28 November 2013
EMA/COMP/630515/2013
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Tivantinib for the treatment of hepatocellular carcinoma

On 13 November 2013, orphan designation (EU/3/13/1202) was granted by the European Commission to Daiichi Sankyo Development Ltd, United Kingdom, for tivantinib 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 scarring of the liver (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 (feeling sick).

Hepatocellular carcinoma is a serious and life-threatening illness that is associated with poor overall survival.

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

At the time of designation, hepatocellular carcinoma affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 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.

*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 512,200,000 (Eurostat 2013).

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The sponsor has provided sufficient information to show that tivantinib might be of significant benefit for patients with hepatocellular carcinoma because early studies show that it may delay the progression of the disease in patients whose disease has stopped responding to, or is resistant to, sorafenib. 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?

Tivantinib works by blocking the action of an enzyme known as c-MET kinase. C-MET kinase is found in high amounts in some cancer cells and is involved in the growth and spread of cancer cells and in the development of new blood vessels to supply them. By blocking this enzyme, the medicine is expected to stop the cancer cells from dividing, and thereby slow down the progression of the disease.

What is the stage of development of this medicine?

The effects of tivantinib have been evaluated in experimental models.

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

At the time of submission, tivantinib was not authorised anywhere in the EU for hepatocellular 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 9 October 2013 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	Tivantinib	Treatment of hepatocellular carcinoma
Bulgarian	Тиватиниб	Лечение на хепатоцелуларен карцином
Czech	Tivantinib	Léčba hepatocelulárního karcinomu
Croatian	Tivantinib	Liječenje hepatocelularnog karcinoma
Danish	Tivantinib	Behandling af hepatocellulært karcinom
Dutch	Tivantinib	Behandeling van hepatocellulair carcinoom
Estonian	Tivantiniib	Hepatotsellulaarse kartsinoomi ravi
Finnish	Tivantinibi	Hepatosellulaarisen karsinooman hoito
French	Tivantinib	Traitement du cancer hépatocellulaire
German	Tivantinib	Behandlung des Leberzellkarzinoms
Greek	Τιβαντινίμπη	Θεραπεία του ηπατοκυτταρικού καρκινώματος
Hungarian	Tivantinib	Hepatocelluláris carcinoma kezelése
Italian	Tivantinib	Trattamento del carcinoma epatocellulare
Latvian	Tivantinibs	Hepatocellulāras karcinomas ārstēšana
Lithuanian	Tivantinibas	Hepatoceliulinės karcinomos gydymas
Maltese	Tivantinib	Kura tal-karċinoma epatoċellulari
Polish	Tyvantyinib	Leczenie raka wątrobowokomórkowego
Portuguese	Tivantinib	Tratamento do carcinoma hepatocelular
Romanian	Tivantinib	Tratamentul carcinomului hepatocelular
Slovak	Tivantinib	Liečba hepatocelulárneho karcinómu
Slovenian	Tivantinib	Zdravljenje hepatocelularnega karcinoma
Spanish	Tivantinib	Tratamiento del carcinoma hepatocelular
Swedish	Tivantinib	Behandling av hepatocellulärt karcinom
Norwegian	Tivantinib	Behandling av hepatocellulært karsinom
Icelandic	Tívantíníb	Meðferð við lifrarfrumukrabbameini

[1] At the time of designation