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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

N-(3-(5-fluoro-2-(4-(2-methoxyethoxy)phenylamino)pyrimidin-4-ylamino)phenyl)acrylamide benzenesulfonic acid salt for the treatment of chronic lymphocytic leukaemia / small lymphocytic lymphoma

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Disclaimer Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in January 2015 on request of the Sponsor.

On 16 March 2014, orphan designation (EU/3/13/1234) was granted by the European Commission to Celgene Europe Limited, United Kingdom, for N-(3-(5-fluoro-2-(4-(2-methoxyethoxy)phenylamino)pyrimidin-4-ylamino)phenyl)acrylamide benzenesulfonic acid salt for the treatment of chronic lymphocytic leukaemia / small lymphocytic lymphoma.

What is chronic lymphocytic leukaemia / small lymphocytic lymphoma?

Chronic lymphocytic leukaemia (CLL) is cancer of a type of white blood cells called B lymphocytes. In this disease, the lymphocytes multiply too quickly and live for too long, so that there are too many of them circulating in the blood. The cancerous lymphocytes look normal, but they are not fully developed and do not work properly. Over a period of time, the abnormal cells replace the normal white cells, red cells and platelets (components that help the blood to clot) in the bone marrow (the spongy tissue inside the large bones in the body, where blood cells are produced). The disease known as 'small lymphocytic lymphoma' (SLL) is essentially the same disease as CLL. The name SLL is normally used when the cancer cells are located mainly in the lymph nodes.



CLL/SLL mainly affects older people and is rare in people under the age of 40 years. It is a long-term debilitating and life-threatening disease because it involves the weakening of the immune system (the body's natural defences), which can leave patients vulnerable to severe infections.

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

At the time of designation, CLL/SLL affected approximately 3.8 to 4.7 in 10,000 people in the European Union (EU). This was equivalent to a total of around 195,000 to 241,000 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?

Treatment for CLL/SLL is complex and depends on a number of factors, including the extent of the disease, whether it has been treated before, and the patient's age, symptoms and general state of health. Patients whose CLL/SLL is not causing any symptoms or is only getting worse very slowly may not need treatment. Treatment for CLL/SLL is only started if symptoms become troublesome. At the time of designation, the main treatment for CLL/SLL was chemotherapy (medicines to treat cancer).

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with CLL/SLL because early studies showed that the medicine was beneficial for patients whose disease did not respond or had come back after treatment with currently authorised medicines. 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 CLL/SLL by blocking the action of an enzyme called Bruton's tyrosine kinase (BTK), which is mostly found in B lymphocytes. BTK is important for the growth and survival of B lymphocytes and their migration to the organs where these cells normally divide. By blocking BTK, the medicine is expected to slow down the migration of B lymphocytes in CLL/SLL and to induce cell death, thereby slowing the progression of the disease.

The medicine is expected to be taken by mouth.

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 in patients with CLL/SLL were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for CLL/SLL 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 12 December 2013 recommending the granting of this designation.

*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. At the time of designation, this represented a population of 512,900,000 (Eurostat 2014).

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

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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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	N-(3-(5-fluoro-2-(4-(2-methoxyethoxy)phenylamino)pyrimidin-4-ylamino) phenyl)acrylamide benzenesulfonic acid salt	Treatment of chronic lymphocytic leukaemia / small lymphocytic lymphoma
Bulgarian	N-(3-(5-флуоро-2-(4-(2-метоксиетокси)фениламино)пиримидин-4-иламино)фенил)акриламидна сол на бензолсулфоновата киселина	Лечение на хронична лимфоцитна левкемия / Дребноклетъчен лимфоцитен лимфом
Czech	sůl kyseliny N-(3-(5-fluoro-2-(4-(2-methoxyethoxy)fenylamino)pyrimidin-4-ylamino)fenyl)akrylamidbenzensulfonové	Léčba chronické lymfatické leukemie / malobuněčného B lymfomu
Croatian	Sol N-(3-(5-fluoro-2-(4-(2-metoksietoksi)fenilamino)pirimidin-4-ilamino)fenil)akrilamid benzensulfonatne kiseline	Liječenje kronične limfocitne leukemije / limfoma malih limfocita
Danish	Salt af N-(3-(5-fluoro-2-(4-(2-methoxyethoxy)phenylamino)pyrimidin-4-ylamino)phenyl)akrylamid-benzensulfonsyre	Behandling af kronisk lymfatisk leukæmi/ Småcellet lymfocytisk lymfom
Dutch	N-(3-(5-fluoro-2-(4-(2-methoxyethoxy)fenylamino)pyrimidine-4-ylamino)fenyl)acrylamide-benzeensulfonaat	Behandeling van chronische lymfocyttaire leukemie/ kleincellig lymfocytair lymfoom
Estonian	N-(3-(5-fluoro-2-(4-(2-metoksüetoksü)fenüülamiin)pürimidiin-4-üülamiin)fenüül)akrüülamiid benseensulfoonhappe sool	Kroonilise lümfoidleukeemia ja väikerakk-lümfotsüütlümfoomi ravi
Finnish	N-(3-(5-fluoro-2-(4-(2-metoksietoksi)fenyyliamino)pyrimidiini-4-yyliamino)fenyyli)akryyliamidi-bentseenisulfonihapposuola	Kroonisen lymfaattisen leukemian japienilymfosyyttisen lymfooman hoito
French	Sel d'acide benzène sulfonique N-(3-(5-fluoro-2-(4-(2-méthoxyéthoxy)phénylamino)pyrimidine-4-ylamino)phényl)acrylamide	Traitement de la leucémie lymphoïde chronique/du lymphome lymphocytaire à petites cellules
German	N-(3-(5-Fluor-2-(4-(2-methoxyethoxy)phenylamino)pyrimidin-4-ylamino)phenyl)acrylamid-Benzolsulfonsäure-Salz	Behandlung der chronischen lymphatischen Leukämie/des kleinzelligen lymphozytischen Lymphoms

¹ At the time of designation

Language	Active ingredient	Indication
Greek	άλας N-(3-(5-φθορο-2-(4-(2-μεθοξυαιθοξυ)φαινυλαμινο)πυριμιδινό-4-υλαμινο)φαινυλο)ακρυλαμιδίου του βενζολοσουλφονικού οξέος	Θεραπεία της χρόνιας λεμφοκυτταρικής λευχαιμίας/ του Λεμφώματος από Μικρά Λεμφοκύτταρα
Hungarian	N-(3-(5-fluoro-2-(4-(2-metoxietoxi)fenilamino)pirimidin-4-ilamino)fenil)akrilamid benzénszulfonsav só	Krónikus lymphoid -leukaemia/kissejtes lymphocytás lymphoma kezelése
Italian	Sale dell'acido N-(3-(5-fluoro-2-(4-(2-metossietossi)fenilammino)pirimidin-4-ilammino)fenil)acrilammide benzensolfonico	Trattamento della leucemia linfocitica cronica/ linfoma a piccoli linfociti
Latvian	N-(3-(5-fluor-2-(4-(2-metoksietoksi)fenilamino)pirimidīn-4-ilamino)fenil)akrilamīda benzolsulfoskābes sāls	Hroniskas limfoleikozes/mazo limfocītu limfomas ārstēšana
Lithuanian	N-(3-(5-fluoro-2-(4-(2-metoksietoksi)fenilamino)pirimidin-4-ilamino)fenil)akrilamido benzensulfoninės rūgšties druska	Lėtinės limfocitinės leukemijos/ smulkių limfocitų limfomos gydymas
Maltese	Melġ ta' N-(3-(5-fluoro-2-(4-(2-methoxyethoxy)phenylamino)pyrimidin-4-ylamino)phenyl)acrylamide benzenesulfonic acid	Kura tal-lewkimja limfoċitika kronika/limfoma limfoċitika żgħira
Polish	N-(3-(5-fluoro-2-(4-(2-metoksyetoksy)fenylamino)pirymidyn-4-ylamino) fenyl)akrylamid benzenosulfonian	Leczenie przewlekłej białaczki limfatycznej/ Chłoniaka z małych limfocytów B
Portuguese	Sal do ácido N-(3-(5-fluoro-2-(4-(2-metoxietoxi)fenilamino)pirimidin-4-ilamino)fenil)acrilamida benzenosulfónico	Tratamento da leucemia linfocítica crónica/linfoma de pequenos linfócitos
Romanian	Sare a acidului N-(3-(5-fluoro-2-(4-(2-metoxietoxi)fenilamino)pirimidin-4-il-amino)fenil)acrilamidă benzensulfonică	Tratamentul leucemiei limfoide cronice / limfomului limfocitar cu celule mici
Slovak	soľ kyseliny N-(3-(5-fluoro-2-(4-(2-metoxyetoxy) fenylamino)pyrimidín-4-ylamino)fenyl)akrylamid benzénsulfónovej	Liečba chronickej lymfocytovej leukémie / malobunkového lymfocytového lymfómu
Slovenian	Sol N-(3-(5-fluoro-2-(4-(2-metoksietoksi)fenilamino)pirimidin-4-ilamino)fenil)akrilamid benzensulfonske kisline	Zdravljenje kronične limfatične levkemije / drobnoceličnega limfocitnega limfoma
Spanish	Sal del ácido benzenosulfónico de N-(3-(5-fluoro-2-(4-(2-metoxietoxi)fenilamino)pirimidina-4-ilamino)fenil)acrilamida	Tratamiento de la leucemia linfocítica crónica linfoma linfocítico pequeño

Language	Active ingredient	Indication
Swedish	N-(3-(5-fluor-2-(4-(2-metoxýetoxý)fenýlamin)pyrimidin-4-ylamin)fenýl)akrylamid-bensensulfonsyra-salt	Behandling av kronisk lymfatisk leukemi/småcelligt lymfocytärt lymfom
Norwegian	N-(3-(5-fluor-2-(4-(2-metoksyetoksy)fenýlamin)pyrimidin-4-ylamin)fenýl)akrylamid benzensulfonsyre salt	Behandling av kronisk lymfatisk leukemi / småcellet lymfocytært lymfom
Icelandic	N-(3-(5-flúóró-2-(4-(2-metoxýetoxý)fenýlamínó)pýrimídín-4-ýlamínó)fenýl)akrýlamíð bensensúlfónsýrusalt	Meðferð á langvinnu eitilfrumuhvítblæði/smáeitilfrumu eitlakraðbameini