7 November 2016
EMA/620940/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

N-[(2S)-5-{[(1R, 2S)-2-(4-fluorophenyl)cyclopropyl]amino}-1-(4-methylpiperazin-1-yl)-1-oxopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamide, bis-tosylate salt for the treatment of myelofibrosis

On 14 October 2016, orphan designation (EU/3/16/1757) was granted by the European Commission to Imago BioSciences Ltd, United Kingdom, for N-[(2S)-5-{[(1R, 2S)-2-(4-fluorophenyl)cyclopropyl]amino}-1-(4-methylpiperazin-1-yl)-1-oxopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamide, bis-tosylate salt (also known as IMG-7289) for the treatment of myelofibrosis.

What is myelofibrosis?

Myelofibrosis is a disease in which fibrous tissue forms in the bone marrow (the spongy tissue inside the large bones where blood cells are produced), interfering with normal blood cell production. This causes some immature blood cells to migrate from the bone marrow to other organs, such as the spleen and liver, which become enlarged. Symptoms of the disease include bone pain, tiredness, weakness, weight loss, fever and bleeding.

Myelofibrosis is a debilitating disease that is long-lasting and 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).

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

At the time of designation, myelofibrosis affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 51,000 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 28), Norway, Iceland and Liechtenstein. This represents a population of 513,700,000 (Eurostat 2016).

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What treatments are available?

At the time of designation, busulfan, hydroxycarbamide and ruxolitinib were authorised in the EU for myelofibrosis. In addition, medicines were authorised to treat the symptoms, including erythropoietin (a hormone that stimulates the production of red blood cells) to treat anaemia, and surgery was used to remove the enlarged spleen. In some patients, haematopoietic (blood) stem cell transplantation was used to treat the disease. This is a procedure where the patient's bone marrow is cleared of cells and replaced with stem cells from a donor to form new bone marrow that produces healthy blood cells.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with myelofibrosis because laboratory studies have shown that the medicine may reduce spleen size and stop fibrous tissue forming in the bone marrow. 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 blocks the activity of an enzyme called 'lysine-specific demethylase 1' (LSD1). LSD1 is present in high quantities in myelofibrosis patients, leading to the production of abnormal immature blood cells. Blocking its activity is expected to allow the production of normal blood cells and cause death of abnormal cells.

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, no clinical trials with the medicine in patients with myelofibrosis had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for myelofibrosis 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 September 2016 recommending the granting of this designation.

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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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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	N-[(2S)-5-{[(1R,2S)-2-(4-fluorophenyl)cyclopropyl]amino}-1-(4-methylpiperazin-1-yl)-1-oxopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamide, bis-tosylate salt	Treatment of myelofibrosis
Bulgarian	N-[(2S)-5-{[(1R,2S)-2-(4-флуорофенил)циклопропил]амино}-1-(4-метилпиперазин-1-ил)-1-оксопентан-2-ил]-4-(1H-1,2,3-триазол-1-yl)бензамид, бис-тосилат	Лечение на миелофиброза
Croatian	N-[(2S)-5-{[(1R,2S)-2-(4-fluorofenil)ciklopropil]amino}-1-(4-metillpiperazin-1-il)-1-oksopentan-2-il]-4-(1H-1,2,3-triazol-1-yl)benzamid, bis-tosilat sol	Liječenje mijelofibroze
Czech	N-[(2S)-5-{[(1R,2S)-2-(4-fluorophenyl)cyclopropyl]amino}-1-(4-methylpiperazin-1-yl)-1-oxopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamide, bis-tosylat sůl	Léčba myelofibrózy
Danish	N-[(2S)-5-{[(1R,2S)-2-(4-fluorophenyl)cyclopropyl]amino}-1-(4-methylpiperazin-1-yl)-1-oxopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamide, bis-tosylate salt	Behandling af myelofibrose
Dutch	N-[(2S)-5-{[(1R,2S)-2-(4-fluorophenyl)cyclopropyl]amino}-1-(4-methylpiperazin-1-yl)-1-oxopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamide, bis-tosylate zout	Behandeling van myelofibrose
Estonian	N-[(2S)-5-{[(1R,2S)-2-(4-fluorofenüül)tsüklopropüül]amino}-1-(4-metüülpiperaziin-1-üül)-1-oksopentaan-2-üül]-4-(1H-1,2,3-triazool-1-üül)benzamiid, bis-tosülaat sool	Müelofibroosi ravi
Finnish	N-[(2S)-5-{[(1R,2S)-2-(4-fluorofenyyli)syklopropyyli]amino}-1-(4-metyylipiperatsin-1-yyli)-1-oksopentan-2-yyli]-4-(1H-1,2,3-triatsol-1-yyli)bentsamidiini, bis-tosylaatin suola	Myelofibroosin hoito
French	Sel de N-[(2S)-5-{[(1R,2S)-2-(4-fluorophényl)cyclopropyl]amino}-1-(4-méthylpipérazin-1-yl)-1-oxopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamide, bis-tosylate	Traitement de la myélofibrose
German	N-[(2S)-5-{[(1R,2S)-2-(4-fluorophenyl)cyclopropyl]amino}-1-(4-methylpiperazin-1-yl)-1-oxopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamide, bis-tosylate salt	Behandlung der Myelofibrose

[1] At the time of designation

Language	Active ingredient	Indication
Greek	N-[(2S)-5-{[(1R,2S)-2-(4-φθοροφαινυλ)κυκλοπρολυλ]αμινο}-1-(4-μεθυλπιπεραζιν-1-υλ)-1-οξοπενταν-2-υλ]-4-(1H-1,2,3-τριαζολ-1-υλ)βενζαμίδιο, δις -τοσυλικό άλας	Θεραπεία της μυελοϊνωσης
Hungarian	N-[(2S)-5-{[(1R,2S)-2-(4-fluorophenyl)cyclopropyl]amino}-1-(4-methylpiperazin-1-yl)-1-oxopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamide, bis-tosylate só	Myelofibrosis kezelése
Italian	N-[(2S)-5-{[(1R,2S)-2-(4-fluorofenil)ciclopropil]amino}-1-(4-metilpiperazin-1-yl)-1-ossopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamide, sale bis-tosilato	Trattamento della mielofibrosi
Latvian	N-[(2S)-5-{[(1R,2S)-2-(4-fluorofenil)ciklopropil]amino}-1-(4-metilpiperazīn-1-il)-1-oksopentān-2-il]-4-(1H-1,2,3-triazol-1-il)benzamīda, bis-tosilāta sāls	Mielofibrozes ārstēšana
Lithuanian	N-[(2S)-5-{[(1R,2S)-2-(4-fluorofenil)ciklopropil]amin}-1-(4-metilpiperazin-1-il)-1-oksopentan-2-il]-4-(1H-1,2,3-triazol-1-il)benzamid, bis-tosilato druska	Mielofibrozės gydymas
Maltese	N-[(2S)-5-{[(1R,2S)-2-(4-fluorophenyl)cyclopropyl]amino}-1-(4-methylpiperazin-1-yl)-1-oxopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamide, bis-tosylate salt	Kura tal-mjelofibroży
Polish	N-[(2S)-5-{[(1R,2S)-2-(4-fluorofenyl)cyklopropyl]amino}-1-(4-metylpiperazyno-1-yl)-1-oksopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamid, sól bis-tosylatu	Leczenie mielofibrozy
Portuguese	Sal bis tosilato da N-[(2*S*)-5-{[(1*R*,2*S*)-2-(4-fluorofenil)ciclopropil]amino}-1-(4-metilpiperazin-1-il)-1-oxopentan-2-il]-4-(1*H*-1,2,3-triazol-1-il)benzamida	Tratamento da mielofibrose
Romanian	Sare de N-[(2S)-5-{[(1R,2S)-2-(4-fluorofenil)ciclopropil]amino}-1-(4-metilpiperazin-1-il)-1-oxopentan-2-il]-4-(1H-1,2,3-triazol-1-il)benzamidă, bis-tosilat	Tratamentul mielofibrozei
Slovak	N-[(2S)-5-{[(1R,2S)-2-(4-fluorofenyl)cyklopropyl]amino}-1-(4-metylpiperazín-1-yl)-1-oxopentán-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamid, bis-tosylát soľ	Liečba myelofibrózy
Slovenian	N-[(2S)-5-{[(1R,2S)-2-(4-fluorofenil)ciklopropil]amino}-1-(4-metilpiperazin-1-il)-1-oksopentan-2-il]-4-(1H-1,2,3-triazol-1-il)benzamide, bis-tozilat	Zdravljenje mielofibroze
Spanish	Sal de bis-tosilate N-[(2S)-5-{[(1R,2S)-2-(4-fluorofenil)ciclopropil]amino}-1-(4-metilpiperazin-1-il)-1-oxopentan-2-il]-4-(1H-1,2,3-triazol-1-yl)benzamide	Tratamiento de la mielofibrosis

Language	Active ingredient	Indication
Swedish	N-[(2S)-5-{[(1R,2S)-2-(4-fluorophenyl)cyclopropyl]amino}-1-(4-methylpiperazin-1-yl)-1-oxopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamide, bis-tosylate salt	Behandling av myelofibros
Norwegian	N-[(2S)-5-{[(1R,2S)-2-(4-fluorofenyl)syklopropyl]amino}-1-(4-metylpiperazin-1-yl)-1-oksopentan-2-yl]-4-(1H-1,2,3-triazol-1-yl)benzamid, bis-tosylatsalt	Behandling av myelofibrose
Icelandic	N-[(2S)-5-{[(1R,2S)-2-(4-flúórófenýl)cýclóprópýl]amínó}-1-(4-methýlpíperazín-1-ýl)-1-oxópentan-2-ýl]-4-(1H-1,2,3-tríazól-1-ýl)benzamíð, bis-tósýlat salt	Meðferð á mýelófíbrósu