



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide for the treatment of chronic lymphocytic leukaemia

On 6 December 2012, orphan designation (EU/3/12/1080) was granted by the European Commission to AbbVie Ltd, United Kingdom, for 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide for the treatment of chronic lymphocytic leukaemia.

What is chronic lymphocytic leukaemia?

Chronic lymphocytic leukaemia (CLL) is cancer of a type of white blood cell 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).

CLL is the most common type of leukaemia and mainly affects older people. It is rare in people under the age of 40 years. CLL is a long-term debilitating and life-threatening disease because some patients develop severe infections.

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

At the time of designation, CLL affected approximately 3 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 152,000 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).

*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 27), Norway, Iceland and Liechtenstein. This represents a population of 506,300,000 (Eurostat 2011).



What treatments are available?

Treatment for CLL 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 is not causing any symptoms or is only getting worse very slowly may not need treatment. Treatment for CLL is only started if symptoms become troublesome. At the time of designation, the main treatment for CLL 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 because it works in a different way to existing treatments and early studies show that it might improve the outcome of patients whose disease does not respond or has come back after 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?

This medicine is expected to work by blocking proteins called Bcl-2. These proteins allow cells to stay alive by preventing the natural process that leads to cell death (apoptosis). Bcl-2 proteins can be found in high concentration in cancer cells. By blocking the action of these proteins, the medicine is expected to make cancer cells more responsive to this natural process, causing their death and slowing the growth of the cancer. As Bcl-2 proteins have been shown to be associated with resistance to conventional chemotherapy, it is expected that this medicine will reduce resistance and allow other medicines to be more effective in their treatment.

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 CLL were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for CLL. Orphan designation of the medicine has been granted in the United States of America for CLL.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 November 2012 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:

AbbVie Ltd
Abbott House
Vanwall Business Park
Vanwall Road
Maidenhead,
Berks, SL6 4XE
United Kingdom
Telephone: +44 1628 644501
Telefax: +44 1628 672624
E-mail: orphandrugs.enquiries@abbvie.com

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 substance	Indication
English	4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide	Treatment of chronic lymphocytic leukaemia
Bulgarian	4-(4-{[2-(4-хлорофенил)-4,4-диметилциклохекс-1-ен-1-ил]метил}пиперазин-1-ил)-N-({3-нитро-4-[(тетраhydro-2H-пиран-4-илметил)амино]фенил}сулфонил)-2-(1H-пироло [2,3-b]пиридин-5-илокси)бензамид	Лечение на хронична лимфоцитна левкемия
Czech	4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]fenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)salicylamid	Léčba chronické lymfatické leukémie
Danish	4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyklohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamid	Behandling af kronisk lymfocytær leukæmi
Dutch	4-(4-{[2-(4-chloorfenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]fenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide	Behandeling van chronische lymfocyttaire leukemie
Estonian	4-(4-{[2-(4-klorofenüül)-4,4-dimetüülsükloheks-1-een-1-üül]metüül}piperasiin-1-üül)-N-({3-nitro-4-[(tetrahydro-2H-püraan-4-üülmetüül)amino]fenüül}sulfonüül)-2-(1H-pürrolo[2,3-b]püridiin-5-üloksü)bensamiid	Kroonilise lümfoidleukeemia ravi
Finnish	4-(4-{[2-(4-klorofenyyli)-4,4-dimetyylisyklo-1-heksen-1-yyli]metyyli}piperatsin-1-yyli)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-yyli]metyyli)amino]fenyyli}sulfonyyli)-2-(1H-pyrrolo[2,3-b]pyridin-5-yylioksi)bentsamidi	Kroonisen lymfosyyttileukemian hoito
French	4-(4-{[2-(4-chlorophényl)-4,4-diméthylcyclohex-1-en-1-yl]methyl}pipérazine-1-yl)-N-({3-nitro-4-[(tétrahydro-2H-pyran-4-ylmethyl)amino]phényl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridine-5-yloxy)benzamide	Traitement de la leucémie lymphoïde chronique

¹ At the time of designation

Language	Active substance	Indication
German	4-(4-{[2-(4-Chlorphenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamid	Behandlung der chronisch-lymphatischen Leukämie
Greek	4-(4-{[2-(4-χλωροφαινυλο)-4,4-διμεθυλοκυκλοεξ-1-εν-1-υλ]μεθυλ}πιπεραζινο-1-yl)-N-({3-νιτρο-4-[(τετραϋδρο-2H-πυρανο-4-υλμεθυλο)αμινο]φαινυλο}σουλφονυλο)-2-(1H-πυρολο[2,3-b]πυριδινο-5-υλοξυ)βενζαμίδη	Θεραπεία της χρόνιας λεμφοκυτταρικής λευχαιμίας
Hungarian	4-(4-{[2-(4-klórfenil)-4,4-dimetilciklohex-1-én-1-il]metil}piperazin-1-il)-N-({3-nitro-4-[(tetrahidro-2H-pirán-4-ilmetil)amino]fenil}szulfonil)-2-(1H-pirroló[2,3-b]piridin-5-iloxi)benzamid	Krónikus lymphoid leukémia kezelése
Italian	4-(4-{[2-(4-clorofenil)-4,4-dimetilcicloes-1-en-1-il]metil}piperazin-1-il)-N-({3-nitro-4-[(tetraidro-2H-piran-4-ilmetil)amino]fenil}sulfonil)-2-(1H-pirroló[2,3-b]piridin-5-ilossi)benzamide	Trattamento della leucemia linfocitica cronica
Latvian	4-(4-{[2-(4-hlorofenil)-4,4-dimetilcikloheks-1-ēn-1-il]metil}piperazīn-1-il)-N-({3-nitro-4-[(tetrahidro-2H-piran-4-ilmetil)amino]fenil}sulfonil)-2-(1H-piroló[2,3-b]piridīn-5-iloksi)benzamīds	Hroniskas limfocitiskās leukēmijas ārstēšana
Lithuanian	4-(4-{[2-(4-chlorofenil)-4,4-dimetilcikloheks-1-en-1-il]metil}piperazin-1-il)-N-({3-nitro-4-[(tetrahidro-2H-piran-4-ilmetil)amino]fenil}sulfonil)-2-(1H-piroló[2,3-b]piridin-5-iloksi)benzamidás	Lėtinės limfocitinės leukemijos gydymas
Maltese	4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide	Kura tal-lewkimja limfoċitika kronika
Polish	4-(4-{[2-(4-chlorofenylo)-4,4-dimetylocykloheks-1-en-1-yl]metylo}piperazyn-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-piran-4-ylmetylo)amino]fenylo}sulfonylo)-2-(1H-pirroló[2,3-b]pirydyn-5-yloksy)benzamid	Leczenie przewlekłej białaczki limfatycznej
Portuguese	4-(4-{[2-(4-clorofenil)-4,4-dimetilciclohex-1-eno-1-il]metil}piperazina-1-il)-N-({3-nitro-4-[(tetrahidro-2H-piran-4-ilmetil)amino]fenil}sulfonil)-2-(1H-pirroló[2,3-b]piridina-5-iloxi)benzamida	Tratamento da leucemia linfocítica crónica
Romanian	4-(4-{[2-(4-clorofenil)-4,4-dimetilciclohex-1-enă-1-il]metil}piperazină-1-il)-N-({3-nitro-4-[(tetrahidro-2H-piran-4-ilmetil)amino]fenil}sulfonil)-2-(1H-piroló[2,3-	Tratamentul leucemiei limfoide cronice

Language	Active substance	Indication
	b]piridin-5-iloxi)benzamidă	
Slovak	4-(4-{[2-(4-chlorofenyl)-4,4-dimetylcyklohex-1-en-1-yl]metyl}piperazín-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyrán-4-ylmetyl)amino]fenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridín-5-yloxy)benzamid	Liečba chronickej lymfocytovej leukémie
Slovenian	4-(4-{[2-(4-klorofenil)-4,4-dimetilcikloheks-1-en-1-il]metil}piperazin-1-il)-N-({3-nitro-4-[(tetrahydro-2H-piran-4-ilmetil)amino]fenil}sulfonyl)-2-(1H-pirolo[2,3-b]piridin-5-iloksi)benzamid	Zdravljenje kronične limfatske levkemije
Spanish	4-(4-{[2-(4-chlorofenil)-4,4-dimetil ciclohex-1-en-1-il]metil}piperazina-1-il)-N-({3-nitro-4-[(tetrahydro-2H-piran-4-ilmetil)amino]fenil}sulfonyl)-2-(1H-pirrol[2,3-b]piridina-5-iloxi)benzamida	Tratamiento de la leucemia linfocítica crónica
Swedish	4-(4-{[2-(4-klorofenyl)-4,4-dimetylcyklohex-1-en-1-yl]metyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmetyl)amino]fenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)bensamid	Behandling av kronisk lymfatisk leukemi
Norwegian	4-(4-{[2-(4-klorfenyl)-4,4-dimetylcykloheks-1-en-1-yl]metyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmetyl)amino]fenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamid	Behandling av kronisk lymfatisk leukemi
Icelandic	4-(4-{[2-(4-klórófenýl)-4,4-dímetylsýklóhex-1-en-1-ýl]metýl}píperazín-1-ýl)-N-({3-nítró-4-[(tetrahýdró-2H-pýran-4-ýlmetýl)amínó]fenýl}súlfónýl)-2-(1H-pýrróló[2,3-b]pýridín-5-ýloxý)benzamið	Meðferð á langvinnu eitilfrumuhvítblæði