20 April 2015
EMA/COMP/360298/2010 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

11-(2-Pyrrolidin-1-yl-ethoxy)-14,19-dioxa-5,7,26-triaza-tetracyclo[19.3.1.1(2,6).1(8,12)] heptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-decaene for the treatment of primary myelofibrosis

First publication	15 October 2010
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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.

On 25 August 2010, orphan designation (EU/3/10/768) was granted by the European Commission to Voisin Consulting S.A.R.L., France, for 11-(2-pyrrolidin-1-yl-ethoxy)-14,19-dioxa-5,7,26-triaza-tetracyclo[19.3.1.1(2,6).1(8,12)] heptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-decaene for the treatment of primary myelofibrosis.

The sponsorship was transferred to Baxter Innovations GmbH, Austria, in March 2015.

What is primary myelofibrosis?

Primary myelofibrosis is a disease of unknown cause in which the bone marrow (the spongy tissue inside the large bones) becomes dense and fibrous, and starts producing abnormal immature blood cells that replace the normal blood cells.

In this disease, some immature blood cells migrate from the bone marrow to other organs, such as the spleen and liver, where they mature. This causes the organs to become enlarged. Patients with primary myelofibrosis can develop several symptoms, including pain in the bones, tiredness, weakness, infections and bleeding.

Primary myelofibrosis is a debilitating disease that is long lasting and may be life threatening because it can lead to severe anaemia (low red blood cell counts) and infections, and can result in leukaemia (cancer of the white blood cells).

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

At the time of designation, primary myelofibrosis affected approximately 0.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 15,000 people*, and is below the threshold 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, hydroxyurea and busulfan (which are also used to treat cancer) were authorised in the EU for primary myelofibrosis. In addition, treatments aimed at relieving the symptoms of the disease were used. These included androgens (male hormones), glucocorticoids (a type of steroid) and erythropoietin (a hormone that stimulates the production of red blood cells) to treat anaemia, and surgery to remove the enlarged spleen. In some patients, haematopoietic (blood) stem-cell transplantation was used. This is a complex procedure where the patient receives stem cells from a matched donor 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 primary myelofibrosis because it works in a different way to existing treatments and because early studies show that it might improve the outcome of patients with this condition. These assumptions 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 thought to work by blocking an enzyme known as Janus kinase 2 (JAK2). This enzyme can be found in some receptors on the surface of cells and is involved in the reproduction and growth of blood cells. In myelofibrosis, JAK2 is overactivated. By blocking this enzyme, this medicine is expected to slow down the abnormal growth of blood cells, reducing the symptoms of the disease.

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 this medicine including patients with primary myelofibrosis were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for primary myelofibrosis. Orphan designation of this medicine had been granted in the United States of America for the treatment of myeloproliferative disorders with the JAK2 V617F mutation.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 2 June 2010 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 506,300,000 (Eurostat 2010).

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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	11-(2-pyrrolidin-1-yl-ethoxy)-14,19-dioxa-5,7,26-triaza-tetracyclo[19.3.1.1(2,6).1(8,12)] heptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-decaene	Treatment of primary myelofibrosis
Bulgarian	11-(2-пиролидин-1-ил-етокси)-14,19-диокса-5,7,26-триаза-тетрацикло[19.3.1.1(2,6).1(8,12)] хептакоза-1(25),2(26),3,5,8,10,12(27),16,21,23-декаен	Лечение на първична миелофиброза
Croatian	11-(2-pirolidin-1-il-etoksi)-14,19-dioksa-5,7,26-triaza-tetraciklo [19.3.1.1(2,6).1(8,12)] heptakoza-1(25),2(26),3,5,8,10,12(27),16,21,23-dekaen	Liječenje primarne mijelofibroze
Czech	11-(2-pyrrolidin-1-yl-ethoxy)-14,19-dioxa-5,7,26-triaza-tetracyklo[19.3.1.1(2,6).1(8,12)] heptakosa-1(25),2(26),3,5,8,10,12(27),16,21,23-dekaen	Léčba primárnímyelofibrózy
Danish	11-(2-pyrrolidin-1-yl-ethoxy)-14,19-dioxa-5,7,26-triaza-tetracyclo[19.3.1.1(2,6).1(8,12)] heptakosa-1(25),2(26),3,5,8,10,12(27),16,21,23-dekaen	Behandling af primær myelofibrose
Dutch	11-(2-pyrrolidine-1-yl-etoxy)-14,19-dioxa-5,7,26-triaza-tetracyclo[19.3.1.1(2,6).1(8,12)] heptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-deceen	Behandeling van primaire myelofibrose
Estonian	11-(2-pürrolidiin-1-üül-etoksü)-14,19-dioksa-5,7,26-triasa-tetratsüklo[19.3.1.1(2,6).1(8,12)] heptakosa-1(25),2(26),3,5,8,10,12(27),16,21,23-dekaeen	Esmase müelofibroosi ravi
Finnish	11-(2-pyrrolidiini-1-yl-etoksi)-14,19-dioksa-5,7,26-triatsa-tetrasyklo[19.3.1.1(2,6).1(8,12)] heptakosa-1(25),2(26),3,5,8,10,12(27),16,21,23-dekeeni	Primaarisen myelofibroosin hoito
French	11-(2-pyrrolidine-1-yl-éthoxy)-14,19-dioxa-5,7,26-triaza-tétracyclo[19.3.1.1(2,6).1(8,12)] heptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-décaène	Traitement de la myélofibrose primitive
German	11-(2-Pyrrolidin-1-yl-ethoxy)-14,19-dioxa-5,7,26-triaza-tetracyclo[19.3.1.1(2,6).1(8,12)] heptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-Decen	Behandlung der primären Myelofibrose
Greek	11-(2-πυρρολιδίν-1-υλ-αιθοξυ)-14,19-διοξα-5,7,26-τριαζα-τετρακυκλο[19.3.1.1(2,6).1(8,12)] επτακοσα-1(25),2(26),3,5,8,10,12(27),16,21,23-δεκαΐνη	Θεραπεία της πρωτογενούς μυελοσκλήρυνσης
Hungarian	11-(2-pirrolidin-1-il-etoxi)-14,19-dioxa-5,7,26-triaza-tetraciklo[19.3.1.1(2,6).1(8,12)] heptakoza-1(25),2(26),3,5,8,10,12(27),16,21,23-decén	Primer mielofibrózis kezelésére
Italian	11-(2-pirrolidin-1-yl-etossi)-14,19-diossa-5,7,26-triaza-tetraciclo[19.3.1.1(2,6).1(8,12)] eptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-decene	Trattamento della mielofibrosi primitiva
Latvian	11-(2-pirolidīn-1-il-etoksi)-14,19-dioksa-5,7,26-triaza-tetraciklo[19.3.1.1(2,6).1(8,12)] heptakosa-1(25),2(26),3,5,8,10,12(27),16,21,23-decēns	Primāras mielofibrozes ārstēšana

[1] At the time of transfer of sponsorship

Language	Active ingredient	Indication
Lithuanian	11-(2-pirolidin-1-il-etoksi)-14,19-dioksa-5,7,26-triazatetraciklo[19.3.1.1(2,6).1(8,12)] heptakoza-1(25),2(26),3,5,8,10,12(27),16,21,23-dekaenas	Pirminės mielofibrozės gydymas
Maltese	11-(2-pyrrolidin-1-yl-ethoxy)-14,19-dioxa-5,7,26-triaza-tetracyclo[19.3.1.1(2,6).1(8,12)] heptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-decaene	Kura tal-mjelofibrożi primarja
Polish	11-(2-pirolidyno-1-yl-etoksy)-14,19-dioksa-5,7,26-triaza-tetracyklo[19.3.1.1(2,6).1(8,12)] heptakoza-1(25),2(26),3,5,8,10,12(27),16,21,23-dekan	Leczenie mielofibrozy pierwotnej
Portuguese	11-(2-pirrolidina-1-yl-etoxi)-14,19-dioxa-5,7,26-triaza-tetraciclo[19.3.1.1(2,6).1(8,12)] heptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-deceno	Tratamento da mielofibrose primária
Romanian	11-(2-pirolidin-1-il-etoxi)-14,19-dioxa-5,7,26-triaza-tetraciclo[19.3.1.12,6.18,12] heptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-decenă	Tratamentul mielofibrozei primitive
Slovak	11-(2-pyrolidín-1-yl-etoxy)-14,19-dioxa-5,7,26-triáza-tetracyklo[19.3.1.1(2,6).1(8,12)] heptakosa-1(25),2(26),3,5,8,10,12(27),16,21,23-dekaén	Liečba primárnej myelofibrózy
Slovenian	11-(2-pirolidin-1-il-etoksi)-14,19-dioksa-5,7,26-triaza-tetraciklo[19.3.1.1(2,6).1(8,12)] heptakoza-1(25),2(26),3,5,8,10,12(27),16,21,23-dekaen	Zdravljenje primarne mielofibroze
Spanish	11-(2-pirrolidina-1-il-etoxi)-14,19-dioxa-5,7,26-triaza-tetraciclo[19.3.1.1(2,6).1(8,12)] heptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-deceno	Tratamiento de la mielofibrosis primaria
Swedish	11-(2-pyrrolidin-1-yl-etoxy)-14,19-dioxa-5,7,26-triaza-tetracyclo[19.3.1.1(2,6).1(8,12)] heptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-deken	Behandling av primär myelofibros
Norwegian	11-(2-pyrrolidin-1-yl-etoksy)-14,19- dioksa -5,7,26-triaza-tetracyclo[19.3.1.1(2,6).1(8,12)] heptacosa-1(25),2(26),3,5,8,10,12(27),16,21,23-Decen	Behandling av primær myelofibrose
Icelandic	11-(2-pýrrólidín-1-yl-ethoxý)-14,19-díoxa-5,7,26-tríaza-tetracýclo[19.3.1.1(2,6).1(8,12)] heptacósa-1(25),2(26),3,5,8,10,12(27),16,21,23-deken	Meðferð á beinmergsnetjuhersli