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EPAR summary for the public

Lysodren

mitotane

This is a summary of the European public assessment report (EPAR) for Lysodren. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Lysodren.

What is Lysodren?

Lysodren is a medicine that contains the active substance mitotane. It is available as tablets (500 mg).

What is Lysodren used for?

Lysodren is used to treat the symptoms of advanced adrenal cortical carcinoma (cancer of the outer layer of the adrenal gland). It is used when the cancer is unresectable (cannot be removed by surgery), is metastatic (has spread to other parts of the body), or has relapsed (returned after treatment).

Because the number of patients with adrenal cortical carcinoma is low, the disease is considered 'rare', and Lysodren was designated an 'orphan medicine' (a medicine used in rare diseases) on 12 June 2002.

The medicine can only be obtained with a prescription.

How is Lysodren used?

Treatment with Lysodren should be started and followed by a specialist who has suitable experience. The recommended starting dose in adults is 2 to 3 g per day, divided into two or three doses, taken with meals containing fatty food. A starting dose of 4 to 6 g per day can be used in patients who need urgent control of Cushing's syndrome (a set of symptoms of adrenal gland cancer caused by high hormone levels). The dose is increased in a stepwise manner until it reaches an 'optimal' dose that

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gives the best results without causing unacceptable side effects. The levels of the active substance in the blood should be monitored frequently, with the final target dose aiming to reach blood levels between 14 and 20 mg per litre. This is usually reached within three to five months. Levels above 20 mg/l may cause severe side effects without increasing the medicine's effectiveness.

The dose may be reduced or treatment interrupted if the patient experiences side effects. Treatment should continue as long as there is a benefit. If there is no improvement in symptoms after three months of treatment at the optimal dose, treatment should be stopped.

There is limited information on the use of Lysodren in children, but a daily starting dose of 1.5 to 3.5 g per square metre body surface area (calculated using the child's height and weight) is recommended.

Lysodren is not recommended for use in patients with severe liver or kidney problems, and it should be used with caution in those with mild or moderate liver or kidney problems. It should also be used with caution in elderly patients, with frequent monitoring of blood levels.

Patients who take Lysodren should receive the 'Lysodren patient card' that they should carry with them in case of emergency, to inform healthcare professionals (such as doctors and nurses) that they are taking the medicine.

How does Lysodren work?

The cortex of the adrenal gland produces steroid hormones. When this area develops cancer, levels of these hormones can increase, causing the symptoms of the disease. The active substance in Lysodren, mitotane, is thought to work by preventing cells in the adrenal gland from working properly, by damaging their mitochondria (the energy-producing components), reducing the production of some steroid hormones. It may also alter the breakdown of these hormones. Together, these effects reduce the levels of the hormones in the body, improving the symptoms of the disease.

How has Lysodren been studied?

Since the active substance in Lysodren, mitotane, is a well-established medicine that has been used in the treatment of adrenal cortical carcinoma in Europe since 1959, the company presented information from the published literature to support its application for Lysodren.

It presented the results of 220 studies published since 1990 on the use of the medicine in unresectable, metastatic adrenal cortical carcinoma. The studies included over 500 adults and children, who were treated for various lengths of time with mitotane, either alone or in combination with other anticancer medicines. The main measures of effectiveness in the studies included survival time, the reduction in tumour size and the time spent free of the symptoms of the disease.

What benefit has Lysodren shown during the studies?

Overall, the studies suggested that Lysodren could provide a benefit in patients with advanced adrenal cortical carcinoma, by increasing survival times (by over five years in a few cases) and causing shrinkage or stabilisation of tumour size in 20 to 30% of patients. It also reduced the symptoms of the disease, particularly in patients whose cancer was producing high hormone levels. There was insufficient evidence to support its use as an add-on to other anticancer medicines. Limited information was available on the use of mitotane in children, but overall, the children remained disease free for an average of seven months when taking the medicine.

What is the risk associated with Lysodren?

The most common side effects with Lysodren (seen in more than 1 patient in 10) are increased blood levels of liver enzymes, cholesterol and triglycerides (a type of fat), leucopenia (low white blood cell counts), prolonged bleeding time, ataxia (difficulty co-ordinating movements), paraesthesia (abnormal sensations like pins and needles), vertigo (a spinning sensation), sleepiness, mucositis (inflammation of the mucous membranes, such as the lining of the mouth), vomiting, diarrhoea, nausea (feeling sick), epigastric discomfort (discomfort around the stomach), skin rash, myasthenia (muscle weakness), adrenal insufficiency (reduced adrenal gland activity), loss of appetite, asthenia (weakness), gynaecomastia (breast enlargement) and confusion. For the full list of all side effects reported with Lysodren, see the package leaflet.

Lysodren must not be used in people who are hypersensitive (allergic) to mitotane or any of the other ingredients. It must not be used in patients who are breast-feeding or who are taking spironolactone (a diuretic).

Why has Lysodren been approved?

The CHMP decided that Lysodren's benefits are greater than its risks for the treatment of advanced adrenal cortical carcinoma, but noted that the effect of Lysodren has not been established in adrenal cortical carcinoma that is not producing high levels of steroid hormones. The Committee recommended that Lysodren be given marketing authorisation.

Other information about Lysodren

The European Commission granted a marketing authorisation valid throughout the European Union for Lysodren on 28 April 2004.

The summary of opinion of the Committee for Orphan Medicinal Products for Lysodren can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designation.

The full EPAR for Lysodren can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports. For more information about treatment with Lysodren, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 07-2013.