



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

2-amino-2-[2-[2-chloro-4-[[3-(phenylmethoxy)phenyl]thio]phenyl]ethyl]-1,3-propanediol hydrochloride for the prevention of graft-versus-host disease

On 14 December 2015, orphan designation (EU/3/15/1583) was granted by the European Commission to Novartis Europharm Limited, United Kingdom, for 2-amino-2-[2-[2-chloro-4-[[3-(phenylmethoxy)phenyl]thio]phenyl]ethyl]-1,3-propanediol hydrochloride for the prevention of graft-versus-host disease.

What is graft-versus-host disease?

Graft-versus-host disease (GvHD) is a complication that can affect patients who have received allogeneic haematopoietic (blood) stem-cell transplantation. This is a complex procedure used to treat diseases of the blood such as leukaemia (a cancer of the white blood cells), whereby a patient receives stem cells from a matched donor to help restore the bone marrow, which produces new blood cells.

In GvHD, the transplanted white blood cells recognise the patient as 'foreign' and attack the patient's organs, such as the stomach, gut, skin and liver, leading to organ damage. GvHD may happen shortly after transplantation or later on, in which case a wider range of organs can be involved.

GvHD is a serious and life-threatening disease with a high mortality rate.

What is the estimated number of patients at risk of developing the condition?

At the time of designation, the number of patients at risk of GvHD was estimated to be less than 1 people in 10,000 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 at risk of developing 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 512,900,000 (Eurostat 2015).



What methods of prevention are available?

At the time of designation, several medicines were authorised in the EU for the prevention of GvHD, such as cyclosporine and antilymphocyte immunoglobulins (ATG). Treatment aimed to reduce the activity of immune cells involved in GvHD, thereby reducing their ability to attack the patient's organs.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients at risk of GvHD because initial studies suggest that it may improve the outcome of these patients. 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?

In GvHD, donor white blood cells migrate to host's immune tissue (such as the thymus and lymph nodes), where they are activated and then released to attack cells throughout the body. Their release is triggered by a substance called sphingosine-1-phosphate, which attaches to so-called S1P1 receptors on the cells. This medicine acts by preventing activation of S1P1 receptors and so keeping most of the donor's white blood cells in the immune tissue where they cannot attack the cells of the body. This is expected to prevent GvHD.

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 in patients at risk of GvHD were ongoing.

At the time of submission, this medicine was not authorised anywhere in the EU for prevention of GvHD 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 12 November 2015 recommending the granting of this designation.

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	2-amino-2-[2-[2-chloro-4-[[3-(phenylmethoxy)phenyl]thio]phenyl]ethyl]-1,3-propanediol hydrochloride	Prevention of graft-versus-host disease
Bulgarian	2-амино-2-[2-[2-хлоро-4-[[3-(фенилметокси)фенил]тио]фенил]етил]-1,3-пропандиол хидрохлорид	Профилактика на болестта на присадката срещу приемателя
Croatian	2-amino-2-[2-[2-kloro-4-[[3-(fenilmetoksi)fenil]tio]fenil]etil]-1,3-propandiolklorid	Prevenција reakcije presatka protiv primatelja
Czech	2-amino-2-[2-[2-chloro-4-[[3-(fenylmethoxy)fenyl]thio]fenyl]ethyl]-1,3-propanediol hydrochlorid	Prevence onemocnění štěpu proti hostiteli
Danish	2-amino-2-[2-[2-chloro-4-[[3-(phenylmethoxy)phenyl]thio]phenyl]ethyl]-1,3-propandiol hydrochlorid	Forebyggelse af graft versus host reaktion
Dutch	2-amino-2-[2-[2-chloro-4-[[3-(fenylmethoxy)fenyl]thio]fenyl]ethyl]-1,3-propaandiol hydrochloride	Preventie van "graft versus host" ziekte
Estonian	2-amino-2-[2-[2-kloro-4-[[3-(fenüülmetsü)fenüül]tio]fenüül]etüül]-1,3-propaandioolvesinikkloriid	<i>Graft versus host</i> haiguse preventatsioon
Finnish	2-amino-2-[2-[2-kloro-4-[[3-(fennyylimetoksi)fennyli]tio]fennyli]etyyli]-1,3-propaanidiolihydrokloridi	Käänteishyljintäreaktion esto
French	2-amino-2-[2-[2-chloro-4-[[3-(phénylméthoxy)phényl]thio]phényl]éthyl]-1,3-propanediol hydrochloride	Prévention de la réaction du greffon contre l'hôte
German	2-Amino-2-[2-[2-chloro-4-[[3-(phenylmethoxy)phenyl]thio]phenyl]ethyl]-1,3-propandiolhydrochlorid	Prävention der Graft-versus-Host-Reaktion
Greek	2-αμινο-2-[2-[2-χλωρο-4-[[3-(φαινυλομεθοξυ)φαινυλ]θειο]φαινυλ]αιθυλο]-1,3-προπανεδιόλη υδροχλωρική	Πρόληψη της αντίδρασης του μοσχεύματος
Hungarian	2-amino-2-[2-[4-[[3-(fenilmetoxi)fenil]szulfanil]-2-fenil]etil]propán-1,3-diol–hidroklorid	Graft-versus-host betegség megelőzése
Italian	2-amino-2-[2-[2-cloro-4-[[3-(fenilmetossi)fenil]tio]fenil]etil]-1,3-propandiolo cloridrato	Prevenzione della reazione del trapianto contro l'ospite
Latvian	2-amino-2-[2-[2-hlor-4-[[3-(fenilmetoksi)fenil]tio]fenil]etil]-1,3-propanediola hidrohlorīds	Saimnieka-transplantāta slimības novēršana

¹ At the time of designation

Language	Active ingredient	Indication
Lithuanian	2-amino-2-[2-[2-chloro-4-[[3-(fenilmetoksi)fenil]tio]fenil]etil]-1,3-propandiol hidrochloridas	Transplantato atmetimo ligos prevencija
Maltese	2-amino-2-[2-[2-chloro-4-[[3-(phenylmethoxy)phenyl]thio]phenyl]ethyl]-1,3-propanediol hydrochloride	Kura tal-marda tat-tessut għat-trapjant kontra dak li jirċievih
Polish	Chlorowodorek 2-amino-2-[2-[2-chloro-4-[[3-(fenylometoksy)fenylo]tio]fenylo]etylo]-1,3-propanediolu	Zapobieganie chorobie przeszczep przeciw gospodarzowi
Portuguese	Cloridrato de 2-amino-2-[2-[2-cloro-4-[[3-(fenilmetoxi)fenil]tio]fenil]etil]-1,3-propanodiol	Prevenção da doença do enxerto contra o hospedeiro
Romanian	Clorhidrat de 2-amino-2-[2-[2-cloro-4-[[3-(fenilmetoxi)fenil]tio]fenil]etil]-1,3-propandiol	Prevenirea bolii grefă contra gazdă
Slovak	2-amino-2-[2-[2-chlóro-4-[[3-(fenylmetoxy)fenyl]tio]fenyl]etyl]-1,3-propándiolhydrochlorid	Prevenca reakcie štepu proti hostiteľovi
Slovenian	2-amino-2-[2-[2-kloro-4-[[3-(fenilmetoksi)fenil]tio]fenil]etil]-1,3-propandiol hidroklorid	Preprečevanje zavrnitvene reakcije pri presaditvi
Spanish	Clorhidrato de 2-amino-2-[2-[2-cloro-4-[[3-(fenilmetoxi)fenil]tio]fenil]etil]-1,3-propanodiol	Prevención de la enfermedad de injerto contra huésped
Swedish	2-amino-2-[2-[2-klor-4-[[3-(fenylmetoxi)-fenyl]-tio]-fenyl]-etyl]-1,3-propandiolhydroklorid	Förebyggande av transplantat-mot-värdsjukdom
Norwegian	2-amino-2-[2-[2-kloro-4-[[3-(fenylmetoksy)fenyl]tio]fenyl]etyl]-1,3-propandiol hydroklorid	Forebygging av graft-versus-host -reaksjon
Icelandic	2-amínó-2-[2-[2-klóró-4-[[3-(fenýlmetoxý)fenýl]thíó]fenýl]etýl]-1,3-própandíól hýdróklóríð	Forvörn gegn hýsilssótt