



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

EMA/COMP/780640/2011 Rev.1  
Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

Brivanib alaninate for the treatment of hepatocellular carcinoma

First publication	22 November 2011
Rev.1: withdrawal from the Community Register	11 June 2013
<b>Disclaimer</b> Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

***Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in April 2013 on request of the Sponsor.***

On 27 October 2011, orphan designation (EU/3/11/918) was granted by the European Commission to Bristol-Myers Squibb Pharma EEIG, United Kingdom, for brivanib alaninate 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 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 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 less than 1 in 10,000 people in the European Union (EU). This is equivalent to a total of 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 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 brivanib alaninate might be of significant benefit for patients with hepatocellular carcinoma because it could provide an alternative for patients who cannot take or for whom existing treatments do not work. Early studies show that it might improve the treatment of patients with this condition, particularly if used when existing treatment had failed. 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?**

Brivanib alaninate belongs to a group of medicines called protein kinase inhibitors. These compounds work by blocking enzymes (specialised proteins) known as protein kinases, which can be found in some receptors (such as VEGFR and FGFR ) on the surface of cancer cells. The protein kinases are involved in the growth and spread of the cancer cells and in the development of new blood vessels that supply the tumours. By blocking these enzymes, brivanib alaninate is expected to reduce the growth and spread of the cancer and cut off the blood supply that keeps cancer cells growing.

Brivanib alaninate is expected to be taken by mouth.

## **What is the stage of development of this medicine?**

The effects of brivanib alaninate have been evaluated in experimental models.

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

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

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 September 2011 recommending the granting of this designation.

---

\*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. At the time of designation, this represented a population of 507,700,000 (Eurostat 2011).

---

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:

Bristol-Myers Squibb Pharma EEIG  
Uxbridge Business Park  
Sanderson Road  
Uxbridge UB8 1DH  
United Kingdom  
Telephone: +44 18 95 52 35 17  
Telefax: +44 20 87 54 35 76  
E-mail: [medical.information@bms.com](mailto:medical.information@bms.com)

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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Brivanib alaninate	Treatment of hepatocellular carcinoma
Bulgarian	Бриваниб аланинат	Лечение на хепатоцелуларен карцином
Czech	Brivanib alaninat	Léčba hepatocelulárního karcinomu
Danish	Brivanibalaninat	Behandling af hepatocellulært karcinom
Dutch	Brivanibalaninaat	Behandeling van hepatocellulair carcinoom
Estonian	Brivaniibalaninaat	Hepatotsellulaarse kartsinoomi ravi
Finnish	Brivanibialaninaatti	Hepatosellulaarisen karsinooman hoito
French	brivanib alaninate	Traitement du cancer hépatocellulaire
German	Brivanibalaninat	Behandlung des Leberzellkarzinoms
Greek	Αλανινική μπριβανίμπη	Θεραπεία του ηπατοκυτταρικού καρκινώματος
Hungarian	Brivanib-alaninát	Hepatocelluláris carcinoma kezelése
Italian	Brivanib alaninato	Trattamento del carcinoma epatocellulare
Latvian	Brivaniba alanināts	Hepatocellulāras karcinomas ārstēšana
Lithuanian	Brivanibo alaninatas	Hepatoceliulinės karcinomos gydymas
Maltese	Brivanib alaninate	Kura tal-karċinoma epatoċellulari
Polish	Alaninian briwanibu	Leczenie raka wątrobowokomórkowego
Portuguese	Alaninato de brivanib	Tratamento do carcinoma hepatocelular
Romanian	Brivanib alaninat	Tratamentul carcinomului hepatocelular
Slovak	Brivanib alaninát	Liečba hepatocelulárneho karcinómu
Slovenian	Brivanib alaninat	Zdravljenje hepatocelularnega karcinoma
Spanish	Brivanib alaninato	Tratamiento del carcinoma hepatocelular
Swedish	Brivanibalaninat	Behandling av hepatocellulärt karcinom
Norwegian	Brivanibalaninat	Behandling av hepatocellulært karsinom
Icelandic	Brivaníð alanínat	Meðferð við lifrarfrumukrabbameini

<sup>1</sup> At the time of designation