



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

(Z)-3-(3-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylohydrazide for the treatment of diffuse large B-cell lymphoma

On 22 August 2014, orphan designation (EU/3/14/1317) was granted by the European Commission to Clinipace GmbH, Germany, for (Z)-3-(3-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylohydrazide for the treatment of diffuse large B-cell lymphoma.

### What is diffuse large B-cell lymphoma?

Diffuse large B-cell lymphoma is the most common cancer of the lymphatic system, a network of vessels that transport fluid (lymph) from tissues through the lymph nodes and into the bloodstream. The cancer 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 initial treatment.

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

At the time of designation, diffuse large B-cell lymphoma affected approximately 2.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 123,000 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).

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\*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 511,100,000 (Eurostat 2014).



## 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), sometimes in combination 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 complex procedure where patients receive their own stem cells to help restore the bone marrow.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with diffuse large B-cell lymphoma because early studies show a positive response in patients with progressive disease who cannot be treated with existing therapies. 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?

This medicine is expected to work in patients with diffuse large B-cell lymphoma by blocking the action of a protein called exportin1 (XPO1). XPO1 is found at higher levels in many cancer cells, where it prevents the actions of proteins that help stop cancer growth. By blocking XPO1, the medicine is expected to enhance the action of these anti-cancer proteins and bring about the death of the cancer cells, thereby slowing the progression of the disease.

## 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. Orphan designation of the medicine had been granted in the United States for the treatment of this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 July 2014 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:

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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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	(Z)-3-(3-(3,5-bis(trifluoromethyl)phenyl)-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylohydrazide	Treatment of diffuse large B-cell lymphoma
Bulgarian	(Z)-3-(3-(3,5-бис(трифлуорометил)фенил-1H-1,2,4-триазол-1-ил)-N'-(пиразин-2-ил)акрил хидразид	Лечение на дифузен В-едроклетъчен лимфом
Croatian	(Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-il)-N'-(pirazin-2-il)akrilhidrazid	Liječenje difuznog limfoma velikih B-stanica
Czech	(Z)-3-(3-(3,5-bis(trifluorometyl)fenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)akrylhydrazid	Léčba velkobuněčného difuzního B-lymfomu
Danish	(Z)-3-(3-(3,5-bis(trifluoromethyl)phenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)akrylhydrazid	Behandling af diffust storcellet B-celle lymfom
Dutch	(Z)-3-(3-(3,5-bis(trifluormethyl)fenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylhydrazide	Behandeling van diffuus grootcellig B-cel-lymfoom
Estonian	(Z)-3-(3-(3,5-bis(trifluorometüül)fenüül-1H-1,2,4-triasool-1-üül)-N'-(pürasiin-2-yl)akrüül-hüdrasiin	Diffuusse suure $\beta$ -rakulise lümfoomi ravi
Finnish	(Z)-3-(3-(3,5-bis(trifluorometyyli)fenyyli-1H-1,2,4-triatsoli-1-yl)-N'-(pyratsiini-2-yl)akryylihydratsidi	Diffuusin suurisoluisen B-solulymfooman hoito
French	(Z)-3-(3-(3,5-bis(trifluorométhyl)phényl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylhydrazide	Traitement du lymphome diffus à grandes cellules B
German	(Z)-3-(3-(3,5-bis(Trifluormethyl)phenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylhydrazid	Behandlung des diffusen großzelligen B-Zell-Lymphoms
Greek	(Z)-3-(3-(3,5-δισ(τριφθορομεθυλο)φαινυλο-1H-1,2,4-τριαζολ-1-υλο)-N'-(πυραζιν-2-υλο)ακρυλυδραζίδιο	Θεραπεία του διάχυτου μεγαλοκυτταρικού λεμφώματος Β-κυττάρου (DLBCL)
Hungarian	(Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-yl)-N'-(pirazin-2-yl)akrilhidrazid	Diffúz nagy B-sejtes lymphoma kezelése
Italian	(Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-yl)-N'-(pirazina-2-yl)acrilidrazide	Terapia del Linfoma non-Hodgkin diffuso a grandi cellule di tipo B (DLBCL)
Latvian	(Z)-3-(3-(3,5-bis(trifluormetil)fenil-1H-1,2,4-triazol-1-il)-N'-(pirazīn-2-il)akrilhidrazīds	Difūzas lielo B šūnu limfomas ārstēšana
Lithuanian	(Z)-3-(3-(3,5-bis(trifluorometil)fenil)-1H-1,2,4-triazol-1-il)-N'-(pirazin-2-il)akrilhidrazidas	Difuzinės stambiujų B ląstelių limfomos gydymas
Maltese	(Z)-3-(3-(3,5-bis(trifluoromethyl)phenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)acrylohydrazide	Kura tal-limfoma taċ-ċelluli tat-tip B kbar mxerrda
Polish	(Z)-3-(3-(3,5-bis(trifluorometylo)fenylo-1H-1,2,4-triazol-1-yl)-N'-(pirazyn-2-yl)akrylohydrazyd	Leczenie rozlanego chłoniaka z dużych limfocytów B
Portuguese	(Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-il)-N'-(pirazin-2-il)acrilhidrazida	Tratamento do linfoma difuso de grandes células B
Romanian	(Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-il)-N'-(pirazin-2-il)acrilhidrazidă	Tratamentul limfomului difuz cu celule B mari

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
Slovak	(Z)-3-(3-(3,5-bis(trifluórometyl)fenyl-1H-1,2,4-triazol-1-yl)-N'-(pirazín-2-yl)akrylhydrazid	Liečba difúzneho veľkobunkového lymfómu z buniek B
Slovenian	(Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-il)-N'-(pirazin-2-il)akrilhidrazid	Zdravljenje razširjenega limfoma velikih B celic
Spanish	(Z)-3-(3-(3,5-bis(trifluorometil)fenil-1H-1,2,4-triazol-1-il)-N'-(pirazina-2-il)acrilhidrazida	Tratamiento del linfoma difuso de células B grandes
Swedish	(Z)-3-(3-(3,5-bis(trifluorometyl)fenyl-1H-1,2,4-triazol-1-yl)-N'-(pyrazin-2-yl)akrylhydrazid	Behandling av diffusa storcelliga B-cells lymfom
Norwegian	(Z)-3-(3-(3,5-bis(trifluormetyl)fenyl-1H-1,2,4-triazol-1-yl)-N'-(pirazin-2-yl)akrylhydrazid	Behandling av diffust storcellet B-celle lymfom
Icelandic	(Z)-3-(3-(3,5-bis(þríflúórómetyl)fenyl-1H-1,2,4-tríasól-1-ýl)-N'-(pýrasín-2-ýl)akrýlhýdrasíð	Til meðferðar á dreifðu stórfrumu B frumu eitlakrabbameini