



COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

**PUBLIC SUMMARY OF
POSITIVE OPINION FOR ORPHAN DESIGNATION
OF**

**defibrotide
for the treatment of hepatic veno-occlusive disease (VOD)**

On 29 July 2004, orphan designation (EU/3/04/212) was granted by the European Commission to, Gentium S.p.A, Italy, for defibrotide for the treatment of hepatic veno-occlusive disease (VOD).

What is hepatic veno-occlusive disease?

Hepatic veno-occlusive disease (VOD) is a disease of the liver in which the small vessels are destroyed. This can occur following liver transplantation but also as an adverse reaction to certain medicines. Examples of the latter one are chemotherapeutic agents (drugs used to kill cancer cells or used in certain circumstances to eliminate cells of the body's defence system) or medicines containing specific proteins called antibodies used to target abnormal cells in certain diseases such as acute myeloid leukaemia. Hepatic veno-occlusive disease (VOD) is characterised by painful enlargement of the liver (hepatomegaly), yellowing of the skin and eyes caused by excess bile products in the blood (jaundice), excess fluid in the abdomen (ascites) and weight gain due to fluid retention by the body.

What are the methods of treatment available?

No satisfactory methods exist that were authorised at the time of application. Supportive measures are aimed at maintaining an adequate functioning of the liver and include dietary restriction of salt and liquids, administration of medicines called diuretics that help removing fluids from the body.

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

According to the information provided by the sponsor, hepatic veno-occlusive disease (VOD) was considered to affect not more than 19,000 persons in the European Union.

How is this medicinal product expected to act?

Defibrotide is expected to act by preventing the clotting (thrombosis) in the blood vessels (antithrombotic activity) or by stimulating the dissolution of the clot (thrombolysis).

What is the stage of development of this medicinal product?

The effects of defibrotide were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with hepatic veno-occlusive disease (VOD) were ongoing.

The medicinal product was not marketed anywhere worldwide for hepatic veno-occlusive disease at the time of submission. Orphan designation of defibrotide was granted in the United States for the treatment of hepatic veno-occlusive disease.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 16 June 2004 a positive opinion recommending the grant of the above-mentioned designation.

Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

For more information:

Sponsor's contact details:

Gentium S.p.A

Piazza XX Settembre, 2

I-22079 Villa Guardia (CO)

Italy

Telephone: +39 031 38 52 17

Telefax: +39 031 38 52 41

E-mail: miacobelli@gentium.it

Patients' association contact point:

British Liver Trust

Portman House

44 High Street

Ringwood

BH24 1AG

United Kingdom

Telephone: +44 14 25 46 30 80

E-mail: info@britishlivertrust.org.uk

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

**Translations of the active ingredient and indication in all EU languages
and Norwegian and Icelandic**

Language	Active Ingredient	Indication
English	Defibrotide	Treatment of hepatic veno-occlusive disease
Czech	Defibrotid	Léčba jaterní veno-okluzivní choroby
Danish	Defibrotid	Behandling af hepatisk veno-okklusiv sygdom
Dutch	Defibrotide	Behandeling van veno-occlusieve leverziekte
Estonian	Defibrotide	Maksa venoos-oklusiivse haiguse ravi
Finnish	Defibrotidi	Maksan laskimotukkeumasairauden hoito
French	Défibrotide	Traitement de la maladie veino-occlusive hépatique
German	Defibrotid	Behandlung des hepatischen Venenverschlusssyndroms
Greek	Δεφιβροτίδη	Θεραπεία φλεβοαποφρακτικής ηπατοπάθειας
Hungarian	Defibrotide	Veno-occlusiv májbetegség kezelése
Italian	Defibrotide	Trattamento della malattia epatica veno-occlusiva
Latvian	Defibrotīds	Aknu vēnu okluzīvas saslimšanas ārstēšanai
Lithuanian	Defibrotidas	Kepenų veninės - okliuzinės ligos gydymas
Maltese	Defibrotide	Treatment of hepatic veno-occlusive disease
Polish	Defibrotyd	Leczenie choroby okluzyjnej żył wątroby
Portuguese	Defibrotide	Tratamento da doença veno-occlusiva hepática
Slovak	Defibrotid	Liečba venookluzívnej choroby pečene
Slovenian	Defibrotide	Zdravljenje okluzivne bolezni hepatičnih ven
Spanish	Defibrotida	Tratamiento de la enfermedad venoocclusiva hepática
Swedish	Defibrotid	Behandling av hepatisk venoockluderande sjukdom
Norwegian	Difibrotid	Behandling av hepatisk veno-okklusiv sykdom
Icelandic	Defibrótíð	Meðferð við bláæðastíflun í lifur