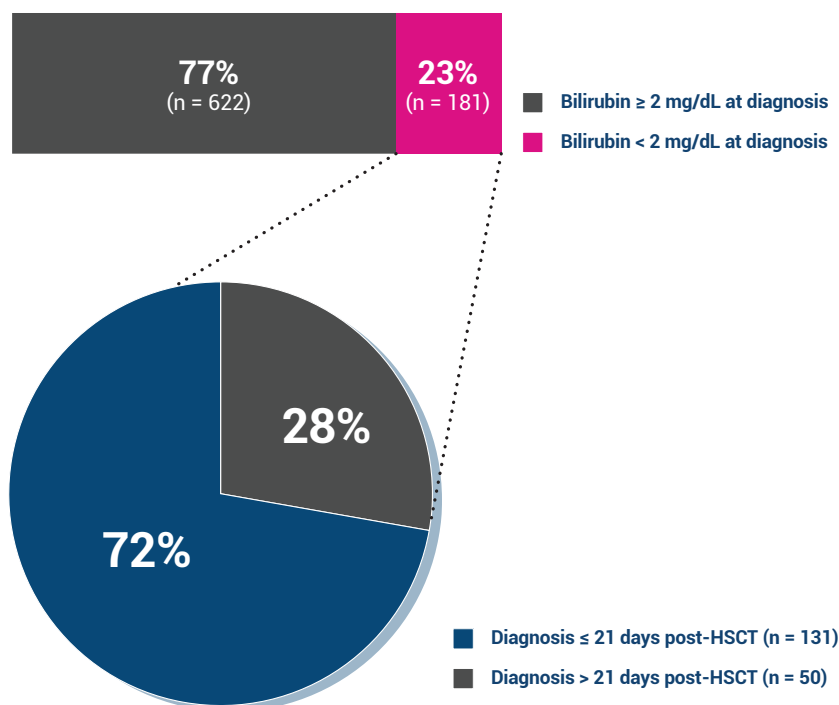


**Prompt identification of VOD without
hyperbilirubinemia can allow for earlier
treatment and improved survival outcomes**

In both adults and pediatric patients, anicteric VOD (defined as bilirubin < 2 mg/dL) can occur before and after Day 21 post-HSCT^{1*}

Incidence of anicteric VOD/SOS in both pediatric and adult patients (N = 803)



Adapted from Corbacioglu, *et al.*

23% of patients in the T-IND study had a bilirubin level < 2 mg/dL at time of VOD diagnosis

- These patients would have been **untreated** if the presence of hyperbilirubinemia was required for VOD diagnosis
- 28% of these anicteric patients experienced late onset VOD (> 21 days)
 - Therefore, it is important to monitor patients for VOD at any time after HSCT

For more information about DEFITELIO, please contact your Jazz Pharmaceutical representative or Jazz Medical Information at jazzcamc@dlss.com

Indications and Clinical Use:

^PrDEFITELIO® (defibrotide sodium) solution for intravenous infusion is indicated for the treatment of adult and pediatric patients with severe hepatic veno-occlusive disease (VOD) also known as sinusoidal obstruction syndrome (SOS), following hematopoietic stem-cell transplantation (HSCT).²

Geriatrics (> 65 years of age): Clinical studies of DEFITELIO did not include sufficient numbers of patients aged 65 years and over to determine whether they respond differently from younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

Pediatrics (≤ 16 years of age): The safety and effectiveness of DEFITELIO in pediatric patients (> 1 month to < 16 years of age) were established in clinical trials in pediatric patients with severe hepatic VOD following HSCT.

Contraindications:

- Concomitant administration with systemic anti-coagulant or fibrinolytic therapy
- Known hypersensitivity to this drug or to any ingredient in the formulation or component of the container

Most Serious Warnings and Precautions:

DEFITELIO must be prescribed and administered to patients by specialized physicians experienced in the diagnosis and treatment of complications of HSCT.

DEFITELIO increased the activity of thrombolytic/fibrinolytic enzymes *in vitro*, and it may increase the risk of bleeding in patients with VOD after HSCT. Do not initiate DEFITELIO in patients with active bleeding. Patients should be closely monitored for signs and symptoms of hemorrhage during treatment with DEFITELIO. In patients who develop active bleeding, discontinue treatment with DEFITELIO until the bleeding is controlled. Discontinue DEFITELIO infusion at least 2 hours prior to an invasive procedure.

Patients treated with DEFITELIO must not receive concomitant medications such as heparin, warfarin, alteplase, or other systemic anticoagulant or fibrinolytic therapy (excluding routine maintenance or reopening of central venous lines) because of the potential increased risk of bleeding.

Other Relevant Warnings and Precautions:

- Anaphylactic reaction has been reported in association with the use of DEFITELIO
- Peri-operative considerations/surgery: There is no known reversal agent for the profibrinolytic effects of DEFITELIO. Discontinue DEFITELIO infusion at least 2 hours prior to an invasive procedure
- Use in pregnant and/or nursing women
- Effective contraception is required for male and female patients during exposure to DEFITELIO and for 1 week subsequent to discontinuation

For More Information:

Please consult the Product Monograph at <https://pp.jazzpharma.com/pi/defitelio.ca.PM-en.pdf> for important information relating to adverse reactions, interactions and dosing information which have not been discussed in this piece.

The Product Monograph is also available by calling Jazz Medical Information at 1-800-520-5568.

^{*}Results T-IND, an open-label, single-arm study. A total of 1154 patients were enrolled across 101 centres in the US. Of these patients, 1137 met the criteria for VOD. A total of 1000 patients (including 570 pediatric patients) with hepatic VOD/SOS, with or without multi-organ dysfunction (MOD), post-HSCT or post-non-transplant associated chemotherapy alone, were treated with DEFITELIO. Patients received 25 mg/kg/day (4 divided doses of 6.25 mg/kg, 2-hour infusion) for ≥ 21 days. Dosing was based on patient's baseline body weight prior to HSCT conditioning: doses were rounded to the nearest 10 mg for adults and pediatric patients > 35 kg and to the nearest 5 mg for pediatric patients < 35 kg.

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Jazz Pharmaceutical representative or Jazz Medical Information at jazzcamc@dlss.com

REFERENCES: 1. Corbacioglu S, Kernan NA, Pagliuca A, *et al.* Incidence of anicteric veno-occlusive disease/sinusoidal obstruction syndrome and outcomes with defibrotide following hematopoietic cell transplantation in adult and pediatric patients. *Biol Blood Marrow Transplant* 2020;26:1342–1349. 2. Current DEFITELIO Product Monograph, Jazz Pharmaceuticals Canada Inc.



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