

13 December 2016
EMA/688679/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Valproic acid for the treatment of diffuse large B-cell lymphoma

On 18 November 2016, orphan designation (EU/3/16/1792) was granted by the European Commission to Valcuria AB, Sweden, for valproic acid for the treatment of diffuse large B-cell lymphoma.

What is diffuse large B-cell lymphoma?

Diffuse large B-cell lymphoma is a type of blood cancer and the most common form of a group of blood cancers known as non-Hodgkin lymphomas.

Diffuse large B-cell lymphoma affects a type of white blood cell called B lymphocytes, or B cells. In patients with this cancer, the B cells multiply too quickly and live for too long, so there are too many of them in the lymph nodes. The first sign of the disease is usually a lump in the neck, under the arm or in the groin area, which is caused by an enlarged lymph node. Patients with diffuse large B-cell lymphoma may also have fever, tiredness, night sweats or weight loss that have no obvious cause.

Although some people with diffuse 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 treatment.

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

At the time of designation, diffuse large B-cell lymphoma affected approximately 4.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 221,000 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 for the treatment of diffuse large B-cell lymphoma in the EU. The main treatment was chemotherapy (medicines to treat cancer) usually in combination with medicines called monoclonal antibodies and sometimes with radiotherapy (treatment with radiation). Autologous haematopoietic (blood) stem-cell transplantation was also used in patients at risk of the disease coming back after treatment. This is a procedure where the patient's bone

*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).

marrow is replaced with the patient's own stem cells to form new bone marrow that produces healthy blood cells.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with diffuse large B-cell lymphoma. This is based on preliminary results in patients showing that the medicine can be added to standard treatment and may prolong survival. 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?

Valproic acid (or valproate) is a well-known medicine used in the EU to treat epilepsy and bipolar disorder. In diffuse large B-cell lymphoma, the medicine is expected to work by blocking the activity of histone deacetylases (HDACs), proteins that promote cell division. By blocking HDACs, the medicine is expected to stop the cancer cells from dividing and multiplying, leading to cell death. Valproic acid is also thought to increase the sensitivity of the cancer cells to standard cancer treatments, for example by increasing production of CD20 receptors, which are the target of the cancer medicine rituximab. This increases the effectiveness of rituximab treatment, helping to control the cancer and improve survival.

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 the medicine in patients with diffuse large B-cell lymphoma were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for diffuse large B-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 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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Valproic acid	Treatment of diffuse large B-cell lymphoma
Bulgarian	Натриев валпроат	Лечение на дифузен В-едроклетъчен лимфом
Croatian	Valproična kiselina	Liječenje difuznog limfoma velikih B-stanica
Czech	Kyselina valproová	Léčba velkobuněčného difuzního B-lymfomu
Danish	Valproesyre	Behandling af diffust storcellet B-celle lymfom
Dutch	Valproïnezuur	Behandeling van diffuus grootcellig B-cel-lymfoom
Estonian	Valproaathape	Diffuusse suure B-rakulise lümfoomi ravi
Finnish	Valproaattihappo	Diffuusin suurisoluisen B-solulymfooman hoito
French	Acide valproïque	Traitement du lymphome diffus à grandes cellules B
German	Valproinsäure	Behandlung des diffusen großzelligen B-Zell-Lymphoms
Greek	βαλπροϊκό οξύ	Θεραπεία του διάχυτου μεγαλοκυτταρικού λεμφώματος Β-κυττάρου (DLBCL)
Hungarian	Valproát sav	Diffúz nagy B-sejtes lymphoma kezelése
Italian	Acido valproico	Terapia del Linfoma non-Hodgkin diffuso a grandi cellule di tipo B (DLBCL)
Latvian	Valproiskābe	Difūzas lielo B šūnu limfomas ārstēšana
Lithuanian	Valproinė rūgštis	Difuzinės stambiųjų B ląstelių limfomos gydymas
Maltese	Valproic acid	Kura tal-limfoma taċ-ċelluli tat-tip B kbar mxerrda
Polish	Kwas walproinowy	Leczenie rozlanego chłoniaka z dużych limfocytów B
Portuguese	Ácido valpróico	Tratamento do linfoma difuso de grandes células B
Romanian	Acid valproic	Tratamentul limfomului difuz cu celule B mari
Slovak	Valproát sodný	Liečba difúzneho veľkobunkového lymfómu z buniek B
Slovenian	Natrijev valproat	Zdravljenje razširjenega limfoma velikih B celic
Spanish	Ácido valproico	Tratamiento del linfoma difuso de células B grandes
Swedish	Natriumvalproat	Behandling av diffusa storcelliga B-cells lymfom
Norwegian	Natriumvalproat	Behandling av diffust storcellet B-celle lymfom
Icelandic	Valpróín sýra	Til meðferðar á dreifðu stórfrumu B frumu eitlakraðbameini

¹ At the time of designation