13 November 2015
EMA/COMP/614807/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2-Chloro-N6-(3-iodobenzyl)adenosine-5'-N-methyluronamide for the treatment of hepatocellular carcinoma

On 9 October 2015, orphan designation (EU/3/15/1565) was granted by the European Commission to PBS Regulatory Consulting Group Limited, United Kingdom, for 2-chloro-N6-(3-iodobenzyl)adenosine-5'-N-methyluronamide 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 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

*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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body (metastatic disease). Nexavar (sorafenib) was authorised in the EU for use in hepatocellular carcinoma.

The sponsor has provided sufficient information to show that 2-chloro-N6-(3-iodobenzyl)adenosine-5'-N-methyluronamide might be of significant benefit for patients with hepatocellular carcinoma. The information provided indicates that the medicine stabilises the disease and may improve survival in some patients in whom previous treatments did not work. 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?

This medicine attaches to receptors known as A_3AR receptors, which are present in abnormally high amounts in liver cancer cells. Once attached to these receptors, the medicine interferes with certain signalling pathways in the cancer cells, resulting in the death of the cells. The medicine is also thought to stimulate the body's immune cells known as 'natural killer cells' to attack the cancer cells, thereby enhancing its anti-cancer effects.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

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

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

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 3 September 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

For details of the current sponsor of the orphan designation please refer to the information on the main web page of this Public Summary of Opinion.

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	2-chloro-N6-(3-iodobenzyl)adenosine-5'-N-methyluronamide	Treatment of hepatocellular carcinoma
Bulgarian	2-хлоро-N6-(3-йодобензил)аденозин-5'-N-метилуронамид	Лечение на хепатоцелуларен карцином
Croatian	2-kloro-N6-(3-jodobenzil)adenozin-5'-N-metiluronamid	Liječenje hepatocelularnog karcinoma
Czech	2-chlor-N6-(3-jodbenzyl)adenosin-5'-N-methyluronamide	Léčba hepatocelulárního karcinomu
Danish	2-chlor-N6-(3-iodbenzyl)adenosin-5'-N-methyluronamid	Behandling af hepatocellulært karcinom
Dutch	2-chloor-N6-(3-joodbenzyl)adenosine-5'-N-methyluronamide	Behandeling van hepatocellulair carcinoom
Estonian	2-kloro-N6-(3-jodobensüül)adenosiin-5'-N-metüüluronamiid	Hepatotsellulaarse kartsinoomi ravi
Finnish	2-kloori-N6-(3-jodibentsyyli)adenosiini-5'-N-metyyliuronamidi	Hepatosellulaarisen karsinooman hoito
French	2-chloro-N6-(3-iodobenzyl)adénosine-5'-N-methyluronamide	Traitement du cancer hépatocellulaire
German	2-Chlor-N6-(3-iodbenzyl)adenosin-5'-N-methyluronamid	Behandlung des Leberzellkarzinoms
Greek	2-χλωρο-Ν6-(3-ιωδοβενζυλο)αδενοσίνη-5'-Ν-μεθυλουρονομίδη	Θεραπεία του ηπατοκυτταρικού καρκινώματος
Hungarian	2-Klór-N6-(3-jód-benzil)adenozin-5'-N-methyluronamide	Hepatocelluláris carcinoma kezelése
Italian	2-cloro-N6-(3-iodobenzil)adenosina-5'-N-methyluronamide	Trattamento del carcinoma epatocellulare
Latvian	2-hloro-N6-(3-jodobenzil)adenozīn-5'-N-metiluronamīds	Hepatocellulāras karcinomas ārstēšana
Lithuanian	2-chloro-N6-(3-jodobenzil)adenozino-5'-N-metiluronamidas	Hepatoceliulinės karcinomos gydymas
Maltese	2-Chloro-N6-(3-iodobenzyl)adenosine-5'-N-methyluronamide	Kura tal-karċinoma epatoċellulari
Polish	2-Chloro-N6-(3-jodobenzylo)adenozyno-5'-N-methyluronamid	Leczenie raka wątrobowokomórkowego
Portuguese	2-Cloro-N6-(3-iodobenzil)adenosina-5'-N-metiluronamida	Tratamento do carcinoma hepatocelular
Romanian	2-clor-N6-(3-iodbenzil)adenozin-5'-N-metiluronamidă	Tratamentul carcinomului hepatocelular
Slovak	2-chlór-N6-(3-jodbenzyl)adenozín-5'-N-methyluronamide	Liečba hepatocelulárneho karcinómu

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	2-kloro-N6-(3-jodobenzil)adenozin-5'-N-metiluronamide	Zdravljenje hepatocelularnega karcinoma
Spanish	2-cloro-N6-(3-yodobencil)adenosina-5'-N-metiluronamida	Tratamiento del carcinoma hepatocelular
Swedish	2-klor-N6-(3-jodbensyl)adenosin-5'-N-methyluronamide	Behandling av hepatocellulärt karcinom
Norwegian	2-klor-N6-(3-jodbenzyl)adenosin-5'-N-methyluronamide	Behandling av hepatocellulært karsinom
Icelandic	2-klór-N6-(3-joðbensýl)adenosín-5'-N-methýúrónamíð	Meðferð við lifrarfrumukrabbameini