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IN BRIEF

Defibrotide *(Defitelio)* for Hepatic Veno-Occlusive Disease

The FDA has approved defibrotide sodium (*Defitelio* – Jazz), a mixture of mostly single-stranded polydeoxyribonucleotide sodium salts, for treatment of adults and children with hepatic veno-occlusive disease (also known as sinusoidal obstruction syndrome) and renal or pulmonary dysfunction following hematopoietic stem cell transplantation (HSCT). It is the first drug to be approved by the FDA for treatment of severe hepatic veno-occlusive disease. Defibrotide was approved earlier by the European Medicines Agency for the same indication.

Hepatic veno-occlusive disease is an uncommon (<2%) complication of HSCT, but it has been associated with a 70-80% mortality rate. Defibrotide has antithrombotic, anti-inflammatory, and antioxidant properties that protect hepatic endothelial cells from the damage associated with HSCT.[1]

Approval of defibrotide was based on the results of three open-label studies in patients with hepatic veno-occlusive disease and multi-organ dysfunction following HSCT. In one trial in 102 adults and children, treatment with defibrotide 6.25 mg/kg every 6 hours for a median of 21.5 days was associated with a 38.2% survival rate (defined as survival at day +100 post-HSCT), compared to a 25.0% survival rate in 32 matched historical controls.[2] In another trial, the survival rate was 44% among 75 patients treated with defibrotide 25 mg/kg/day.[3] In an unpublished study (summarized in the package insert), the survival rate was 45% among 351 patients treated with defibrotide as part of an expanded access program.

Compared with historical controls, the overall incidence of adverse effects was similar with defibrotide. The most common serious adverse effects have been hypotension and hemorrhage, particularly pulmonary alveolar hemorrhage (7%). Concurrent use of defibrotide and a systemic anticoagulant or fibrinolytic drug is contraindicated. The recommended dosage of defibrotide is 6.25 mg/kg given as a 2-hour IV infusion every 6 hours for a minimum of 21 days. The cost of 21 days of treatment with defibrotide for a patient weighing 70 kg is $155,925.[4]

1. M Palomo et al. What is going on between defibrotide and endothelial cells? Snapshots reveal the hot spots of their romance. Blood 2016; 127:1719.
2. PG Richardson et al. Phase 3 trial of defibrotide for the treatment of severe veno-occlusive disease and multi-organ failure. Blood 2016; 127:1656.
3. PG Richardson et al. Defibrotide for the treatment of severe hepatic veno-occlusive disease and multiorgan failure after stem cell transplantation: a multicenter, randomized, dose-finding trial. Biol Blood Marrow Transplant 2010; 16:1005.
4. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. August 5, 2016. Reprinted with permission by First Databank, Inc. All rights reserved. ©2016. www.fdbhealth.com/policies/drug-pricing-policy.

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