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Questions and answers

Questions and answers on the outcome of an extension of indication application for Lysodren (mitotane)

On 30 May 2013, the Committee for Medicinal Products for Human Use (CHMP) finalised its assessment of an application to modify the approved use of Lysodren, which would have extended its use in the treatment of adrenal cortical carcinoma to include 'non-functional' disease. The CHMP did not consider the data submitted to be sufficient to recommend this change. However, the Committee concluded that new information relating to blood concentrations of the medicine and side effects should be included in the prescribing information.

What is Lysodren?

Lysodren is an orphan medicine (a medicine used in rare diseases) that contains the active substance mitotane. It is available as tablets (500 mg). It is used to treat the symptoms of advanced adrenal cortical carcinoma (cancer of the adrenal cortex, the outer layer of the adrenal gland, which is responsible for producing steroid hormones). It is used when the cancer cannot be removed by surgery, is metastatic (has spread to other parts of the body) or has relapsed (returned after treatment).

What was Lysodren expected to be used for?

Lysodren is currently indicated to treat the symptoms of 'functional' adrenal cortical carcinoma, which is when the tumour produces excess levels of steroid hormones, causing related symptoms (such as Cushing's syndrome). The prescribing information contains a statement that Lysodren's effects have not been established in 'non-functional' adrenal cortical carcinoma (when hormone production is not altered and the only symptoms are caused by the size of the tumour). Lysodren was expected to be used in non-functional as well as functional adrenal cortical carcinoma, and therefore the company was requesting to remove this statement from the prescribing information.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8668
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

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What did the company present to support its application?

The company presented the results of one main study involving 304 patients with advanced adrenocortical carcinoma (166 with functional disease and 138 with non-functional disease). The study compared two treatment regimens where Lysodren was given with other anticancer medicines: one consisted of Lysodren together with etoposide, doxorubicin and cisplatin, while the other consisted of Lysodren together with streptozocin.

What were the conclusions of the CHMP?

The CHMP concluded that the data provided was not sufficient to determine the effects of Lysodren in patients with non-functional disease. It was not possible to assess whether the treatment's effect in terms of controlling the disease was caused by Lysodren or not, as the study was not designed to demonstrate this. Moreover, relevant data on the sub-group of patients with non-functional disease were not provided. Therefore, there was not enough evidence to support the proposed change to the prescribing information.

At the same time, the newly submitted results provided further information on the relationship between the amount of the medicine in the blood and its effects, and on certain side effects seen in patients treated with Lysodren. Therefore, the CHMP recommended including the relevant data in the prescribing information for Lysodren.

What consequences does this refusal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that there are no ongoing clinical trials or compassionate use programmes with Lysodren in patients with non-functional disease.

What is happening with Lysodren for treatment of functional adrenal cortical carcinoma?

There are no consequences for the use of Lysodren in its authorised indications.

The full European Public Assessment Report for Lysodren can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.