



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Linsitinib for the treatment of adrenal cortical carcinoma

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in February 2013 on request of the Sponsor.

On 2 April 2012, orphan designation (EU/3/12/977) was granted by the European Commission to Astellas Pharma Europe B.V., the Netherlands, for linsitinib for the treatment of adrenal cortical carcinoma.

What is adrenal cortical carcinoma?

Adrenal cortical carcinoma is a cancer of the adrenal cortex, which is the outside layer of the adrenal glands, small glands located above the kidneys. The adrenal cortex produces several steroid hormones, including sex hormones (which cause the body to have masculine or feminine characteristics), aldosterone (which helps to regulate the body's blood pressure) and cortisol (also known as the stress hormone because it is released in response to stress). In adrenal cortical carcinoma too much of one or more of these steroid hormones are produced. Symptoms associated with adrenal cortical carcinoma may include weakening of the muscles and bones, high blood pressure and the development of abnormal masculine or feminine features if the sex hormones are affected.

Adrenal cortical carcinoma is a long-term debilitating and life-threatening disease due to poor overall survival which ranges between one and two years in the advanced stages of the disease.

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

At the time of designation, adrenal cortical carcinoma affected approximately 0.05 in 10,000 people in the European Union (EU). This was equivalent to a total of 2,500 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).

*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 (EU 27), Norway, Iceland and Liechtenstein. At the time of designation, this represented a population of 509,000,000 (Eurostat 2012).



What treatments are available?

At the time of designation, mitotane was authorised in the EU to treat the symptoms of adrenal cortical carcinoma, when the cancer is unrespectable (cannot be removed by surgery), is metastatic (has spread to other parts of the body) or has relapsed (returned after treatment). For small tumours, surgery was used to remove the cancer cells.

The sponsor has provided sufficient information to show that linsitinib might be of significant benefit for patients with adrenal cortical carcinoma because it works in a different way to existing treatments and early studies show that it may improve the outcome of patients whose disease is advanced for whom no other effective therapy exists. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Linsitinib is a 'protein tyrosine kinase inhibitor', which means that it works by blocking enzymes known as tyrosine kinases. These enzymes can be found in some receptors on the surface of cancer cells, including the insulin-like growth factor 1 receptor (IGF-1R) which is a receptor for a protein called insulin-like growth factor (IGF). IGF-1R is involved in stimulating the cells to divide uncontrollably. By blocking these receptors, linsitinib is expected to stop cell division and lead to cell death. This is expected to slow down the growth or cause the shrinkage of adrenal cortical carcinoma tumours.

What is the stage of development of this medicine?

The effects of linsitinib have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with linsitinib in patients with adrenal cortical carcinoma were ongoing.

At the time of submission, linsitinib was not authorised anywhere in the EU for adrenal cortical carcinoma or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 February 2012 recommending the granting of this designation.

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Linsitinib	Treatment of adrenal cortical carcinoma
Bulgarian	Линзитиниб	Лечение на надбъбречен кортикален карцином.
Czech	Linsitinib	Léčba adrenokortikálního karcinomu
Danish	Linsitinib	Behandling af adrenokortikalt carcinom
Dutch	Linsitinib	Behandeling van bijniercortex carcinoom
Estonian	Linsitinib	Neerupealise koore kartsinoomi ravi
Finnish	Linsitinibi	Lisämunuaisen kuorikerroksen karsinooman hoito.
French	Linsitinib	Traitement du carcinome cortico-surrénalien
German	Linsitinib	Behandlung des adrenokortikalen Karzinoms.
Greek	Λινσιτινίμπη	Θεραπεία του καρκινώματος του φλοιού των επινεφριδίων.
Hungarian	Linsitinib	Mellékvesekéreg karcinoma kezelése
Italian	Linsitinib	Trattamento del carcinoma surrenalico
Latvian	Linsitinībs	Adrenokortikālās karcinomas ārstēšana
Lithuanian	Linsitinibas	Antinksčių žievės karcinomos gydymas
Maltese	Linsitinib	Kura ta' karċinoma tal-kortiċi adrenalni
Polish	Linsytynib	Leczenie raka kory nadnercza
Portuguese	Linsitinib	Tratamento do carcinoma adreno cortical
Romanian	Linsitinib	Tratamentul carcinomului corticosuprarenalian
Slovak	Linsitinib	Liečba karcinómu kôry nadobličky
Slovenian	linsitinib	Zdravljenje karcinoma nadledvične žleze
Spanish	Linsitinib	Tratamiento de carcinoma adreno cortical
Swedish	Linsitinib	Behandling av binjurebarkskarcinom
Norwegian	Linsitinib	Behandling av adrenokortikalt karsinom
Icelandic	Linsitínib	Meðferð nýrnaheftubarkar krabbameins

¹ At the time of designation