- difficulty of coordinating muscles

Frequency Not Known

- 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, vision blurred, double vision, distortion of images, complain of glare
- fungal infection
- liver damage (may cause yellowing of the skin and eyes, dark coloured urine)
- decreased uric acid in blood tests
- bladder inflammation with bleeding
- presence of blood in urine, presence of proteins in urine
- balance disorder
- distortion of the 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 which binds sex hormones) increased in blood tests
- decreased free testosterone (sex hormone) in blood tests in males

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

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system (see below). By reporting side effects you can help provide more information on the safety of the medicine.

United Kingdom

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard

Ireland

HPRA Pharmacovigilance

Earlsfort Terrace

IRL - Dublin 2

Tel: +353 1 6764971

Fax: +353 1 6762517

Website: www.hpra.ie

e-mail: medsafety@hpra.ie

5. How to store Lysodren

Keep out of the sight and reach of children.

Store in the original packaging.

Do not use after the expiry date which is stated on the carton and the bottle after EXP.

Any unused product or waste material should be disposed of in accordance with local requirements for cytotoxic medicines.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Lysodren contains

- The active substance is mitotane. Each tablet contains 500 mg of mitotane.
- The other ingredients are maize starch, microcrystalline cellulose (E 460), macrogol 3350 and silica colloidal anhydrous.

What Lysodren looks like and contents of the pack

Lysodren tablets are white, biconvex, round and scored.

Lysodren is available in plastic bottles of 100 tablets.

Marketing Authorisation Holder

Laboratoire HRA Pharma
15 rue Béranger
F - 75003 Paris
France

Manufacturer

Corden Pharma Latina S.p.A.
Via del Murillo Km. 2.800
04010 Sermoneta (Latina)
Italy

or

CENTRE SPECIALITES PHARMACEUTIQUES

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United Kingdom

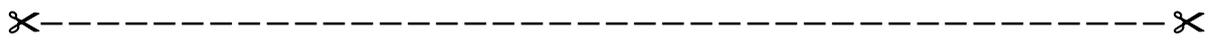
HRA Pharma UK & Ireland Ltd
Tel: 0800 917 9548

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency (EMA) web site: <http://www.emea.europa.eu/>. There are also links to other websites about rare diseases and treatments.

This leaflet is available in all European languages on the EMA website.



LYSODREN PATIENT CARD

<p>I am on Lysodren (mitotane) treatment</p> <p>I am prone to acute adrenal insufficiency</p> <p>In case I need emergency care, adequate precautionary measures should be taken</p>	<p>The name of my Doctor is:</p> <p>Phone:</p> <p>For information on the product, please contact: <i>Laboratoire HRA Pharma</i> <i>Tel: + 33 1 40 33 11 30</i> <i>lysodren@hra-pharma.com</i></p>
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