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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Ibrutinib for the treatment of graft-versus-host disease

On 18 November 2016, orphan designation (EU/3/16/1780) was granted by the European Commission to Janssen-Cilag International N.V, Belgium, for ibrutinib for the treatment of graft-versus-host disease.

What is graft-versus-host disease?

Graft-versus-host disease is a complication that can affect patients who have had allogeneic haematopoietic (blood) stem-cell transplantation to treat diseases of the blood such as leukaemia (a cancer of the white blood cells). The procedure involves a patient receiving stem cells from a donor to help restore the bone marrow, which produces new healthy blood cells.

Graft-versus-host disease occurs when transplanted cells recognise the patient's body as 'foreign' and attack the patient's organs, such as the stomach, gut, skin and liver, leading to organ damage. The disease may happen shortly after transplantation or later on, in which case a wider range of organs can be involved.

Graft-versus-host disease is a serious and life-threatening disease with a high mortality rate.

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

At the time of designation, graft-versus-host disease affected approximately 0.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 21,000 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 European Union (EU) for the treatment of graft-versus-host disease, such as ciclosporin and corticosteroids. Treatment aimed to

*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 513,700,000 (Eurostat 2016).

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reduce the activity of transplanted cells involved in graft-versus-host disease, thereby reducing their ability to attack the patient's organs.

The sponsor has provided sufficient information to show that ibrutinib might be of significant benefit for patients with graft-versus-host disease because early studies found improvement in patients who had not improved on medicines authorised for the condition. 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?

Ibrutinib blocks two enzymes. The first is called Bruton's tyrosine kinase (Btk), which is mostly found in B cells, and the second is interleukin-2-inducible T-cell kinase (ITK), which stimulates T cells. B cells and T cells are part of the immune system, the body's natural defences. Both B cells and T cells in the transplant are thought to be involved in the attack on the patient's organs. By blocking Btk and ITK, ibrutinib is expected to reduce the activity of both types of cells and improve the symptoms of graft-versus-host disease.

What is the stage of development of this medicine?

The effects of ibrutinib have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with ibrutinib in patients with graft-versus-host disease were ongoing.

At the time of submission, ibrutinib was authorised in the EU under the name Imbruvica for mantle cell lymphoma, chronic lymphocytic leukaemia and Waldenström's macroglobulinaemia.

At the time of submission, the medicine was not authorised anywhere in the EU for graft-versus-host disease. Orphan designation of ibrutinib had been granted in the United States for graft-versus-host disease.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 6 October 2016 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:

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	Ibrutinib	Treatment of graft-versus-host disease
Bulgarian	Ибрутиниб	Лечение на болестта на присадката срещу приемателя
Croatian	Ibrutinib	Liječenje reakcije presatka protiv primatelja
Czech	Ibrutinib	Léčba reakce štěpu proti hostiteli
Danish	Ibrutinib	Behandling af graft versus host reaktion
Dutch	Ibrutinib	Behandeling van graft versus host ziekte
Estonian	Ibrutiniib	Graft versus host haiguse ravi
Finnish	Ibrutinibi	Käänteishyljintäreaktion hoito
French	Ibrutinib	Traitement de la réaction du greffon contre l'hôte
German	Ibrutinib	Behandlung der Graft-versus-Host-Reaktion
Greek	Ιβρουτινίμπη	Θεραπεία της αντίδρασης του μοσχεύματος
Hungarian	Ibrutinib	Graft-versus-host betegség kezelése
Italian	Ibrutinib	Trattamento della reazione del trapianto contro l'ospite
Latvian	Ibrutinibs	Saimnieka-transplantāta slimības ārstēšana
Lithuanian	Ibrutinibas	Transplantato atmetimo ligos gydymas
Maltese	Ibrutinib	Kura tal-marda tat-tessut għat-trapjant kontra dak li jirċievih
Polish	Ibrutynib	Leczenie choroby przeszczep przeciw gospodarzowi
Portuguese	Ibrutinib	Tratamento da reacção do enxerto contra o hospedeiro
Romanian	Ibrutinib	Tratamentul reacţiei grefei contra gazdei
Slovak	Ibrutinib	Liečba reakcie štepu proti hostiteľovi
Slovenian	Ibrutinib	Zdravljenje bolezni presadka proti gostitelju
Spanish	Ibrutinib	Tratamiento de la enfermedad de injerto contra huésped
Swedish	Ibrutinib	Behandling av graft-värd host reaktion
Norwegian	Ibrutinib	Behandling av graft-versus-host -reaksjon
Icelandic	Íbrútíníb	Til meðferðar á hýsilssótt

[1] At the time of designation