



EUROPEAN MEDICINES AGENCY
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Public summary of opinion on orphan designation

5-(4,6-dimorpholino-1,3,5-triazin-2-yl)-4-(trifluoromethyl)pyridin-2-amine
for the treatment of diffuse large B-cell lymphoma

On 27 February 2017, orphan designation (EU/3/17/1830) was granted by the European Commission to Voisin Consulting S.A.R.L., France, for 5-(4,6-dimorpholino-1,3,5-triazin-2-yl)-4-(trifluoromethyl)pyridin-2-amine (also known as PQR309) 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 222,000 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

*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).



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 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 based on preliminary results in patients who did not respond to previous treatment or whose disease came back after it, and who responded to this medicine. 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?

The medicine works by blocking the activity of 'mammalian target of rapamycin' (mTOR) and 'phosphoinositide-3-kinases' (PI3K), two types of enzymes involved in controlling cell growth. In many cancers including diffuse large B-cell lymphoma, the biological pathway involving mTOR and PI3K is overactive and enables the uncontrolled growth and spread of cancer cells. By blocking the actions of these enzymes, the medicine is expected to help slow down the growth and spread of the cancer.

What is the stage of development of this medicine?

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

At the time of submission of the application for orphan designation, clinical trials with the medicine including 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 19 January 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	5-(4,6-dimorpholino-1,3,5-triazin-2-yl)-4-(trifluoromethyl)pyridin-2-amine	Treatment of diffuse large B-cell lymphoma
Bulgarian	5-(4,6-диморфолино-1,3,5-триазин-2-ил)-4-(трифлуорометил)пиридин-2-амин	Лечение на дифузен В-едроклетъчен лимфом
Croatian	5-(4,6-dimorfolino-1,3,5-triazin-2-yl)-4-(trifluorometil)piridin-2-amin	Liječenje difuznog limfoma velikih B-stanica
Czech	5-(4,6-dimorpholino-1,3,5-triazin-2-yl)-4-(trifluoromethyl)pyridin-2-amine	Léčba velkobuněčného difuzního B-lymfomu
Danish	5-(4,6-dimorpholino-1,3,5-triazin-2-yl)-4-(trifluoromethyl)pyridin-2-amine	Behandling af diffust storcellet B-celle lymfom
Dutch	5-(4,6-dimorpholino-1,3,5-triazin-2-yl)-4-(trifluoromethyl)pyridin-2-amine	Behandeling van diffuus grootcellig B-cel-lymfoom
Estonian	5-(4,6-dimorfolino-1,3,5-triaziin-2-üül)-4-(trifluorometüül)püridiin-2-amiin	Diffuusse suure β -rakulise lümfoomi ravi
Finnish	5-(4,6-dimorfoliini-1,3,5-triaziin-2-yyli)-4-(trifluorometyyli)pyridiini-2-amiini	Diffuusin suurisoluisen B-solulymfooman hoito
French	5-(4,6-dimorpholino-1,3,5-triazin-2-yl)-4-(trifluorométhyl)pyridin-2-amine	Traitement du lymphome diffus à grandes cellules B
German	5-(4,6-dimorpholino-1,3,5-triazin-2-yl)-4-(trifluoromethyl)pyridin-2-amine	Behandlung des diffusen großzelligen B-Zell-Lymphoms
Greek	5-(4,6-διμορφολινο-1,3,5-τριαζιν-2-υλ)-4-(θφορομεθυλ)πυροδιν-2-αμίνη	Θεραπεία του διάχυτου μεγαλοκυτταρικού λεμφώματος Β-κυττάρου (DLBCL)
Hungarian	5-(4,6-dimorpholino-1,3,5-triazin-2-yl)-4-(trifluoromethyl)pyridin-2-amin	Diffúz nagy B-sejtes lymphoma kezelése
Italian	5-(4,6-dimorfolino-1,3,5-triazin-2-yl)-4-(trifluorometil)piridin-2-amina	Terapia del Linfoma non-Hodgkin diffuso a grandi cellule di tipo B (DLBCL)
Latvian	5-(4,6-dimorfolīna-1,3,5-triaziin-2-il)-4-(trifluorometil)piridīn-2-amīns	Difūzas lielo B šūnu limfomas ārstēšana
Lithuanian	5-(4,6-dimorfolino-1,3,5-triazin-2-il)-4-(trifluorometil)piridin-2-aminas	Difuzinės stambių B ląstelių limfomos gydymas
Maltese	5-(4,6-dimorfolino-1,3,5-triazin-2-il)-4-(trifluorometil)piridin-2-amina	Kura tal-limfoma tač-ċelluli tat-tip B kbar mxerrda
Polish	5-(4,6-dimorfolino-1,3,5-triazin-2-ylo)-4-(trifluorometylo)pyridyno-2-amina	Leczenie rozlanego chłoniaka z dużych limfocytów B
Portuguese	5-(4,6-dimorfolino-1,3,5-triazin-2-il)-4-(trifluorometil)piridin-2-amina	Tratamento do linfoma difuso de grandes células B
Romanian	5-(4,6-dimorfolino-1,3,5-triazin-2-il)-4-(trifluorometil)piridin-2-amină	Tratamentul limfomului difuz cu celule B mari
Slovak	5-(4,6-dimorfolino-1,3,5-triazin-2-yl)-4-(trifluorometyl)pyridín-2-amin	Liečba difúzneho veľkobunkového lymfómu z buniek B

¹ At the time of designation

Language	Active ingredient	Indication
Slovenian	5-(4,6-dimorfolino-1,3,5-triazin-2-yl)-4-(trifluorometil)piridin-2-amin	Zdravljenje razširjenega limfoma velikih B celic
Spanish	5-(4,6-dimorpholino-1,3,5-triazin-2-yl)-4-(trifluoromethyl)pyridin-2-amina	Tratamiento del linfoma difuso de células B grandes
Swedish	5-(4,6-dimorpholino-1,3,5-triazin-2-yl)-4-(trifluoromethyl)pyridin-2-amin	Behandling av diffusa storcelliga B-cells lymfom
Norwegian	5-(4,6-dimorfolino-1,3,5-triazin-2-yl)-4-(trifluorometyl)pyridin-2-amin	Behandling av diffust storcellet B-celle lymfom
Icelandic	5-(4,6-dímorfólínó-1,3,5-tríazín-2-ýl)-4-(triflúórómethýl)pýridín-2-amín	Til meðferðar á dreifðu stórfrumu B frumu eitlakkabbameini