



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

2 March 2015
EMA/COMP/219979/2012 Rev.2
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

1-[(3R)-3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4 d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-one for the treatment of chronic lymphocytic leukaemia

First publication	5 June 2012
Rev.1: transfer of sponsorship	7 March 2013
Rev.2: information about Marketing Authorisation	2 March 2015
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.	

On 26 April 2012, orphan designation (EU/3/12/984) was granted by the European Commission to Nexus Oncology Ltd, United Kingdom, for 1-[(3R)-3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4 d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-one for the treatment of chronic lymphocytic leukaemia.

The sponsorship was transferred to Janssen-Cilag International N.V, Belgium, in January 2013.

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 was equivalent to a total of around 153,000 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 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 has progressed or 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 an enzyme called Bruton's tyrosine kinase (Btk), which is mostly found in B-lymphocytes. Btk activates 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 and to induce cell death, thereby delaying or stopping 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 1-[(3R)-3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4 d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-one have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with this medicine in patients with CLL were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for CLL 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 8 March 2012 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 27), Norway, Iceland and Liechtenstein. At the time of designation, this represented a population of 509,000,000 (Eurostat 2012).

Update: 1-[(3R)-3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4 d]pyrimidin-1-yl]-1-piperidiny]-2-propen-1-one, ibrutinib (Imbruvica) has been authorised in the EU since 21 October 2014 for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy, or in first line in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemo immunotherapy.

More information on Imbruvica can be found in the European public assessment report (EPAR) on the Agency's website: [ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports](http://ema.europa.eu/Find%20medicine/Human%20medicines/European%20Public%20Assessment%20Reports)

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	1-[(3R)-3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4 d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-one	Treatment of chronic lymphocytic leukaemia
Bulgarian	1-[(3R)-3-[4-амино-3-(4-феноксифенил)-1H-пиразоло[3,4 d]пиримидин-1-ил]-1-пиперидинил]-2-пропен-1-он	Лечение на хронична лимфоцитна левкемия
Czech	1-[(3R)-3-[4-amino-3-(4-fenoxyfenyl)-1H-pyrazolo[3,4d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-on	Léčba chronické lymfatické leukémie
Danish	1-[(3R)-3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4 d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-one	Behandling af kronisk lymfocytær leukæmi
Dutch	1-[(3R)-3-[4-amino-3-(4-fenoxyfenyl)-1H-pyrazolo[3,4 d]pyrimidine-1-yl]-1-piperidinyl]-2-propeen-1-on	Behandeling van chronische lymfocyttaire leukemie
Estonian	1-[(3R)-3-[4-amino-3-(4-fenoksüfenüül)-1H-pürasolo[3,4-d]pürimidiin-1-üül]-1-piperidinüül]-2-propen-1-oon	Kroonilise lümfoidleukeemia ravi
Finnish	1-[(3R)-3-[4-amino-3-(4-fenoksifenyyli)-1H-pyratsoli[3,4 d]pyrimidiini-1-yl]-1-piperidinyyli]-2-propeeni-1-oni	Kroonisen lymfaattisen leukemian hoito
French	1-[(3R)-3-[4-amino-3-(4-phénoxyphényl)-1H-pyrazolo[3,4d]pyrimidin-1-yl]-1-pipéridinyl]-2-propène-1-one	Traitement de la leucémie lymphoïde chronique
German	1-[(3R)-3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4 d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-one	Behandlung der chronisch-lymphatischen Leukämie
Greek	1-[(3R)-3-[4-αμινό-3-(4-φαινοξυφαινυλο)-1H-πυραζολο[3,4 d]πυριμιδινό-1-yl]-1-πιπεριδινυλο]-2-προπεν-1-όνη	Θεραπεία της χρόνιας λεμφοκυτταρικής λευχαιμίας
Hungarian	1-[(3R)-3-[4-amino-3-(4-fenoxifenil)-1H-pirazolo[3,4-d]pirimidin-1-il]-1-piperidinil]-2-propén-1-on	Krónikus lymphoid leukémia kezelése
Italian	1-[(3R)-3-[4-amino-3-(4-fenossifenil)-1H-pirazolo[3,4 d]pirimidin-1-il]-1-piperidinil]-2-propen-1-one	Trattamento della leucemia linfocitica cronica
Latvian	1-[(3R)-3-[4-amino-3-(4-fenoksifenil)-1H-pirazolo[3,4 d]pirimidīn-1-il]-1-piperidinil]-2-propen-1-ons	Hroniskas limfocītiskās leukēmijas ārstēšana
Lithuanian	1-[(3R)-3-[4-amino-3-(4-fenoksifenil)-1H-pirazolo[3,4 d]pirimidin-1-il]-1-piperidinil]-2-propen-1-onas	Lėtinės limfocitinės leukemijos gydymas

¹ At the time of designation

Language	Active ingredient	Indication
Maltese	1-[(3R)-3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4 d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-one	Kura tal-lewkimja limfoċitika kronika
Polish	1-[(3R)-3-[4-amino-3-(4-fenoksyfenilo)-1H-pirazolo[3,4 d]pirymidyno-1-ilo]-1-piperydynilo]-2-propen-1-on	Leczenie przewlekłej białaczki limfatycznej
Portuguese	1-[(3R)-3-[4-amino-3-(4-fenoxifenil)-1H-pirazolo[3,4 d]pirimidina-1-il]-1-piperidinil]-2-propen-1-ona	Tratamento da leucemia linfocítica crónica
Romanian	1-[(3R)-3-[4-amino-3-(4-fenoxifenil)-1H-pirazolo[3,4 d]pirimidin-1-il]-1-piperidinil]-2-propen-1-onă	Tratamentul leucemiei limfoide cronice
Slovak	1-[(3R)-3-[4-amino-3-(4-fenoxyfenyl)-1H-pyrazolo[3,4 d]pyrimidín-1-yl]-1-piperidinyl]-2-propén-1-ón	Liečba chronickej lymfocytovej leukémie
Slovenian	1-[(3R)-3-[4-amino-3-(4-fenoksifenil)-1H-pirazolo[3,4 d]pirimidin-1-il]-1-piperidinil]-2-propen-1-on	Zdravljenje kronične limfatske levkemije
Spanish	1-[(3R)-3-[4-amino-3-(4-fenoxifenil)-1H-pirazolo[3,4 d]pirimidin-1-il]-1-piperidinil]-2-propen-1-ona	Tratamiento de la leucemia linfocítica crónica
Swedish	1-[(3R)-3-[4-amino-3-(4-fenoxyfenyl)-1H-pyrazol[3,4 d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-on	Behandling av kronisk lymfatisk leukemi
Norwegian	1-[(3R)-3-[4-amino-3-(4-fenoksyfenyl)-1H-pyrazolo[3,4 d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-on	Behandling av kronisk lymfatisk leukemi
Icelandic	1-[(3R)-3-[4-amínó-3-(4-fenoxýfenýl)-1H-pýrasóló[3,4 d]pýrímídín-1-ýl]-1-píperídínýl]-2-própen-1-ón	Meðferð á langvinnu eitilfrumuhvítblæði