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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Florilglutamic acid (^{18}F) for diagnosis of hepatocellular carcinoma

On 21 March 2016, orphan designation (EU/3/16/1632) was granted by the European Commission to Piramal Imaging GmbH, Germany, for florilglutamic acid (^{18}F) for the diagnosis 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 debilitating in the long term and life-threatening, with patients surviving on average for around 6 to 20 months after diagnosis.

What is the estimated number of patients eligible for diagnosis of the condition?

At the time of designation, the number of patients eligible for diagnosis of hepatocellular carcinoma was estimated to be approximately 2 people in 10,000 in the European Union (EU). This was equivalent to a total of around 103,000 people*, and is below the ceiling for orphan designation. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What methods of diagnosis are available?

At the time of designation, several methods were used for the diagnosis of hepatocellular carcinoma, including histopathology (examining a tissue under the microscope) and biochemical testing (measuring substances produced by tumours), as well as imaging methods such as magnetic

*Disclaimer: For the purpose of the designation, the number of patients eligible for diagnosis of 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 513,700,000 (Eurostat 2016).

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resonance imaging (MRI) and computer tomography (CT) using so-called contrast agents to obtain better images of organs and tissues.

The sponsor has provided sufficient information to show that florilglutamic acid (^{18}F) might be of significant benefit for patients with hepatocellular carcinoma, with preliminary data showing it could improve the detection of small cancer lesions that are currently missed when using authorised contrast agents in MRI scans. 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?

Florilglutamic acid (^{18}F) is a radioactive compound for use with an imaging method known as positron emission tomography (PET). Florilglutamic acid (^{18}F) enters cells through a transport system known as x_C^- which is more abundant in cancer tissue. When injected into the patient, florilglutamic acid (^{18}F) is more effectively taken up by the cancer cells in the liver from where it is expected to emit radiation that can be detected in a PET scan, thereby allowing the cancer to be diagnosed.

What is the stage of development of this medicine?

The effects of florilglutamic acid (^{18}F) 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 diagnosing hepatocellular carcinoma or designated as an orphan medicinal product elsewhere for this indication.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 18 February 2016 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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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	Florilglutamic acid (^{18}F)	Diagnosis of hepatocellular carcinoma
Bulgarian	Флорилглутаминова киселина (^{18}F)	Диагноза на хепатоцелуларен карцином
Croatian	Fluoril glutaminska kiselina (^{18}F)	Dijagnosticiranje hepatocelularnog karcinoma
Czech	Florilglutamová kyselina (^{18}F)	Diagnóza hepatocelulárního karcinomu
Danish	Florilglutaminsyre (^{18}F)	Diagnose af hepatocellulært karcinom
Dutch	Florilglutaminezuur (^{18}F)	Diagnose van hepatocellulair carcinoom
Estonian	Fluoriilglutamiinhape (^{18}F)	Hepatotsellulaarse kasvaja diagnoosimine
Finnish	Florilglutamiinihappo[^{18}F]	Hepatosellulaarisen karsinooman diagnosointi
French	Acide florilglutamique (*^{18}F*)	Diagnostic du cancer hépatocellulaire
German	Fluoropropyl-Glutaminsäure (^{18}F)	Diagnose des Leberzellkarzinoms
Greek	Φθοριλογλουταμινικό οξύ (^{18}F)	Διάγνωση του ηπατοκυτταρικού καρκινώματος
Hungarian	Florilglutaminsav (^{18}F)	Hepatocelluláris carcinoma diagnosztizálása
Italian	Acido florilglutamico (^{18}F)	Diagnosi del carcinoma epatocellulare
Latvian	Florilglutamīnskābe (^{18}F)	Hepatocelulāras karcinomas diagnostika
Lithuanian	Florilglutamo rūgštis (^{18}F)	Hepatoceliulinės karcinomos diagnostika
Maltese	Florilglutamic acid (^{18}F)	Dijanjosi tal-karċinoma epatoċellulari
Polish	Kwas florylglutaminowy (^{18}F)	Rozpoznawanie raka wątrobowokomórkowego
Portuguese	Ácido florilglutâmico (^{18}F)	Diagnóstico do carcinoma hepatocellular
Romanian	Acid fluorilglutamic (^{18}F)	Diagnosticul carcinomului hepatocelular
Slovak	Kyselina Florilglutámová (^{18}F)	Diagnóza hepatocelulárneho karcinómu
Slovenian	Florilglutamična kislina (^{18}F)	Diagnosticiranje hepatocelularnega karcinoma
Spanish	Ácido florilglutámico (^{18}F)	Diagnóstico del carcinoma hepatocellular
Swedish	Florilglutaminsyra (^{18}F)	Diagnos av hepatocellulärt karcinom
Norwegian	Florilglutaminsyre (^{18}F)	Diagnose av hepatocellulært karsinom
Icelandic	Flórilglútamínsýra (^{18}F)	Sjúkdómsgreining lifrarfrumukrabbameins

[1] At the time of designation