EMA/COMP/601661/2010 Rev.2
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 post-essential thrombocythaemia myelofibrosis

First publication	14 December 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 26 November 2010, orphan designation (EU/3/10/810) 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 post-essential thrombocythaemia 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 post-essential thrombocythaemia myelofibrosis?

Myelofibrosis is a disease 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. It can develop as a reaction to essential thrombocythaemia (overproduction of platelets, components that help the blood to clot). 'Essential' means that the thrombocythaemia is not caused by any known condition.

In myelofibrosis, 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 myelofibrosis can develop several symptoms, including pain in the bones, fever, tiredness, weakness, weight loss, infections and bleeding.

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

Post-essential thrombocythaemia 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).

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

At the time of designation, post-essential thrombocythaemia myelofibrosis affected less than 0.15 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 7,600 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, although hydroxyurea and busulfan were authorised in the EU for primary myelofibrosis (myelofibrosis of unknown cause), there were no treatments authorised specifically for post-essential thrombocythaemia myelofibrosis.

Treatments for this disease were aimed at relieving symptoms. They 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 or radiation to remove or shrink the enlarged spleen. In some patients, allogeneic 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.

How is this medicine expected to work?

This medicine is thought to work by blocking an enzyme known as Janus kinase 2 (JAK2), which can be found in some receptors on the surface of cells and is involved in the production 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 this medicine 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 post-essential thrombocythaemia myelofibrosis were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for post-essential thrombocythaemia 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 9 September 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

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 post-essential thrombocythaemia 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 миелофиброза след есенциална тромбоцитемия
Czech	Monohydrát dichloridu N-tert-butyl-3-[(5-metyl-2-{[4-(2-pyrrolidin-1-ylethoxy)fenyl]amino}pyrimidin-4-yl)amino] benzensulfonamidu	Léčba post-esenciální trombocytémické 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 post essentiel thrombocythæmi myelofibrose
Dutch	N-tert-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)fenyl]amino}pyrimidin-4-yl)amino] benzeensulfonamidedihydrochloride-monohydraat	Behandeling van myelofibrosis volgend op essentiële trombocytemie
Estonian	N-tert-butüül-3-[(5-metüül-2-{[4-(2-pürrolidiin-1-üületoksü)fenüül]amino}pürimidiin-4-üül)amino] benseensulfoonamiid divesinikkloriid monohüdraat	Postessentsiaalse trombotsüteemia müelofibroosi ravi
Finnish	N-tert-butyyli-3-[(5-metyyli-2-{[4-(2-pyrrolidin-1-yylietoksi)fenyyli]amino}pyrimidin-4-yyli)amino] bentseenisulfonamididihydrokloridimonohydraatti	Essentiaalisen trombosytemian jälkeisen 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 consécutive à une thrombocytémie essentielle
German	N-tert-butyl-3-[(5-methyl-2-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}pyrimidin-4-yl)amino] Benzolsulfonamid Hydrochlorid-Monohydrat	Behandlung einer Myelofibrose nach essentieller Thrombozythämie
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 μυελοϊνωσης από ιδιοπαθή θρομβοκυττάρωση
Hungarian	N-terc-butil-3-[(5-metil-2-{[4-(2-pirrolidin-1-ylethoxy)fenil]amino}pirimidin-4-yl)amino]-benzolszulfonamid-dihidroklorid-monohidrát	Esszenciális thrombocytaemiát követő 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 post-trombocitemia essenziale
Latvian	N-terc-butil-3-[(5-metil-2-{[4-(2-pirolidīn-1-iletoksi)fenil]amino}pirimidīn-4-il)amino] benzēnasulfonamīda dihidrohlorīda monohidrāts	Pēc-esenciālas trombocitēmijas mielofibrozes ārstēšana
Lithuanian	N-tert-butil-3-[(5-metil-2-{[4-(2-pirolidin-1-iletoksi)fenil]amino}pirimidin-4-il)amino] benzensulfonamido dihidrochlorido monohidratas	Mielofibrozės gydymas po esencialinės trombocitemijos

[1] At the time of designation

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 konsegwenti għal trombocitemija essenzjali
Polish	Dwuchlorowodorek N-tert-butylo-3-[(5-metylo-2-{[4-(2-pirolidyno-1-yletoksy)fenylo]amino}pirymidyno-4-yl)amino] benzenosulfonamidu jednowodny	Leczenie mielofibrozy wywołanej nadpłytkowością samoistną
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 devida a trombocitémia essencial
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 post-trombocitemie esenţială
Slovak	N-tert-butyl-3-[(5-metyl-2-{[4-(2-pyrolidín-1-yletoxy)fenyl]amino}pyrimidín-4-yl)amino] benzénsulfonamid dihydrochlorid monohydrát	Liečba myelofibrózy po esenciálnej trombocytémii
Slovenian	N-terc-butil-3-[(5-metil-2-{[4-(2-pirolidin-1-iletoksi)fenil]amino}pirimidin-4-il)amino] benzenesulfonamid dihidroklorid monohidrata	Zdravljenje mielofibroze, nastale po esecialni trombocitemiji
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 secundaria a trombocitemia esencial
Swedish	N-tert-butyl-3-[(5-metyl-2-{[4-(2-pyrrolidin-1-yletoxi)fenyl]amino}pyrimidin-4-yl)amino]bensensulfonamiddihydrokloridmonohydrat	Behandling av post-essentiell trombocytemi myelofibros
Norwegian	N-tert-butyl-3-[(5-metyl-2-{[4-(2-pyrrolidin-1-yletoksy)fenyl]amino}pyrimidin-4-yl)amino] benzensulfonamiddihydrokloridmonohydrat	Behandling av myelofibrose sekundært til essensiell trombocytemi
Icelandic	N-tert-bútýl-3-[(5-metýl-2-{[4-(2-pýrrólídín-1-ýletoxý)fenýl]amínó}pýrimídín-4-ýl)amínó] benzensúlfónamíð díhýdróklóríð einhýdrat	Meðferð á mýelófíbrósu í kjölfar eðlislægs blóðflagnadreyra