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EMA/COMP/406301/2011
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Peretinoin for the treatment of hepatocellular carcinoma

On 5 August 2011, orphan designation (EU/3/11/890) was granted by the European Commission to Kowa Pharmaceutical Europe Co. Ltd, United Kingdom, for peretinoin 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 a cancer that has spread to the liver from another location 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 following 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 severe and life-threatening disease 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 is 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, several medicines were authorised in the EU for the treatment of hepatocellular carcinoma. The choice of treatment depended mainly on how advanced the disease was. The only therapies to cure the cancer were surgery to remove the tumour and liver transplantation, but these could only be carried out in very few patients. Other treatments included chemotherapy (medicines to treat cancer) and immunotherapy (medicines that stimulate the immune system to kill

*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. This represents a population of 506,300,000 (Eurostat 2011).

the cancer cells). Radiofrequency ablation (using a probe placed into the tumour to heat and destroy cancer cells) and ethanol injection were also used to remove small tumours.

The sponsor has provided sufficient information to show that peretinoin might be of significant benefit for patients with hepatocellular carcinoma because this medicine works in a different way to existing treatments and early studies show that it might improve the treatment of patients with this condition in preventing the cancer coming back after it has been removed. 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?

Peretinoin belongs to the group of retinoids, substances that are derived from vitamin A. The medicine is thought to activate a protein called the retinoic acid receptor (RAR), which is attached to the DNA in the cells, where it is involved in regulating normal cell growth. This regulation does not take place normally in cancer cells. By activating RAR in cells, peretinoin is expected to stop the growth of cancerous cells, bringing about their regulated cell death and stopping pre-cancerous cells from becoming cancerous.

What is the stage of development of this medicine?

The effects of peretinoin have been evaluated in experimental models.

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

At the time of submission, peretinoin 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 5 May 2011 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	Peretinoin	Treatment of hepatocellular carcinoma
Bulgarian	Перетиноин	Лечение на хепатоцелуларен карцином
Czech	Peretinoin	Léčba hepatocelulárního karcinomu
Danish	Peretinoin	Behandling af hepatocellulært karcinom
Dutch	Peretinoïne	Behandeling van hepatocellulair carcinoom
Estonian	Peretinoiin	Hepatotsellulaarse kartsinoomi ravi
Finnish	Peretinoiini	Hepatosellulaarisen karsinooman hoito
French	Péretinoïne	Traitement du cancer hépatocellulaire
German	Peretinoin	Behandlung des Leberzellkarzinoms
Greek	Περετινοΐνη	Θεραπεία του ηπατοκυτταρικού καρκινώματος
Hungarian	Peretinoin	Hepatocellularis carcinoma kezelése
Italian	Peretinoina	Trattamento del carcinoma epatocellulare
Latvian	Peretinoīns	Hepatocelulāras karcinomas ārstēšana
Lithuanian	Peretinoinas	Hepatoceliulinės karcinomos gydymas
Maltese	Peretinoin	Kura tal-karċinoma epatoċellulari
Polish	Peretynoina	Leczenie raka wątrobowokomórkowego
Portuguese	Peretinoína	Tratamento do carcinoma hepatocelular
Romanian	Peretinoin	Tratamentul carcinomului hepatocelular
Slovak	Peretinoín	Liečba hepatocelulárneho karcinómu
Slovenian	Peretinoin	Zdravljenje hepatocelularnega karcinoma
Spanish	Peretinoína	Tratamiento del carcinoma hepatocelular
Swedish	Peretinoin	Behandling av hepatocellulärt karcinom
Norwegian	Peretinoin	Behandling av hepatocellulært karsinom
Icelandic	Peretínóin	Meðferð við lifrarfrumukrabbameini

¹ At the time of designation