Prescribing Information for the United Kingdom

Defitelio® ▼ 80 mg/mL concentrate for solution for infusion (Defibrotide)

Consult the Summary of Product Characteristics (SMPC) before prescribing.

Indication: Defitelio® is indicated for the treatment of severe hepatic veno-occlusive disease (VOD) also known as sinusoidal obstruction syndrome in haematopoietic stem-cell transplantation (HSCT) therapy. It is indicated in adults and in adolescents, children and infants over 1 month of age. **Presentation:** Each 2.5 mL vial contains 200 mg defibrotide concentrate for solution for infusion. **Dosage and administration:** Defitelio® must be prescribed and administered by specialised physicians experienced in the diagnosis and treatment of complications of HSCT. For adults and children over 1 month of age, 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. **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. **Interactions:** ***For potential interactions please refer to the information provided in the SmPC.*** **Fertility, pregnancy, and lactation:** Effective contraception is required for patients and partners of patients during exposure to Defitelio® and for one week subsequent to discontinuation. No data on use in pregnant women. Not to be used during pregnancy unless benefits outweigh risks. It is not known if Defitelio® is excreted in human milk. Risk to infant not expected. It may be used in breastfeeding. **Effects on ability to drive and use machines:** Defitelio® has no or negligible influence on the ability to drive and operate machines. **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 (cerebral haemorrhage, pulmonary haemorrhage, epistaxis, gastro-intestinal haemorrhage, mouth haemorrhage, catheter site haemorrhage); vomiting; diarrhoea; nausea; haematemesis; rash; pruritis; petechiae; haematuria; pyrexia. **Legal category:** POM. **UK List price:** 10 x 2.5mL vials, £3650. **Marketing authorisation number:** PLGB 31626/0005. **Marketing authorisation holder:** Jazz Pharmaceuticals UK Limited, 80 Charlotte Street, London, United Kingdom, W1T 4DF. **Date of preparation:** November 2024. **Job Code:** UK-DEF-2400040. Defitelio® is a registered trademark.

Adverse events should be reported.

Reporting forms and information can be found at:
https://yellowcard.mhra.gov.uk/

Adverse events should also be reported to Jazz Pharmaceuticals by phone: +44 (0)8081890387 (freephone) or by e-mail to medinfo-uk@jazzpharma.com

UK-DEF-2400060
Date of preparation: November 2024

Prescribing Information for The Republic of Ireland

Defitelio® ▼ 80 mg/mL concentrate for solution for infusion (Defibrotide)

Consult the Summary of Product Characteristics (SMPC) before prescribing.

Indication: Defitelio® is indicated for the treatment of severe hepatic veno-occlusive disease (VOD) also known as sinusoidal obstruction syndrome in haematopoietic stem-cell transplantation (HSCT) therapy. It is indicated in adults and in adolescents, children and infants over 1 month of age. **Presentation:** Each 2.5 mL vial contains 200 mg defibrotide concentrate for solution for infusion. **Dosage and administration:** Defitelio® must be prescribed and administered by specialised physicians experienced in the diagnosis and treatment of complications of HSCT. For adults and children over 1 month of age, 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. **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. **Interactions:** ***For potential interactions please refer to the information provided in the SmPC.*** **Fertility, pregnancy, and lactation:** Effective contraception is required for patients and partners of patients during exposure to Defitelio® and for one week subsequent to discontinuation. No data on use in pregnant women. Not to be used during pregnancy unless benefits outweigh risks. It is not known if Defitelio® is excreted in human milk. Risk to infant not expected. It may be used in breastfeeding. **Effects on ability to drive and use machines:** Defitelio® has no or negligible influence on the ability to drive and operate machines. **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 (cerebral haemorrhage, pulmonary haemorrhage, epistaxis, gastro-intestinal haemorrhage, mouth haemorrhage, catheter site haemorrhage); vomiting; diarrhoea; nausea; haematemesis; rash; pruritis; petechiae; haematuria; pyrexia. **Legal category:** POM. **List price:** 10 x 2.5mL vials: price on application. **Marketing authorisation number:** EU/1/13/878/001. **Marketing authorisation holder:** Gentium S.r.l, Piazza XX Settembre 2, 22079 Villa Guardia, Como, Italy. **Date of preparation:** November 2024. **Job Code:** IE-DEF-2400004. Defitelio® is a registered trademark.

Adverse events should be reported.

Reporting forms and information can be found at:
https://www.hpra.ie/homepage/about-us/report-an-issue

Adverse events should also be reported to Jazz Pharmaceuticals by phone: +44 (0)8081890387 (freephone) or +353 1 968 1631 (Republic of Ireland- charges may apply) or by e-mail to medinfo-uk@jazzpharma.com

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Date of preparation: November 2024