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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

N-tert-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino] benzenesulfonamide dihydrochloride monohydrate for the treatment of primary myelofibrosis

First publication	12 October 2010
Rev.1: transfer of sponsorship	15 March 2011
Rev.2: sponsor's name and address change	5 April 2013

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 1 October 2010, orphan designation (EU/3/10/794) was granted by the European Commission to Dr Ulrich Granzer, Germany, for N-tert-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino] benzenesulfonamide dihydrochloride monohydrate for the treatment of primary myelofibrosis.

The sponsorship was transferred to Sanofi Aventis, France, in February 2011. In October 2012, Sanofi Aventis changed name to Sanofi-Aventis Groupe.

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 results in severe anaemia (low red blood cell counts) and infections, and can lead to leukaemia (cancer of the white blood cells).

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

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 may represent an alternative treatment for patients with this condition. 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 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, the 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 N-tert-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino] benzenesulfonamide dihydrochloride monohydrate 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 primary myelofibrosis were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for primary myelofibrosis. Orphan designation of the medicine had been granted in the United States of America for the treatment of secondary and primary myelofibrosis.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 July 2010 recommending the granting of this designation.

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[*]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:

Sanofi-Aventis Groupe
54 rue de la Boétie
75008 Paris
France
Telephone: +33 1 53 77 40 00
Telefax: +33 1 53 77 41 33
www.sanofi-aventis.com/contact/contact.asp

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-tert-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino] benzenesulfonamide dihydrochloride monohydrate	Treatment of primary myelofibrosis
Bulgarian	N-терт-бутил-3-[(5-метил-2-{[4-(2-пиролидин-1-илетокси)фенил]амино}пиримидин-4-ил)амино] бензенсулфонамид дихидрохлорид монохидрат	Лечение на първична миелофиброза
Czech	Monohydrát dichloridu N-tert-butyl-3-[(5-metyl-2-{[4-(2-pyrrolidin-1-ylethoxy)fenyl]amino}pyrimidin-4-yl)amino] benzensulfonamidu	Léčba primární myelofibrózy
Danish	N-tert-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino] benzensulfonamid-dihydrochlorid-monohydrat	Behandling af primær myelofibrose
Dutch	N-tert-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)fenyl]amino}pyrimidin-4-yl)amino] benzeensulfonamidedihydrochloride-monohydraat	Behandeling van primaire myelofibrose
Estonian	N-tert-butüül-3-[(5-metüül-2-{[4-(2-pürrolidiin-1-üületoksü)fenüül]amino}pürimidiin-4-üül)amino] benseensulfoonamiid divesinikkloriid monohüdraat	Esmase müelofibroosi ravi
Finnish	N-tert-butyyli-3-[(5-metyyli-2-{[4-(2-pyrrolidin-1-yylietoksi)fenyyli]amino}pyrimidin-4-yyli)amino] bentseenisulfonamididihydrokloridimonohydraatti	Primaarisen myelofibroosin hoito
French	Dichlorhydrate de N-tert-butyl-3-[(5-méthyl-2-{[4-(2-pyrrolidin-1-yléthoxy)phényl]amino}pyrimidin-4-yl)amino] benzènesulfonamide monohydraté	Traitement de la myélofibrose primitive
German	N-tert-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino] Benzolsulfonamid Hydrochlorid-Monohydrat	Behandlung der primären Myelofibrose
Greek	N-tert-βουτυλο-3-[(5-μεθυλο-2-{[4-(2-πυρρολιδίνη-1-υλ)εθοξυ)φαινυλο]αμινο}πυριδίνη-4-υλ)αμινο] ένυδρο διυδροχλωρικό σουλφοναμιδικό βενζόλιο	Θεραπεία της πρωτογενούς μυελοσκλήρυνσης
Hungarian	N-terc-butil-3-[(5-metil-2-{[4-(2-pirrolidin-1-ylethoxy)fenil]amino}pirimidin-4-yl)amino]-benzolszulfonamid-dihidroklorid-monohidrát	Primer mielofibrózis kezelésére
Italian	N-terz-butil-3-[(5-metil-2-{[4-(2-pirrolidin-1-iletossi)fenil]amino}pirimidin-4-il)amino] dicloridrato monoidrato di benzensulfonamide	Trattamento della mielofibrosi primitiva

[1] At the time of designation

Latvian	N-terc-butil-3-[(5-metil-2-{[4-(2-pirolidīn-1-iletoksi)fenil]amino}pirimidīn-4-il)amino] benzēnasulfonamīda dihidrohlorīda monohidrāts	Primāras mielofibrozes ārstēšana
Lithuanian	N-tert-butil-3-[(5-metil-2-{[4-(2-pirolidin-1-iletoksi)fenil]amino}pirimidin-4-il)amino] benzensulfonamido dihidrochlorido monohidratas	Pirminės mielofibrozės gydymas
Maltese	N-tert-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino] benzenesulfonamide dihydrochloride monohydrate	Kura tal-mjelofibrożi primarja
Polish	Dwuchlorowodorek N-tert-butylo-3-[(5-metylo-2-{[4-(2-pirolidyno-1-yletoksy)fenylo]amino}pirymidyno-4-yl)amino] benzenosulfonamidu jednowodny	Leczenie mielofibrozy pierwotnej
Portuguese	N-terc-butil-3-[(5-metil-2-{[4-(2-pirrolidina-1-iletoxi)fenil]amino}pirimidin-4-il)amino] benzenosulfonamida diidrocloreto de monoidrato	Tratamento da mielofibrose primária
Romanian	Diclorhidrat de N-tert-butil-3-[(5-metil-2-{[4-(2-pirolidin-1-iletoxi)fenil]amino}pirimidin-4-il)amino] benzensulfonamidă monohidrat	Tratamentul mielofibrozei primitive
Slovak	N-tert-butyl-3-[(5-metyl-2-{[4-(2-pyrolidín-1-yletoxy)fenyl]amino}pyrimidín-4-yl)amino] benzénsulfonamid dihydrochlorid monohydrát	Liečba primárnej myelofibrózy
Slovenian	N-terc-butil-3-[(5-metil-2-{[4-(2-pirolidin-1-iletoksi)fenil]amino}pirimidin-4-il)amino] benzenesulfonamid dihidroklorid monohidrata	Zdravljenje primarne mielofibroze
Spanish	Diclorhidrato de N-tert-butil-3-[(5-metil-2-{[4-(2-pirrolidin-1-iletoxi)fenil]amino}pirimidin-4-il)amino] bencenosulfonamida monohidrato	Tratamiento de la mielofibrosis primaria
Swedish	N-tert-butyl-3-[(5-metyl-2-{[4-(2-pyrrolidin-1-yletoxi)fenyl]amino}pyrimidin-4-yl)amino]bensensulfonamid-dihydrokloridmonohydrat	Behandling av primär myelofibros
Norwegian	N-tert-butyl-3-[(5-metyl-2-{[4-(2-pyrrolidin-1-yletoksy)fenyl]amino}pyrimidin-4-yl)amino] benzensulfonamiddihydrokloridmonohydrat	Behandling av primær myelofibrose
Icelandic	N-tert-bútýl-3-[(5-metýl-2-{[4-(2-pýrrólídín-1-ýletoxý)fenýl]amínó}pýrimídín-4-ýl)amínó] benzensúlfónamíð díhýdróklóríð einhýdrat	Meðferð á beinmergsnetjuhersli