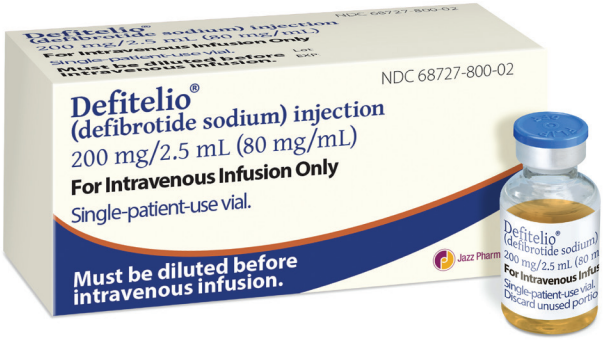
Defitelio® (defibrotide sodium) Fact Sheet

DEFITELIO® (DEFIBROTIDE SODIUM)

Defitelio® (defibrotide sodium) is the first and only FDA-approved therapy in the United States for the treatment of adult and pediatric patients with hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS), with renal or pulmonary dysfunction following hematopoietic stem-cell transplantation (HSCT).



INDICATION[1]

Defitelio is indicated for the treatment of adult and pediatric patients with hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS), with renal or pulmonary dysfunction following hematopoietic stem cell transplantation (HSCT).

ABOUT HEPATIC VOD

HSCT is a potentially curative procedure to treat patients with malignant and non-cancerous hematologic (blood-based) disorders such as leukemia, lymphoma, and aplastic anemia; congenital immunodeficiencies (disorders, present at birth, that compromise the body's ability to fight infections and other diseases); and metabolic disorders.[2]

Hepatic VOD is an early and life-threatening complication of HSCT affecting the sinusoidal endothelial cells that line small veins in the liver. As a result, the small veins, known as sinusoids, become blocked, leading to liver dysfunction.[3] VOD typically occurs within the first 21 days following HSCT and may progress to VOD with multi-organ dysfunction (MOD) in about 30-50% of cases.[4-6]

MOD is characterized by the presence of renal or pulmonary dysfunction.[1] VOD with MOD is associated with an overall mortality (death) rate of 84%.[3] VOD is often characterized by sudden weight gain, hepatomegaly (abnormally enlarged liver), and elevated bilirubin (a substance formed when red blood cells are broken down; abnormal buildup of bilirubin causes jaundice), among other symptoms.[3,6-7]

MECHANISM OF ACTION[1]

Although the exact mechanism of action of Defitelio is not fully known, laboratory studies suggest that the active substance of the drug, known as defibrotide sodium, reduces activation of endothelial cells (inner lining of blood vessels), promotes the breakdown of a blood-clotting protein called fibrin, and also protects endothelial cells from harmful effects of chemotherapy.

CONTRAINDICATIONS[1]

Defitelio should not be given to patients who are:

- Currently taking anti-coagulants or fibrinolytics
- Allergic to Defitelio or any of its ingredients

DOSING[1]

The recommended dose of Defitelio for adult and pediatric patients is 6.25 mg/kg every 6 hours, given as a 2-hour intravenous infusion. Dosing should be based on the patient's baseline body weight, defined as the patient's weight prior to the preparative regimen for HSCT. Defitelio should be given for a minimum of 21 days and continued until the signs and symptoms of VOD have resolved or up to a maximum of 60 days.

Please see full Prescribing Information for Defitelio and discuss with your doctor.

CLINICAL DATA[1]

The efficacy of Defitelio was investigated in three studies:

- **Study 1:** In a prospective study, Defitelio (n=102) was associated with 38% Day +100 survival after transplantation
- **Study 2:** In another prospective study, Defitelio (n=75) was associated with 44% Day +100 survival after transplantation
- **Study 3:** In an expanded access study, Defitelio (n=351) was associated with 45% Day +100 survival after transplantation

SAFETY[1]

The safety of Defitelio was determined in 176 adult and pediatric patients with hepatic VOD with pulmonary and/or renal dysfunction following HSCT who were treated with 6.25 mg/kg of Defitelio every 6 hours. The most common adverse reactions (incidence ≥10% and independent of causality) with Defitelio treatment were hypotension (low blood pressure), diarrhea, vomiting, nausea and epistaxis (nose bleeds). The most common serious adverse reactions (incidence ≥5% and independent of causality) were hypotension (11%) and pulmonary alveolar hemorrhage (7%).

ADDITIONAL IMPORTANT SAFETY INFORMATION FOR DEFITELIO[1]

Defitelio should not be given to patients who are:

- Currently taking anti-coagulants or fibrinolytics
- Allergic to Defitelio or any of its ingredients

Defitelio may increase the risk of bleeding in patients with VOD and should not be given to patients with active bleeding. During treatment with Defitelio, patients should be monitored for signs of bleeding. In the event that bleeding occurs during treatment with Defitelio, treatment may be temporarily or permanently stopped. Patients should tell the doctor right away about any signs or symptoms of hemorrhage such as unusual bleeding, easy bruising, blood in urine or stool, headache, confusion, slurred speech, or altered vision.

Defitelio may cause allergic reactions including anaphylaxis. Patients who develop signs and symptoms of anaphylaxis such as trouble breathing, severe itching, skin rash or hives, or swelling of the face, lips, mouth or tongue should seek medical attention immediately.

The most common side effects of Defitelio are decreased blood pressure, diarrhea, vomiting, nausea and nose bleeds.

Jazz Pharmaceuticals®

REFERENCES

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6. Carreras E. Early complications after HSCT. In: Apperley J, Carreras E, Gluckman E, et al, eds. *The EBMT Handbook*. 6th ed. Paris, France: European School of Haematology; 2012:176-195.
7. NCI Dictionary of Cancer Terms. Bethesda, MD: National Cancer Institute; 2015. http://www.cancer.gov/publications/dictionaries/cancer-terms.

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Please see full Prescribing Information for Defitelio and discuss with your doctor.

DEFITELIO® (defibrotide sodium) injection 80 mg/mL