23 February 2015
EMA/COMP/736554/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Bevacizumab for the treatment of hereditary haemorrhagic telangiectasia

On 16 December 2014, orphan designation (EU/3/14/1390) was granted by the European Commission to Sophie Dupuis-Girod, France, for bevacizumab for the treatment of hereditary haemorrhagic telangiectasia.

What is hereditary haemorrhagic telangiectasia?

Hereditary haemorrhagic telangiectasia (HHT, also known as Rendu-Osler-Weber syndrome) is a genetic disease that causes abnormalities in the capillaries (small blood vessels that connect arteries with veins). This results in direct connections between arteries and veins, which are fragile, increasing the risk of bleeding. The most common symptoms of the disease are spontaneous and frequent nosebleeds, and red spots on the skin, particularly on the face and hands and in the mouth. Bleeding can also occur in the stomach, gut, brain, liver and lungs, and often leads to anaemia (low red blood cell counts).

HHT is a long-term debilitating disease that may be life threatening because of its complications, such as internal bleeding and effects on organs such as the brain, liver and lungs.

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

At the time of designation, HHT affected not more than 2 in 10,000 people in the European Union (EU). This was equivalent to a total of not more than 102,000 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, no satisfactory methods were authorised in the EU for the treatment of HHT. Different methods were used to control bleeding, which depend mainly on where in the body it occurred. For nosebleeds, patients used nasal humidifiers and lubricants. Laser treatment and surgery were used to stop internal bleeding. In patients with severe liver problems, liver transplantation was

*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 511,100,000 (Eurostat 2014).

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performed. When bleeding caused anaemia, patients were given iron supplements and blood transfusions.

How is this medicine expected to work?

Patients with HHT normally have a genetic mutation (defect) that leads to excess activity of VEGF (vascular endothelial growth factor), a protein that circulates in the blood which is involved in the growth of blood vessels. Excess VEGF activity causes the abnormal growth of blood vessels seen in these patients.

Bevacizumab is a monoclonal antibody (a type of protein) that has been designed to recognise and attach to VEGF and to block its action. By blocking VEGF, bevacizumab is expected to prevent the growth of abnormal blood vessels thus relieving the symptoms of bleeding in HHT.

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 HHT were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for HHT. Orphan designation of the medicine had been granted in the United States for HHT. Bevacizumab is authorised in the EU for the treatment of several types of cancer, including lung, kidney and breast cancer.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 November 2014 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

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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	Bevacizumab	Treatment of hereditary haemorrhagic telangiectasia
Bulgarian	Бевацизумаб	Лечение на наследствена хеморагична телангиектазия
Croatian	Bevacizumab	Liječenje hereditarne hemoragijske teleangiektazije
Czech	Bevacizumab	Léčba hereditární hemoragické telangiektázie
Danish	Bevacizumab	Behandling af hereditær hæmoragisk telangiektasi
Dutch	Bevacizumab	Behandeling van hereditaire hemorrhagische telangiëctasie
Estonian	Bevatsisumaab	Päriliku hemorraagilise teleangiektaasia ravi
Finnish	Bevasitsumabi	Perinnöllisen hemorragisen telangiektasian hoito
French	Bevacizumab	Traitement de la télangiectasie hémorragique héréditaire
German	Bevacizumab	Behandlung der hereditären hämorrhagischen Teleangiektasie
Greek	Μπεβασιζουμάμπη	Θεραπεία της κληρονομικής αιμορραγικής τηλαγγειεκτασίας
Hungarian	Bevacizumab	Örökletes vérzéses hajszálértágulat kezelése
Italian	Bevacizumab	Trattamento della telangiectasia emorragica ereditaria
Latvian	Bevacizumabs	Iedzimtas hemorāģiskas teleangiektāzijas ārstēšana
Lithuanian	Bevacizumabas	Paveldimos hemoraginės telangiektazijos gydymas
Maltese	Bevacizumab	Kura tat-telanġektasija ereditarja emorraġika
Polish	Bewacyzumab	Leczenie wrodzonej naczyniakowatości krwotocznej
Portuguese	Bevacizumab	Tratamento das telangiectasias hemorrágicas hereditárias
Romanian	Bevacizumab	Tratamentul teleangiectaziei hemoragice ereditare
Slovak	Bevacizumab	Liečba hereditárnej hemoragickej teleangiektázie
Slovenian	Bevacizumab	Zdravljenje dedne hemoragične teleangiektazije
Spanish	Bevacizumab	Tratamiento de la telangiectasia hemorrágica hereditaria
Swedish	Bevacizumab	Behandling av ärftlig hemoragisk telangiektasia
Norwegian	Bevasizumab	Behandling av Hereditær hemoragisk telangiektasi
Icelandic	Bevacízúmab	Meðhöndlun á arfgengri blæðinga-háræðavíkkun

[1] At the time of designation