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Public summary of opinion on orphan designation

Lisocabtagene maraleucel for the treatment of primary mediastinal large B-cell lymphoma

On 19 November 2018, orphan designation (EU/3/18/2099) was granted by the European Commission to Celgene Europe Limited, United Kingdom, for lisocabtagene maraleucel for the treatment of primary mediastinal large B-cell lymphoma.

What is primary mediastinal large B-cell lymphoma?

Primary mediastinal large B-cell lymphoma is an aggressive cancer of a type of white blood cell called B lymphocytes, or B cells. In patients with this cancer, the B cells multiply quickly and live for too long. Patients usually present with a tumour mass in the chest cavity, which may cause breathlessness, coughing and swelling in the face and arms.

The disease is more common in women and typically affects people younger than 40 years. Although some people with primary mediastinal large B-cell lymphoma can be cured, it remains a serious and life-threatening disease, particularly when the disease is diagnosed late or has come back after initial treatment.

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

At the time of designation, primary mediastinal large B-cell lymphoma affected approximately 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 26,000 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 medicine Yescarta (axicabtagene ciloleucel) was authorised for the treatment of primary mediastinal large B-cell lymphoma. Chemotherapy (medicines to treat cancer) was also used, usually in combination with other medicines called monoclonal antibodies 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 517,400,000 (Eurostat 2018).



sometimes in combination with radiotherapy (treatment with radiation). Autologous haematopoietic (blood) stem-cell transplantation was used in patients at risk of the disease coming back after treatment. This is a complex procedure where patients receive their own stem cells to help restore the bone marrow so that it can produce healthy blood cells.

The sponsor has provided sufficient information to show that lisocabtagene maraleucel might be of significant benefit for patients with primary mediastinal large B-cell lymphoma. Preliminary studies showed that patients whose cancer came back despite several previous treatments responded to the medicine. Also, in patients treated with the medicine there were fewer reports of a serious side effect called 'cytokine release syndrome' than with the authorised treatment Yescarta.

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?

The abnormal B cells in patients with primary mediastinal large B-cell lymphoma produce a protein on their surface called CD19.

This medicine is made up of immune cells (called T cells) which are taken from the patient. The T cells are modified in the laboratory with a virus that carries a gene into the T cells so that they can recognise and attach to CD19. The modified T cells are then given back to the patient, and they are expected to attach to CD19 on the cancer cells and kill them. These T cells are also expected to activate other T cells from the patient to act against the cancer cells.

The type of virus used in this medicine ('lentivirus') is modified in order not to cause disease in humans.

What is the stage of development of this medicine?

The effects of lisocabtagene maraleucel 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 primary mediastinal large B-cell lymphoma were ongoing.

At the time of submission, lisocabtagene maraleucel was not authorised anywhere in the EU for primary mediastinal large B-cell lymphoma. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 18 October 2018 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Lisocabtagene maraleucel	Treatment of primary mediastinal large-B-cell lymphoma
Bulgarian	Лизокабтаген маралеуцел	Лечение на първичен медиастинален В-едроклетъчен лимфом
Croatian	Lizokaptagen maraleucel	Liječenje primarnog mediastinalnog B-velikostaničnog limfoma
Czech	Lisocabtagen maraleucel	Léčba primárního mediastinálního velkobuněčného B lymfomu
Danish	Lisocabtagenmaraleucel	Behandling af primært mediastinalt storcellet B-celle lymfom
Dutch	Lisocabtagene maraleucel	Behandeling van primair mediastinaal grootcellig B-cellymfoom
Estonian	Lisokabtageen maraleutseel	Esmase mediastinaalse B-suurrakkliimfoomi ravi
Finnish	Lisocabtagene maraleucel	Primaarin mediastinaalisen suurisoluisen B-solulymfooman hoitoon
French	Lisocabtagene maraleucel	Traitement du lymphome médiastinal primitif à grandes cellules B
German	Lisocabtagen maraleucel	Behandlung des primär mediastinalen großzelligen B-Zell-Lymphoms
Greek	Lisocabtagene maraleucel	Θεραπεία πρωτοπαθούς λεμφώματος μεσοθωρακίου από μεγάλα Β-κύτταρα
Hungarian	Lisocabtagen maraleucel	Elsődleges mediastinalis nagysejtes B-sejt lymphoma kezelése
Italian	Lisocabtagene maraleucel	Trattamento del linfoma primitivo del mediastino a grandi cellule B
Latvian	Lizokabtagēna maraleicels	Videnes lielo B šūnu primārās limfomas ārstēšana
Lithuanian	Lizokabtagenas maraleucelis	Pirminės tarpuplaučio didelių B ląstelių limfomos gydymas
Maltese	Lisokabtaġen maralewċel	Kura tal-limfoma primarja medjastinali taċ-ċelloli B kbar
Polish	Lizokabtagen maraleucel	Leczenie pierwotnego śródpiersiowego chłoniaka dużych komórek B
Portuguese	Lisocabtagene maraleucel	Tratamento do linfoma primário do mediastino de grandes células B
Romanian	Lisocabtagen maraleucel	Tratamentul limfomului primar mediastinal cu celule B mari
Slovak	Lisocabtagen maraleucel	Liečba primárneho mediastinálneho veľkobunkového B-lymfómu
Slovenian	Lizokabtagen maraleucel	Zdravljenje primarnega mediastinalnega velikoceličnega B-limfoma

¹ At the time of designation

Language	Active ingredient	Indication
Spanish	Lisocabtagene maraleucel	Tratamiento del linfoma mediastínico primario de células B grandes
Swedish	Lisocabtagen maraleucel	Behandling av primärt mediastinalt storcelligt B-cellslymfom
Norwegian	Lisokabtagen maraleucel	Behandling av primært mediastinalt storcellet B-cellelymfom
Icelandic	Lísókabtagen maralefsel	Meðferð á frumkomnu stórfrumu B-eitilfrumukrabbameini í miðmæti

Withdrawn