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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Acalabrutinib for the treatment of lymphoplasmacytic lymphoma

On 21 March 2016, orphan designation (EU/3/16/1626) was granted by the European Commission to Acerta Pharma, BV, the Netherlands, for acalabrutinib for the treatment of lymphoplasmacytic lymphoma.

What is lymphoplasmacytic 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 lymphoplasmacytic lymphoma?

At the time of designation, lymphoplasmacytic lymphoma affected less than 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 5,000 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, 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

*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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combinations of immunotherapy with chemotherapy (medicines intended to kill cancer cells). A technique called plasmapheresis was also used to replace the patient's plasma (the liquid part of the blood which contains the IgM paraprotein) with healthy plasma.

The sponsor has provided sufficient information to show that acalabrutinib might be of significant benefit for patients with lymphoplasmacytic lymphoma, because early studies showed that patients whose disease had come back after previous treatment responded to treatment with this medicine. In addition, preliminary results indicate that there might be fewer side effects with acalabrutinib than with the medicine ibrutinib, which is authorised for this condition. 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?

Acalabrutinib is expected to work by blocking an enzyme called Bruton's tyrosine kinase (Btk), which is found in B cells. Btk promotes growth and survival of B cells. By blocking Btk, acalabrutinib is expected to slow down the build-up of cancerous B cells in lymphoplasmacytic lymphoma, thereby delaying or stopping the progression of the disease.

The medicine is expected to be taken by mouth.

What is the stage of development of this medicine?

The effects of acalabrutinib have been evaluated in experimental models.

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

At the time of submission, acalabrutinib was not authorised anywhere in the EU for lymphoplasmacytic lymphoma. Orphan designation of acalabrutinib had been granted in the United States for Waldenström macroglobulinaemia.

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	Acalabrutinib	Treatment of lymphoplasmacytic lymphoma
Bulgarian	Акалабрутиниб	Лечение на лимфоплазмоцитен лимфом
Croatian	Akalabrutinib	Liječenje limfoplazmocitnog limfoma
Czech	Acalabrutinib	Liječenje limfoplazmocitnog limfoma
Danish	Acalabrutinib	Behandling af Waldenströms makroglobulinæmi
Dutch	Acalabrutinib	Behandeling van lymfoplasmacytair lymfoom
Estonian	Akalabrutiniib	Lümfoplasmatsütaarse lümfoomi ravi
Finnish	Akalabrutinibi	Lymfoplasmasyyttisen lymfooman hoito
French	Acalabrutinib	Traitement du lymphome lymphoplasmocytaire
German	Acalabrutinib	Behandlung des lymphoplasmazytoiden Lymphoms
Greek	Ακαλαβρουτινίμπη	Θεραπεία του λεμφοπλασματοκυτταρικού λεμφώματος
Hungarian	Akalabrutinib	Lymphoplasmacytás lymphoma kezelése
Italian	Acalabrutinib	Trattamento del linfoma linfoplasmacitico
Latvian	Akalabrutinibs	Limfoplazmocitārās limfomas ārstēšana
Lithuanian	Akalabrutinibas	Limfoplazmacitinės limfomos gydymas
Maltese	Acalabrutinib	Kura tal-limfoma limfoplasmaċitika
Polish	Akalabrutynib	Leczenie chłoniaków limfoplazmocytowych
Portuguese	Acalabrutinib	Tratamento do linfoma linfoplasmocítico
Romanian	Acalabrutinib	Tratamentul limfomului limfoplasmocitar
Slovak	Akalabrutinib	Liečba lymfoplazmacytového lymfómu
Slovenian	Akalabrutinib	Zdravljenje limfoplazmacitnega limfoma
Spanish	Acalabrutinib	Tratamiento del linfoma linfoplasmacítico
Swedish	Acalabrutinib	Behandling av lymfoplasmacytiskt lymfom
Norwegian	Acalabrutinib	Behandling av lymfoplasmacytisk lymfom
Icelandic	Acalabrútíníb	Meðferð við eitilfrumu- og plasmafrumueitlakrabbameini

[1] At the time of designation