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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Mitotane for the treatment of adrenal cortical carcinoma

First publication	6 January 2003
Rev.1: administrative update	8 January 2003
Rev.2: administrative update	11 March 2003
Rev.3: information about Marketing Authorisation	29 November 2005
Rev:3: withdrawal from the Community Register	6 June 2014

Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in April 2014 at the end of the period of market exclusivity.

On 12 June 2002, orphan designation (EU/3/02/102) was granted by the European Commission to Laboratoire HRA Pharma, France, for mitotane for the treatment of adrenal cortical carcinoma.

What is adrenal cortical carcinoma?

Cancer of the adrenal cortex is a disease in which cancer (malignant) cells are found in the adrenal cortex, which is the outside layer of the adrenal gland. Cancer of the adrenal cortex is also called adrenal cortical carcinoma. There are two adrenal glands, one above each kidney in the back of the upper abdomen. The adrenal cortex produces steroid hormones. Steroid hormones include sex hormones and hormones used to control minerals and sugar in the body. Cancer cells in the adrenal cortex may make too much of one or more hormones, which can cause symptoms such as high blood pressure, weakening of the bones, or diabetes. If male or female hormones are affected, the body may go through changes such as a deepening of the voice, growing hair on the face, swelling of the sex organs, or swelling of the breasts. Cancers that make hormones are called functioning tumours. Many cancers of the adrenal cortex do not make extra hormones and are called non-functioning tumours.

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Adrenal cortical carcinoma is a life-threatening condition, mainly due to frequent spreading of the cancer cells (metastasis).

What is the estimated number of patients affected by the condition?

At the time of designation, adrenal cortical carcinoma affected approximately 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 3,800 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

The methods of treatment used include surgery, chemotherapy (using drugs to kill the cancer cells) and radiotherapy (using x-rays or other high-energy rays to kill cancer cells). An anticancer medicinal product had been authorised for the treatment of the symptoms of the condition in the Community at the time of the submission of the application for orphan designation. However, there is no authorised treatment available to target adrenocortical carcinoma.

How is this medicine expected to work?

The potential of mitotane to be toxic to the adrenal cells, and therefore to limit tumour growth has been known since several decades but the exact mechanism of action is not known. Mitotane may be of potential significant benefit for the treatment of adrenocortical carcinoma, particularly based on the effect, which have been demonstrated in experimental models of the condition and in several small clinical studies.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, clinical trials in patients with adrenal cortical carcinoma had been completed.

Mitotane had been marketed in the United States and Canada for the treatment of the condition at the time of the orphan application.

Mitotane had not been designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 30 April 2002 recommending the granting of this designation.

Update: Mitotane (Lysodren) has been authorised in the EU since 28 April 2004 for for symptomatic treatment of advanced (unresectable, metastatic or relapsed) adrenal cortical carcinoma. The effect of Lysodren on non-functional adrenal cortical carcinoma is not established.

More information on Lysodren can be found in the European public assessment report (EPAR) on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union.
At the time of designation, this represented a population of 380,600,000 (Eurostat 2002).

Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Sponsor's contact details:

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For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Mitotane	Treatment of adrenal cortical carcinoma
Danish	Mitotane	Behandling af adrenale corticale carcinomer
Dutch	Mitotane	Behandeling van bijniercortex carcinoom
Finnish	Mitotaani	Lisämunuaisen kuorikerroksen karsinooman hoito.
French	Mitotane	Traitement du carcinome cortico-surrénalien
German	Mitotane	Behandlung des adrenokortikalen Karzinoms.
Greek	Mitotane	Θεραπεία του καρκινώματος του φλοιού των επινεφριδίων.
Italian	Mitotane	Trattamento del carcinoma surrenalico
Portuguese	Mitotane	Tratamento do carcinoma adreno cortical
Spanish	Mitotane	Tratamiento de carcinoma adreno cortical
Swedish	Mitotane	Behandling av adrenala cortikala tumörer

[1] At the time of designation