# VOD Risk Factor Awareness

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Patient information:

Patient ID

Name

Date of Birth

Risk factors checked by:

Name

Role

Date

Notes:

| | Transplant-related | OR | Patient and disease-related | OR | Hepatic-related | OR |
|---|---|---|---|---|---|---|
| OR ≥ 10 | | | ☐ Treatment with norethisterone | 10.1 | ☐ Bilirubin >26 μmol/L before BMT<br>Previous use of:<br>☐ Inotuzumab ozogamicin<br>☐ Gemtuzumab ozogamicin | 23.5<br><br>22<br>19.8 |
| 4 ≤ OR < 10 | ☐ Oral or high-dose busulfan-based regimen<br>☐ Myeloablative-conditioning regimen | up to 8.8<br><br>up to 7.9 | ☐ Age <6.7 years in children<br>☐ Genetic factors (GSTM1 polymorphism)<br>☐ Thalassaemia | 9.5<br>up to 4.1<br>up to 4.0 | ☐ Transaminases >2.5 ULN | up to 4.6 |
| OR <4 | ☐ High-dose TBI-based regimen<br>☐ Non T-cell-depleted transplant<br>☐ Previous HSCT<br>☐ HLA-mismatched donor<br>☐ Unrelated donor | 2.8<br>2.2<br>1.9<br>1.4<br>1.4 | ☐ Karnofsky score below 90%<br>☐ Advanced disease (beyond second CR or relapse/refractory) | 2.7<br>up to 1.7 | ☐ Pre-existing liver disease<br>☐ Abdominal irradiation<br>☐ Active viral hepatitis | 3.4<br>2.9<br>2.0 |
| OR unknown | | | ☐ Metabolic syndrome<br>☐ Older age in adults<br>Genetic factors:<br>☐ C282Y allele<br>☐ MTHFR 677CC/1298CC haplotype | Unknown | ☐ Cirrhosis<br>☐ Hepatotoxic drugs<br>☐ Hepatic irradiation | Unknown |

**The outlined risk factors may apply to adults, children, or both.**

Abbreviations: BMT, bone marrow transplant; CR, complete response; HLA, human leukocyte antigens; HSCT, haematopoietic stem cell transplant; OR, odds ratio; TBI, total body irradiation; ULN, upper limit of normal; VOD, veno-occlusive disease.

Adapted from: Mohty M, *et al.* Bone Marrow Transplant 2016;51(7):906–912, Dalle JH, Giralt SA. Biol Blood Marrow Transplant 2016;22(3):400–409, Cesaro S, *et al.* Haematologica. 2005;90(10):1396–1404. and Corbacioglu S, *et al.* Biol Blood Marrow Transplant 2019;25(7):1271–1280.

# Why is it important to be aware of the risk factors of VOD?

Risk stratification is a useful way to help identify which of your patients may be most at risk of developing VOD related to their HSCT.[1]
The presence of risk factors is also important when grading VOD using the EBMT severity grading criteria.[1]

This form lists risk factors for VOD as recognised by the EBMT.[1] Use this form to familiarise yourself with the VOD risk factors.
It is intended to gather information that can support you when conducting risk assessment for post-HSCT VOD.

**Please be aware this is not a validated tool to assess the likelihood of VOD – it should only be used to collate information.**

**Indication**
Defitelio® is indicated for the treatment of severe hepatic veno-occlusive disease (VOD) also known as sinusoidal obstructive syndrome (SOS) in haematopoietic stem-cell transplantation (HSCT) therapy.

It is indicated in adults and in adolescents, children and infants over 1 month of age.

**Prescribing Information**

**Defitelio® ▼80 mg/mL concentrate for solution for infusion**
**(Defibrotide)**
Please refer to the Summary of Product Characteristics before Prescribing.

**Presentation:** Each 2.5 mL vial contains 200 mg defibrotide. Concentrate for solution for infusion. **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 treatment of complications of HSCT. The recommended dose is 6.25 mg/kg body weight every 6 hours (recommended max: 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 impairment: Dose adjustment is not required for patients with renal impairment or who are on intermittent haemodialysis. Hepatic impairment: no dose adjustment recommended but careful monitoring of the patients should be undertaken. Paediatric population: The use of Defitelio® in children aged less than one month is not recommended. **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. A bolus administration of Defitelio® may cause flushing or a sensation of "generalised heat". **Fertility, Pregnancy and Lactation:** No data on use in pregnant women. Not to be used during pregnancy unless benefits outweighs risk. It is not known if Defitelio is excreted in human milk. Risk to infant not expected. It may be used in breast feeding. **Undesirable effects:** ***Please refer to the full SmPC for the complete list of undesirable effects.*** Very common (≥1/10): hypotension. Common (≥1/100 to <1/10): coagulopathy, haemorrhage including cerebral, pulmonary, mouth and gastrointestinal haemorrhage, catheter site haemorrhage, epistaxis, haematemesis, haematuria, petechiae, rash, pruritus, pyrexia, diarrhoea, nausea, vomiting. Uncommon (≥1/1000 to < 1/100): hypersensitivity, anaphylactic reaction, cerebral haematoma, conjunctival and injection site haemorrhage, haemothorax, melaena, ecchymosis. **Overdose:** There is no specific antidote for overdose and treatment should be symptomatic. Defibrotide is not removed by dialysis. **Storage and Handling:** This medicinal product does not need any special storage condition. Do not freeze. Defitelio® is for single use only. Shelf life of unopened vials: 3 years. Any unused medicinal product or waste material should be disposed of in accordance with local requirements. **Legal category:** POM. Package Quantity and Cost: 10 x 2.5mL vials. UK: £3650. IE: Price on Application. **Marketing authorisation number:** EU/1/13/878/001. **Marketing Authorisation Holder:** Gentium Srl., Piazza XX Settembre 2, 22079 Villa Guardia (Co)- Italy Tel +39 0315373200. **Date of preparation:** February 2019. **Job Code:** EURW-UKIREDEF-0001.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

**Adverse events should be reported. Healthcare professionals are asked to report any suspected adverse reactions.**

**For the UK, reporting forms and information can be found at: www.mhra.gov.uk/yellowcard.**

**For Ireland, reporting forms and information can be found at: www.hpra.ie.**

**Adverse events should also be reported by email: AEreporting@jazzpharma.com or by fax to +44 (0) 1865 598765.**

References: 1. Mohty M, *et al.* Bone Marrow Transplant 2016;51(7):906–912.