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Public summary of opinion on orphan designation

Zanubrutinib for the treatment of lymphoplasmatic lymphoma

On 29 May 2019, orphan designation (EU/3/19/2167) was granted by the European Commission to BeiGene Ireland Limited, Ireland, for zanubrutinib, also known as (BGB-3111), for the treatment of lymphoplasmatic lymphoma.

What is lymphoplasmatic lymphoma?

Lymphoplasmacytic lymphoma is a cancer of a type of white blood cell called B lymphocytes or B cells. In lymphoplasmacytic lymphoma, the B cells multiply too quickly and live for too long, so there are too many of them in places like the bone marrow, lymph nodes or spleen. The first signs of the disease are usually weakness and tiredness. In the most common type of lymphoplasmacytic lymphoma, called Waldenström's macroglobulinaemia, the abnormal B cells produce too much of a type of blood protein called immunoglobulin-type-M paraprotein (IgM paraprotein), which makes the blood too thick and can lead to disorders such as eye problems, heart failure, haemolytic anaemia (destruction of red blood cells) and effects on the nervous system.

Lymphoplasmacytic lymphoma is a life-threatening and long-term debilitating disease due to damage to the bone marrow and other organs.

What is the estimated number of patients affected by lymphoplasmatic lymphoma?

At the time of designation, lymphoplasmatic lymphoma affected approximately 1.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 73,000 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).

*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 518,400,000 (Eurostat 2019).

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What treatments are available?

At the time of designation, the main treatments for diseases such as lymphoplasmacytic lymphoma available in the EU included immunotherapy (medicines that act on the body's immune system), and combinations of immunotherapy with chemotherapy (medicines to treat cancer). A technique called plasmapheresis was also used to remove unwanted IgM paraprotein from the plasma (the liquid part of the blood).

The sponsor has provided sufficient information to show that zanubrutinib might be of significant benefit for patients with lymphoplasmacytic lymphoma. Early studies showed that patients whose disease did not respond to or had come back after previous treatment responded to treatment with this medicine. In addition, indirect comparisons with data from a currently authorised medicine suggest improved outcomes with this medicine. These assumptions 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?

Zanubrutinib is expected to work in patients with lymphoplasmacytic lymphoma by blocking the action of an enzyme known as Bruton's tyrosine kinase (BTK). BTK is important for the growth of B cells, including the abnormal B cells of the cancer. By blocking the action of BTK, it is expected that the medicine will slow the progression of the disease.

What is the stage of development of this medicine?

The effects of zanubrutinib have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with zanubrutinib in patients with lymphoplasmatic lymphoma were ongoing.

At the time of submission, zanubrutinib was not authorised anywhere in the EU for the treatment of lymphoplasmatic lymphoma or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 17 April 2019, 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	Zanubrutinib	Treatment of lymphoplasmatic lymphoma
Bulgarian	Занубрутиниб	Лечение на лимфоплазмоцитен лимфом
Croatian	Zanubrutinib	Liječenje limfoplazmocitnog limfoma
Czech	Zanubrutinib	Léčba lymfoplazmatického lymfomu
Danish	Zanubrutinib	Behandling af Waldenströms makroglobulinæmi
Dutch	Zanubrutinib	Behandeling van lymfoplasmacytair lymfoom
Estonian	Zanubrutiniib	Lümfoplasmaatilise luümfoomi ravi
Finnish	Zanubrutinibi	Lymfoplasmasyyttisen lymfooman hoito
French	Zanubrutinib	Traitement du lymphome lymphoplasmocytaire
German	Zanubrutinib	Behandlung des lymphoplasmazytoiden Lymphoms
Greek	Ζανουμπρουτινίμπη	Θεραπεία του λεμφοπλασματοκυτταρικού λεμφώματος
Hungarian	Zanubrutinib	Lymphoplasmacytás lymphoma kezelése
Italian	Zanubrutinib	Trattamento del linfoma linfoplasmacitico
Latvian	Zanubrutinibs	Limfoplazmocitārās limfomas ārstēšana
Lithuanian	Zanubrutinibas	Limfoplazmocitinės limfomos gydymas
Maltese	Zanubrutinib	Kura tal-limfoma limfoplasmatika
Polish	Zanubrutynib	Leczenie chłoniaków limfoplazmocytowych
Portuguese	Zanubrutinib	Tratamento do linfoma linfoplasmocítico
Romanian	Zanubrutinib	Tratamentul limfomului limfoplasmocitar
Slovak	Zanubrutinib	Liečba lymfoplazmacytového lymfómu
Slovenian	Zanubrutinib	Zdravljenje limfoplazmocitnega limfoma
Spanish	Zanubrutinib	Tratamiento del linfoma linfoplasmacítico
Swedish	Zanubrutinib	Behandling av lymfoplasmacytiskt lymfom
Norwegian	Zanubrutinib	Behandling av lymfoplasmacytisk lymfom
Icelandic	Zanubrutinib	Meðferð við eitilfrumu- og plasmafrumueitlakrabbameini

[1] At the time of designation