6 May 2015
EMA/COMP/132959/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Lenvatinib for the treatment of hepatocellular carcinoma

On 19 March 2015, orphan designation (EU/3/15/1460) was granted by the European Commission to Eisai Europe Limited, United Kingdom, for lenvatinib for the treatment of hepatocellular carcinoma.

What is hepatocellular carcinoma?

Hepatocellular carcinoma is a primary cancer of the liver (a cancer that starts in the liver, rather than one that has spread to the liver from elsewhere in the body). It is more common in men than in women, and occurs mostly in people who have liver scarring (cirrhosis) or after infection with the hepatitis B or C viruses. Symptoms of the disease include pain and swelling in the abdomen, weight loss, weakness, loss of appetite and nausea.

Hepatocellular carcinoma is a serious disease and is life-threatening because it is often diagnosed at an advanced stage.

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

At the time of designation, hepatocellular carcinoma affected approximately 0.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 31,000 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?

At the time of designation, some patients with early stage hepatocellular carcinoma were treated with surgery to remove part of the liver. Chemotherapy (medicines to treat cancer) was generally used after surgery or on its own if surgery was not possible or the disease had spread to other parts of the body (metastatic disease). Sorafenib was authorised in the EU for use in hepatocellular carcinoma.

The sponsor has provided sufficient information to show that lenvatinib might be of significant benefit for patients with hepatocellular carcinoma because early studies show that patients with advanced

*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 28), Norway, Iceland and Liechtenstein. This represents a population of 512,900,000 (Eurostat 2015).

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cancer may partially respond to treatment or their disease may be stabilised. 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?

Lenvatinib is expected to work by blocking the activity of several enzymes known as tyrosine kinases, but particularly a tyrosine kinase that is present in a receptor called VEGF. The VEGF receptor is involved in the development of blood vessels and is found in high amounts in hepatocellular carcinoma cells. By blocking the tyrosine kinase in the VEGF receptor, lenvatinib is expected to prevent or slow the development of blood vessels that the cancer tissue needs to continue growing and spreading within the body.

What is the stage of development of this medicine?

The effects of lenvatinib have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with lenvatinib in patients with hepatocellular carcinoma were ongoing.

At the time of submission, lenvatinib was not authorised anywhere in the EU for hepatocellular carcinoma. Orphan designation had been granted in the United States for unresectable hepatocellular carcinoma.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 February 2015 recommending the granting of this designation.

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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	Lenvatinib	Treatment of hepatocellular carcinoma
Bulgarian	Ленватиниб	Лечение на хепатоцелуларен карцином
Croatian	Lenvatinib	Liječenje hepatocelularnog karcinoma
Czech	Lenvatinib	Léčba hepatocelulárního karcinomu
Danish	Lenvatinib	Behandling af hepatocellulært karcinom
Dutch	Lenvatinib	Behandeling van hepatocellulair carcinoom
Estonian	Lenvatinib	Hepatotsellulaarse kartsinoomi ravi
Finnish	Lenvatinibi	Hepatosellulaarisen karsinooman hoito
French	Lenvatinib	Traitement du cancer hépatocellulaire
German	Lenvatinib	Behandlung des Leberzellkarzinoms
Greek	Λενβατινίμπη	Θεραπεία του ηπατοκυτταρικού καρκινώματος
Hungarian	Lenvatinib	Hepatocelluláris carcinoma kezelése
Italian	Lenvatinib	Trattamento del carcinoma epatocellulare
Latvian	Lenvatinibs	Hepatocellulāras karcinomas ārstēšana
Lithuanian	Lenvatinibas	Hepatoceliulinės karcinomos gydymas
Maltese	Lenvatinib	Kura tal-karċinoma epatoċellulari
Polish	Lenwatynib	Leczenie raka wątrobowokomórkowego
Portuguese	Lenvatinib	Tratamento do carcinoma hepatocelular
Romanian	Lenvatinib	Tratamentul carcinomului hepatocelular
Slovak	Lenvatinib	Liečba hepatocelulárneho karcinómu
Slovenian	Lenvatinib	Zdravljenje hepatocelularnega karcinoma
Spanish	Lenvatinib	Tratamiento del carcinoma hepatocelular
Swedish	Lenvatinib	Behandling av hepatocellulärt karcinom
Norwegian	Lenvatinib	Behandling av hepatocellulært karsinom
Icelandic	Lenvatíiníib	Meðferð við lifrarfrumukrabbameini

[1] At the time of designation