

28 November 2013
EMA/COMP/627684/2013
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Defibrotide for the prevention of graft-versus-host disease

On 13 November 2013, orphan designation (EU/3/13/1201) was granted by the European Commission to Gentium S.p.A., Italy, for defibrotide 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 such as leukaemia or multiple myeloma (cancers 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 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 approximately 0.23 people in 10,000 in the European Union (EU). This was equivalent to a total of around 12,000 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).

What methods of prevention are available?

At the time of designation, several medicines were authorised in the European Union (EU) for the prevention of GvHD, such as ciclosporin and antilymphocyte immunoglobulins (ATG). Treatment aimed

*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 512,200,000 (Eurostat 2013).

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 defibrotide might be of significant benefit for patients at risk of GvHD because preliminary clinical studies show that it may reduce the occurrence of GvHD in patients undergoing transplantation. 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?

Defibrotide is expected to work by reducing formation of blood clots and increasing their breakdown in the blood. It may also protect the cells lining blood vessels, which are damaged in patients undergoing stem-cell transplantation.

What is the stage of development of this medicine?

The effects of defibrotide have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with defibrotide in patients at risk of GvHD were planned.

At the time of submission, defibrotide was not authorised anywhere in the EU for 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 9 October 2013 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:

Gentium S.p.A.
Piazza XX Settembre, 2
22079 Villa Guardia (CO)
Italy
Tel. +39 031 5373 200
Fax +39 031 481 784
E-mail: gentium@gentium.it

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	Defibrotide	Prevention of graft-versus-host disease
Bulgarian	Дефибротид	Профилактика на болест на присадката срещу приемателя
Czech	Defibrotid	Prevence onemocnění štěpu proti hostiteli
Croatian	Defibrotid	Prevenција reakcije presatka protiv primatelja
Danish	Defibrotid	Forebyggelse af graft versus host reaktion
Dutch	Defibrotide	Preventie van "graft versus host" ziekte
Estonian	Defibrotiid	<i>Graft versus host</i> haiguse preventsoon
Finnish	Defibrotidi	Käänteishyljintäreaktion esto
French	Défibrotide	Prévention de la réaction du greffon contre l'hôte
German	Defibrotid	Prävention der Graft-versus-Host-Reaktion
Greek	Ντεφιμπροτιδή	Πρόληψη της αντίδρασης του μοσχεύματος
Hungarian	Defibrotid	Graft-versus-host betegség megelőzése
Italian	Defibrotide	Prevenzione della reazione del trapianto contro l'ospite
Latvian	Defibrotīds	Saimnieka-transplantāta slimības novēršana
Lithuanian	Defibrotidas	Transplantato atmetimo ligos prevencija
Maltese	Defibrotide	Kura tal-marda tat-tessut għat-trapjant kontra dak li jirċievih
Polish	Defibrotyd	Zapobieganie chorobie przeszczep przeciw gospodarzowi
Portuguese	Defibrotide	Prevenção da doença do enxerto contra o hospedeiro
Romanian	Defibrotidă	Prevenirea bolii grefă contra gazdă
Slovak	Defibrotid	Prevenia reakcie štepů proti hostiteľovi
Slovenian	Defibrotid	Preprečevanje zavrnitvene reakcije pri presaditvi
Spanish	Defibrotida	Prevención de la enfermedad de injerto contra huésped
Swedish	Defibrotid	Förebyggande av graft-värd host reaktion
Norwegian	Defibrotid	Forebygging av graft-versus-host -reaksjon
Icelandic	Defibrótíð	Forvörn gegn hýsilssótt

¹ At the time of designation