



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

2 March 2015
EMA/COMP/101688/2013 Rev.1
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 mantle cell lymphoma

First publication	26 March 2013
Rev.1: 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 12 March 2013, orphan designation (EU/3/13/1115) was granted by the European Commission to Janssen-Cilag International N.V., Belgium, 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 mantle cell lymphoma.

What is mantle cell lymphoma?

Mantle cell lymphoma is an aggressive cancer of a type of white blood cell called B-lymphocytes, or B cells. In mantle cell lymphoma, 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, caused by an enlarged lymph node. Patients may also have fever, weight loss, tiredness and night sweats.

Mantle cell lymphoma is usually diagnosed in people aged over 50 years. It is more common in men than women. Mantle cell lymphoma is a long-term debilitating and life-threatening disease that is associated with poor overall survival.



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

At the time of designation, mantle cell lymphoma affected approximately 0.17 to 0.56 in 10,000 people in the European Union (EU). This was equivalent to a total of around 9,000 and 29,000 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, temsirolimus was specifically authorised in the EU for the treatment of mantle cell lymphoma that has come back after previous treatment or has not responded to other treatments. The main treatments for mantle cell lymphoma included chemotherapy (medicines to treat cancer), immunotherapy (medicines that stimulate the body's own immune system to kill the cancer cells) and radiotherapy (treatment with radiation). Haematopoietic (blood) stem cell transplantation was also used. This is a complex procedure where patients receive stem cells to help restore the bone marrow.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with mantle cell lymphoma because early studies show that it might improve the outcome of patients whose disease does not respond to 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 an enzyme called Bruton's tyrosine kinase (Btk), which is mostly found in B-lymphocytes. Btk promotes 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 mantle cell lymphoma 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 the medicine including patients with mantle cell lymphoma were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for mantle cell lymphoma. Orphan designation of this medicine had been granted in the United States of America for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 6 February 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 512,200,000 (Eurostat 2013).

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 relapsed or refractory mantle cell lymphoma (MCL).

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

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](http://orphanet.eu), a database containing information on rare diseases which includes a directory of patients' organisations registered in Europe.
- [European Organisation for Rare Diseases \(EURORDIS\)](http://eurordis.eu), 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 mantle cell lymphoma
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 мантелно-клетъчна лимфом
Czech	1-[(3R)-3-[4-amino-3-(4-fenoxyfenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-on	Léčba lymfomu z plášťové zóny
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 mantelcellelymfom
Dutch	1-[(3R)-3-[4-amino-3-(4-fenoxyfenyl)-1H-pyrazolo[3,4-d]pyrimidine-1-yl]-1-piperidinyl]-2-propeen-1-one	Behandeling van mantelcellymfoom
Estonian	1-[(3R)-3-[4-amino-3-(4-fenoksüfenüül)-1H-pürasolo[3,4-d]pürimidiin-1-üül]-1-piperidinüül]-2-propen-1-oon	Mantelrakulise lümfoomi ravi
Finnish	1-[(3R)-3-[4-amino-3-(4-fenoksifenyyli)-1H-pyratsoli[3,4-d]pyrimidiini-1-yl]-1-piperidinyyli]-2-propeeni-1-oni	Manttelisolu-lymfooman hoito
French	1-[(3R)-3-[4-amino-3-(4-phénoxyphényl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-pipéridinyl]-2-propène-1-one	Traitement des lymphomes du manteau
German	1-[(3R)-3-[4-Amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-one	Behandlung von Mantelzelllymphom
Greek	1-[(3R)-3-[4-αμινό-3-(4-φαινοξυφαινυλο)-1H-πυραζολο[3,4-d]πυριμιδινό-1-yl]-1-πιπεριδινυλο]-2-προπεν-1-όνη	Θεραπεία του λεμφώματος μανδυκών κυττάρων
Hungarian	1-[(3R)-3-[4-amino-3-(4-fenoxifenil)-1H-pirazolo[3,4-d]pirimidin-1-il]-1-piperidinil]-2-propén-1-on	Köpenysejtes lymphoma kezelése
Italian	1-[(3R)-3-[4-ammino-3-(4-fenossifenil)-1H-pirazolo[3,4-d]pirimidin-1-il]-1-piperidinil]-2-propen-1-one	Trattamento del linfoma con cellule a mantello
Latvian	1-[(3R)-3-[4-amino-3-(4-fenoksifenil)-1H-pirazolo[3,4-d]pirimidīn-1-il]-1-piperidinil]-2-propen-1-ons	Mantijšūnu limfomas ārstēšana
Lithuanian	1-[(3R)-3-[4-amino-3-(4-fenoksifenil)-1H-pirazolo[3,4-d]pirimidin-1-il]-1-piperidinil]-2-propen-1-onas	Mantijos ląstelių limfomos 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-linfoma tač-čelloli tal-mantell
Polish	1-[(3R)-3-[4-amino-3-(4-fenoksyfenilo)-1H-pirazolo[3,4-d]pirymidyn-1-ylo]-1-piperydynylo]-2-propen-1-on	Leczenie chłoniaków z komórek płaszczowych
Portuguese	1-[(3R)-3-[4-amino-3-(4-fenoxifenil)-1H-pirazolo[3,4-d]pirimidina-1-il]-1-piperidinil]-2-propen-1-ona	Tratamento de linfoma de células do manto
Romanian	1-[(3R)-3-[4-amino-3-(4-fenoxifenil)-1H-pirazolo[3,4-d]pirimidin-1-il]-1-piperidinil]-2-propen-1-onă	Tratamentul limfomului cu celule în manta
Slovak	1-[(3R)-3-[4-amino-3-(4-fenoxyfenyl)-1H-pyrazolo[3,4-d]pyrimidín-1-yl]-1-piperidinyl]-2-propén-1-ón	Liečba lymfómu plášťovej zóny
Slovenian	1-[(3R)-3-[4-amino-3-(4-fenoksifenil)-1H-pirazolo[3,4-d]pirimidin-1-il]-1-piperidinil]-2-propen-1-on	Zdravljenje limfoma plaščnih celic
Spanish	1-[(3R)-3-[4-amino-3-(4-fenoxifenil)-1H-pirazolo[3,4-d]pirimidin-1-il]-1-piperidinil]-2-propen-1-ona	Tratamiento del linfoma de células del manto
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 mantelcellslymfom
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 mantelcelle-lymfom
Icelandic	1-[(3R)-3-[4-aminó-3-(4-fenoxýfenýl)-1H-pýrasóló[3,4-d]pýrímídín-1-ýl]-1-píperídínýl]-2-própen-1-ón	Meðferð möttulfrumu eitlakrabbameins