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EMA/742235/2017

Public summary of opinion on orphan designation

Venetoclax for the treatment of mantle cell lymphoma

On 12 December 2017, orphan designation (EU/3/17/1954) was granted by the European Commission to Abbvie Ltd., United Kingdom, for venetoclax for the treatment of mantle cell lymphoma.

What is mantle cell lymphoma?

Mantle cell lymphoma is an aggressive cancer of a type of white blood cell called B lymphocytes, or B cells. In mantle cell lymphoma, the B cells multiply quickly and live for too long, so they build up in the lymph nodes. The first sign of the disease is usually a lump in the neck, under the arm or in the groin, caused by an enlarged lymph node. Patients may also have fever, weight loss, tiredness and night sweats. Mantle cell lymphoma is usually diagnosed in people aged over 50 years. It is more common in men than in women.

Mantle cell lymphoma is a long-term debilitating and life-threatening disease associated with poor survival.

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

At the time of designation, mantle cell lymphoma affected less than 0.6 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 31,000 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 mantle cell lymphoma included chemotherapy (medicines to treat cancer), immunotherapy (medicines that act on the body's immune system) and radiotherapy (treatment with radiation). Bortezomib, ibrutinib, lenalidomide and temsirolimus were specifically authorised in the EU for the treatment of mantle cell lymphoma that has come back after previous treatment or has not responded to other treatments. Haematopoietic (blood) stem-cell

*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 515,700,000 (Eurostat 2017).

transplantation was also used. This is a procedure where cells in the patient's bone marrow are replaced by stem cells to form new bone marrow that produces healthy blood cells.

The sponsor has provided sufficient information to show that venetoclax might be of significant benefit for patients with mantle cell lymphoma. This is because early studies show that venetoclax might improve the outcome of patients whose disease has come back or not improved with previous treatment. 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?

Venetoclax is expected to work by blocking proteins called Bcl-2. These proteins prevent the natural process that leads to cell death (apoptosis). Bcl-2 proteins can be found in high levels in cancer cells. By blocking the action of these proteins, the medicine is expected to make cancer cells more responsive to the natural process that causes their death, and this can slow down the growth of the cancer.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with venetoclax in patients with mantle cell lymphoma were ongoing.

At the time of submission, the medicine was authorised in the EU as Venclyxto for chronic lymphocytic leukaemia.

Venetoclax was not authorised anywhere in the EU for mantle cell lymphoma or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 31 October 2017 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	Venetoclax	Treatment of mantle cell lymphoma
Bulgarian	Венетоклакс	Лечение на мантелно-клетъчна лимфом
Croatian	Venetoklaks	Liječenje limfoma plaštenih stanica
Czech	Venetoclax	Léčba lymfomu z pláštěvé zóny
Danish	Venetoclax	Behandling af mantelcellymfom
Dutch	Venetoclax	Behandeling van mantelcellymfoom
Estonian	Venetoklaks	Mantelrakulise lümfoomi ravi
Finnish	Venetoklaksi	Manttelisolu-lymfooman hoito
French	Venetoclax	Traitement des lymphomes du manteau
German	Venetoclax	Behandlung von Mantelzelllymphom
Greek	Βενετοκλάξη	Θεραπεία του λεμφώματος μανδύκων κυττάρων
Hungarian	Venetoklax	Köpenysejtes lymphoma kezelése
Italian	Venetoclax	Trattamento del linfoma con cellule a mantello
Latvian	Venetoklaks	Mantijšūnu limfomas ārstēšana
Lithuanian	Venetoklaksas	Mantijos ląstelių limfomos gydymas
Maltese	Venetoclax	Kura tal-linfoma taċ-ċelloli tal-mantell
Polish	Wenetoklaks	Leczenie chłoniaków z komórek płaszczowych
Portuguese	Venetoclax	Tratamento de linfoma de células do manto
Romanian	Venetoclax	Tratamentul limfomului cu celule în manta
Slovak	Venetoklax	Liečba lymfómu pláštovej zóny
Slovenian	Venetoklaks	Zdravljenje limfoma plaščnih celic
Spanish	Venetoclax	Tratamiento del linfoma de células del manto
Swedish	Venetoclax	Behandling av mantelcellslymfom
Norwegian	Venetoclax	Behandling av mantelcelle-lymfom
Icelandic	Venetóklax	Meðferð möttulfrumu eitlakrabbameins

¹ At the time of designation