Launch of Defitelio®▼ (defibrotide) in the EU Information on an EBMT Registry

Defitelio® (defibrotide) has recently been granted a Marketing Authorization for the treatment of severe hepatic veno-occlusive disease (sVOD) in adults and children (over 1 month) in hematopoietic stem cell transplantation.

As part of its post-marketing obligations, the Marketing Authorization Holder (Gentium SpA) has collaborated with the European Society for Blood and Marrow Transplantation (EBMT) to set up a disease registry to collect data in sVOD patients who are either treated with Defitelio® or managed through supportive care only, and to better understand how Defitelio® is being used in clinical practice.

This multi-centre, multi-national, prospective, observational registry is now launched and will:

- focus on specific participating sites which have been selected from the major transplant centres (defined as those performing at least 100 transplants per year) in order to optimise recruitment of severe VOD patients
- open until June 2018 and is planned to recruit 300 patients treated with Defitelio® and 300 patients managed through supportive care only who will act as a control group
- collect data on serious adverse events (SAEs) of interest as well as endpoints of interest in relation to clinical outcome and standard baseline information

The EBMT will also consider additional centres which may be interested in contributing data to this registry. *(Please note that further approvals at a European and a national level may be required for participation of additional sites.)*

For further information on this Registry please contact Emmanuelle Polge, EBMT Operations Manager, via email at jessica.lemaitre@upmc.fr

DEFITELIO® 80 mg/mL concentrate for solution for infusion
Abbreviated Prescribing Information

Refer to Summary of Product Characteristics before prescribing. Presentation: Defitelio® 80 mg/mL concentrate for solution for infusion. Each 2.5 mL vial contains 200 mg defibrotide. For intravenous injection. Indication: Defitelio® is indicated in the treatment of severe hepatic veno-occlusive disease (VOD) in haematopoietic stem-cell transplantation (HSCT) therapy.

Dosage and administration: For adults and children over 1 month of age. Defitelio® must be prescribed and administered by specialised physicians experienced in the diagnosis and treatments of complications of HSCT. The recommended dose is 6.25 mg/kg body weight every 6 hours (25 mg/kg/day) administered over a 2-hour intravenous infusion. Defitelio® must always be diluted with 5% glucose solution for infusion or sodium chloride 9 mg/mL (0.9%) solution for infusion prior to use. Defitelio® should be administered for a minimum of 21 days and continued until symptoms and signs of severe VOD resolve. Renal and hepatic impairment: no dose adjustment recommended but careful monitoring of the patients should be undertaken. Contraindications: Hypersensitivity to the active substance or to any of the excipients. Concomitant use of thrombolytic therapy (e.g. t-PA). Warnings and precautions: Use of medicinal products that increase the risk of haemorrhage within 24 hours of Defitelio® administration (within 12 hours in the case of unfractionated heparin) is not recommended. Concomitant systemic anticoagulant therapy (e.g. heparin, warfarin, direct thrombin inhibitors and direct factor Xa inhibitors), except for routine maintenance or reopening of central venous line, requires careful monitoring. Medicinal products that affect platelet aggregation (e.g. non– steroidal anti-inflammatory agents) should be administered with care. In patients who have or develop clinically significant acute bleeding requiring blood transfusion, Defitelio® is not recommended or should be discontinued. Temporary discontinuation of Defitelio® is recommended in patients who undergo surgery or invasive procedures at significant risk of major bleeding. Administration of Defitelio® to patients who have haemodynamic instability, defined as inability to maintain mean arterial pressure with single pressor support, is not recommended. The use of Defitelio® in children aged less than one month is not recommended. A bolus administration of Defitelio® may cause flushing or a sensation of "generalised heat". Undesirable effects: common (≥1/100 to <1/10): coagulopathy, cerebral, pulmonary and gastrointestinal haemorrhage, epistaxis, haematuria, catheter site haemorrhage, vomiting, hypotension. Uncommon (≥1/1000 to <1/100): hypersensitivity, anaphylactic reaction, cerebral haematoma, conjunctiva, mouth and injection site haemorrhage, haemothorax, haematemesis, melaena, diarrhoea, nausea, ecchymosis, petechiae, rash, pruritus, pyrexia. Legal category: POM. Marketing authorisation number: EU/1/13/878/001. Package quantity: cartons containing 10 × 2.5 mL vials. Further information is available from Gentium SpA, Piazza XX Settembre 2, 22079 Villa Guardia (Co)- Italy Tel +39 0315373200.

Date of prescribing information: March 2015. Defitelio® is a registered trade mark.

For medical information requests, please email: medical-enquiries@gentium.it or phone +39 031 5373 112

Reporting suspected adverse reactions after authorisation of the medicinal product is important.
It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via
IMB Pharmacovigilance - Earlsfort Terracce, IRL – Dublin 2;
Tel: +353 1 6764971; Fax +353 1 6762517; Website: www.imb.ie; e-mail: imbpharmacovigilance@imb.ie
Adverse events should also be reported to Gentium. E-mail: pharmacovigilance@gentium.it
Tel: +39 (0) 31 5373 200 Fax: +39 (0) 31 5373 241
Adverse events should be reported.
For the UK only, adverse events reporting forms can be found at www.yellowcard.gov.uk