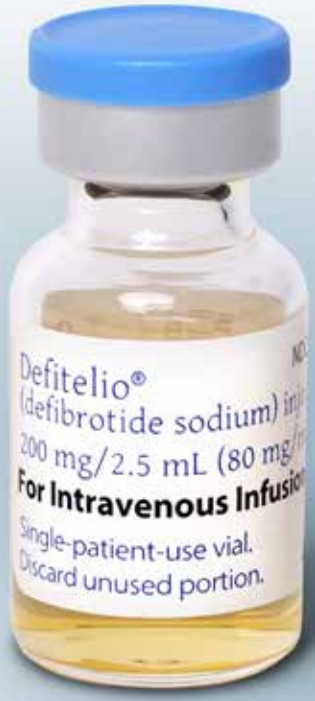
PHARMACY DOSING AND ORDERING GUIDE



DEFITELIO®
(defibrotide sodium) injection 80 mg/mL

FIRST AND ONLY APPROVED TREATMENT FOR PATIENTS WITH VOD

WITH RENAL OR PULMONARY DYSFUNCTION POST HSCT

VOD=veno-occlusive disease

Indication

Defitelio® (defibrotide sodium) 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).

IMPORTANT SAFETY INFORMATION

Contraindications

Defitelio is contraindicated in the following conditions:

- Concomitant administration with systemic anticoagulant or fibrinolytic therapy
- Known hypersensitivity to Defitelio or to any of its excipients

Please see additional Important Safety Information on page 11 and click here for full Prescribing Information.

Description and dosing

Defibrotide sodium is an oligonucleotide mixture with profibrinolytic properties. The chemical name of defibrotide sodium is polydeoxyribonucleotide, sodium salt. Defibrotide sodium is a polydisperse mixture of predominantly single-stranded polydeoxyribonucleotide sodium salts derived from porcine intestinal tissue having a mean weighted molecular weight of 13-20 kDa and a potency of 27-39 and 28-38 biological units per mg as determined by 2 separate assays measuring the release of a product formed by contact between defibrotide sodium, plasmin, and a plasmin substrate.[1]

Defitelio is a clear, light yellow to brown, sterile, preservative-free solution in a single-patient-use vial for intravenous use.[1]

DOSING FOR DEFITELIO[1]

Dosage
6.25 mg/kg every 6 hours (total dose 25 mg/kg/day)
Dosing based on baseline body weight prior to preparative regimen for HSCT

Administration
2-hour intravenous infusion

Days on therapy
Minimum of 21 days
Continue Defitelio until VOD resolution or up to a maximum of 60 days

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Hemorrhage—Defitelio may increase the risk of bleeding in patients with VOD after HSCT. Do not initiate Defitelio in patients with active bleeding. Monitor patients on Defitelio for signs of bleeding. If bleeding occurs, withhold or discontinue Defitelio.

Concomitant systemic anticoagulant or fibrinolytic therapy may increase the risk of bleeding and should be discontinued prior to Defitelio treatment. Consider delaying Defitelio administration until the effects of the anticoagulant have abated.

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Treatment modifications for specific events or procedures

TREATMENT MODIFICATIONS FOR TOXICITY OR INVASIVE PROCEDURES[1]

Event	Recommended action
Hypersensitivity reaction • Severe or life-threatening (anaphylaxis)	**1.** Discontinue Defitelio permanently; do not resume treatment.
Bleeding • Persistent, severe, or potentially life-threatening	**1.** Withhold Defitelio. **2.** Treat the cause of bleeding and give supportive care as clinically indicated. **3.** Consider resuming treatment (at the same dose and infusion volume) when bleeding has stopped and the patient is hemodynamically stable.
• Recurrent significant bleeding	**1.** Discontinue Defitelio permanently; do not resume treatment.
Invasive procedures	**1.** There is no known reversal agent for the profibrinolytic effects of Defitelio. Discontinue Defitelio infusion at least 2 hours prior to an invasive procedure. **2.** Resume Defitelio treatment after the procedure, as soon as any procedure-related risk of bleeding is resolved.

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Preparation

DEFITELIO MUST BE DILUTED PRIOR TO INFUSION[1]	
Dilute Defitelio with either	• 0.9% Sodium Chloride Injection, USP • 5% Dextrose Injection, USP Administer the diluted solution over 2 hours.
Final concentration of Defitelio	Range of 4 mg/mL to 20 mg/mL

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Hypersensitivity Reactions—Hypersensitivity reactions including rash, urticaria, and angioedema have occurred in less than 2% of patients treated with Defitelio. One case of an anaphylactic reaction was reported in a patient who had previously received Defitelio. Monitor patients for hypersensitivity reactions, especially if there is a history of previous exposure. If a severe hypersensitivity reaction occurs, discontinue Defitelio, treat according to the standard of care, and monitor until symptoms resolve.

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PREPARATION INSTRUCTIONS[1]

1. Determine the dose (mg) and number of vials based on the individual patient's baseline weight (weight prior to the preparative regimen for HSCT).

2. Calculate the volume of Defitelio needed, withdraw this amount from the vial(s), and add it to the infusion bag containing 0.9% Sodium Chloride Injection or 5% Dextrose Injection for each dose to make a final concentration of 4 mg/mL to 20 mg/mL.

3. Gently mix the solution for infusion.

4. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Only clear solutions without visible particles should be used. Depending on the type and amount of diluent, the color of the diluted solution may vary from colorless to light yellow.

STORAGE AND HANDLING[1]

- Supplied in a single-patient-use, clear glass vial
- Vials contain no antimicrobial preservatives
- Up to 4 doses may be prepared at one time, if refrigerated
- Use the diluted Defitelio solution within 4 hours if stored at room temperature or within 24 hours if stored under refrigeration
- Partially used vials should be discarded
- Store unused vials at 20°C-25°C (68°F-77°F)

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Information on single dose vs total daily dose

Refer to the vial chart for single-dose and total daily-dose preparation to identify patient vial combinations that may help inform you on minimization of waste.

VIAL CHART FOR DEFITELIO

Single-dose preparation

Patient weight (kg)[a]	Vials required	
	Per 6 hours	Per 24 hours
>3 – 32	1	4
>32 – 64	2	8
>64 – 96	3	12
>96	4	16

Daily-dose preparation

Patient weight (kg)[a]	Vials required per 24 hours
>3 – 8	1
>8 – 16	2
>16 – 24	3
>24 – 32	4
>32 – 40	5
>40 – 48	6
>48 – 56	7
>56 – 64	8
>64 – 72	9
>72 – 80	10
>80 – 88	11
>88 – 96	12
>96	13

[a]Dosing based on baseline body weight prior to preparative regimen for HSCT.[1]

IMPORTANT SAFETY INFORMATION

Most Common Adverse Reactions

The most common adverse reactions (incidence ≥10% and independent of causality) with Defitelio treatment were hypotension, diarrhea, vomiting, nausea, and epistaxis.

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Vial usage

For a patient weighing 72 kg (6.25 mg/kg dose x 72 kg = 450 mg), preparation of a **single dose** requires 3 vials (200 mg/vial) or a total of **12 vials** if all doses are prepared at individual times. For that same patient, preparation of all **4 daily doses** at the same time (25 mg/kg x 72 kg = 1,800 mg) requires **9 vials**. Each vial contains 200 mg/2.5 mL (at a concentration of 80 mg/mL) of defibrotide sodium.[1]

- Use the vial chart to determine the vials required for each patient. Look at the patient's weight in kilograms and the number of vials required to prepare the appropriate dosage for single-dose preparation or total daily-dose preparation. Remember to discard any unused solution remaining in the single-use vials.
- Use the diluted Defitelio solution within 4 hours if stored at room temperature or within 24 hours if stored under refrigeration. Up to 4 doses of Defitelio solution may be prepared at one time, if refrigerated.[1]
- It is solely the responsibility of the treating healthcare professional and/or institution to determine the appropriate dosage for each patient and to appropriately account for any unused drug or wastage in accordance with any applicable law, regulation, or policy.
- Healthcare professionals should calculate all doses before administration. This vial usage chart is merely a guide and is not a substitute for, nor intended to influence, the independent judgement of healthcare professionals. Neither Jazz Pharmaceuticals nor its contractors accept any responsibility for the applicability of the information provided to any particular clinical situation or for any actions or decisions taken in calculating or administering the dose.

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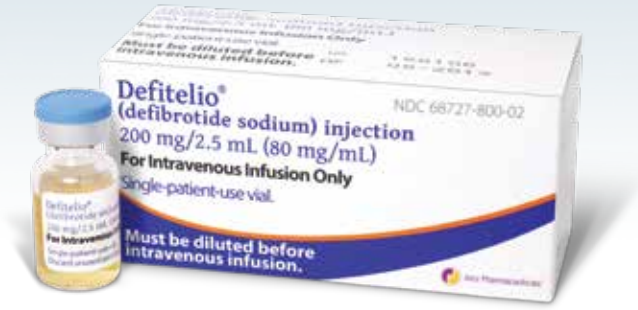
How Defitelio is supplied



Defitelio is supplied in a single-patient-use, clear glass vial.[1]

PACKAGING INFORMATION

Vial volume	2.5 mL vial (200 mg defibrotide sodium)
Carton quantity	10 vials
Carton dimensions (L x W x H)	3-33/64” x 1-43/64” x 1-27/32”

Consider that patients receiving Defitelio should be treated for a minimum of 21 days or until VOD resolution, up to a maximum of 60 days.[1]

NDC INFORMATION[1]

Billing	Single-patient-use vial: 200 mg/2.5 mL (concentration of 80 mg/mL) NDC 68727-800-01[a]
Ordering	Carton: (10 vials) NDC 68727-800-02[a]

[a]NDC number is for billing purposes only.
NDC=National Drug Code.

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CODING INFORMATION

Bone marrow transplant–associated DRG codes	014: Allogeneic bone marrow transplant 016: Autologous bone marrow transplant with CC/MCC 017: Autologous bone marrow transplant without CC/MCC
Hepatic veno-occlusive disease–associated DRG codes	441: Disorder of liver except malignancy, cirrhosis, or alcoholic hepatitis with MCC 442: Disorder of liver except malignancy, cirrhosis, or alcoholic hepatitis with CC 443: Disorder of liver except malignancy, cirrhosis, or alcoholic hepatitis without CC/MCC
Hepatic veno-occlusive disease–associated ICD-10 code	K76.5: Hepatic veno-occlusive disease
J codes: In the event that a J code may be needed, the codes at right may be applicable	J3490: not otherwise classified drug J9999: not otherwise classified drug, antineoplastic J7599: not otherwise classified drug, immunosuppressive

Please confirm with the specific payer as they may require additional information prior to adjudication.
CC=complication or comorbidity; DRG=diagnosis-related group; ICD-10=International Classification of Diseases, Tenth Revision; MCC=major complication or comorbidity.

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How to order Defitelio

ORDER THROUGH MCKESSON PLASMA AND BIOLOGICS

Phone:
1-877-625-2566

Fax:
1-888-752-7626

Email:
MPBOrders@mckesson.com

Email for all other information requests:
MPB@mckesson.com

- Orders can be placed Monday through Friday, 9 AM to 7:30 PM ET
  - Overnight delivery is available for orders placed by 7:30 PM ET
  - For emergency orders after hours of service, call 1-877-625-2566 (24/7/365)
- Verify your institution has a contract with McKesson Plasma and Biologics before ordering; if not, contact McKesson Plasma and Biologics or your Jazz Access and Reimbursement Manager (ARM) in your territory for information about setting up an account

Based on the potential for rapid progression of VOD, it is advisable to have enough product on hand to treat an average-size patient for up to 48 hours.

JazzCares™
Making a difference in Patients' lives, one Patient at a time

JazzCares is sponsored by Jazz Pharmaceuticals and provides information about coverage and reimbursement. Specialists are available to answer your questions. For additional questions regarding reimbursement, contact your Jazz ARM in your territory.

Contact JazzCares specialists at 1-855-593-3955, Monday through Friday, 8 AM to 8 PM ET.

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Please click here for full Prescribing Information.

For additional information, visit defitelio.com or call Jazz Pharmaceuticals Customer Service at 1-800-833-3533.

Reference: 1. Defitelio [package insert]. Palo Alto, CA: Jazz Pharmaceuticals.

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