TRUVEN HEALTH ANALYTICS
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COMPENDIA TRANSPARENCY TRACKING FORM

DATE: 11/14/2018

PACKET: 1817

DRUG: Defibrotide Sodium

USE: Condition Qualifier: Prophylaxis, PEDIATRIC, Veno-occlusive disease of the liver in patients undergoing hematopoietic stem cell transplantation

COMPENDIA TRANSPARENCY REQUIREMENTS	
1	Provide criteria used to evaluate/prioritize the request (therapy)
2	Disclose evidentiary materials reviewed or considered
3	Provide names of individuals who have substantively participated in the review or disposition of the request and disclose their potential direct or indirect conflicts of interest
4	Provide meeting minutes and records of votes for disposition of the request (therapy)

EVALUATION/PRIORITIZATION CRITERIA: S, P *to meet requirement 1

CODE	EVALUATION/PRIORITIZATION CRITERIA
A	Treatment represents an established standard of care or significant **advance** over current therapies
C	**Cancer** or cancer-related condition
E	Quantity and robustness of **evidence** for use support consideration
L	**Limited** alternative therapies exist for condition of interest
P	**Pediatric** condition
R	**Rare** disease
S	**Serious**, life-threatening condition

Note: a combination of codes may be applied to fully reflect points of consideration [eg, therapy may represent an advance in the treatment of a life-threatening condition with limited treatment alternatives (ASL)]

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EVIDENCE CONSIDERED:

*to meet requirements 2 and 4

CITATION	STUDY-SPECIFIC COMMENTS	LITERATURE CODE
Al Jefri,A.H., et al: Veno-occlusive disease/sinusoidal obstruction syndrome after haematopoietic stem cell transplantation: Middle East/North Africa regional consensus on prevention, diagnosis and management. Bone Marrow Transplant Apr 2017; Vol 52, Issue 4; pp. 588-591.		4
Zhang,L.: Defibrotide for the prevention of hepatic veno-occlusive disease after hematopoietic stem cell transplantation: A systematic review. Clinical Transplantation Jul 2012; Vol 26, Issue 4; pp. 511-519.	Comments: This was a systematic review that included a total of 13 studies: one randomized controlled trial, eight studies case series, and four cohort studies. The quality of the studies was assessed with the risk of bias tool and Newcastle-Ottawa Scale. This systematic review conducted a comprehensive literature search and provided information on eligibility criteria, study characteristics, and heterogeneity. The appropriate statistical tests were used.	S
Corbacioglu,S., et al: Defibrotide for prophylaxis of hepatic veno-occlusive disease in paediatric haemopoietic stem-cell transplantation: an open-label, phase 3, randomised controlled trial. Lancet Apr 07, 2012; Vol 379, Issue 9823; pp. 1301-1309.	Comments: This was a phase 3, open-label, randomized controlled trial that included patients at 28 European university hospitals or academic medical centers. The independent review committee adjudicated masked ultrasound reports and clinical data for suspected and diagnosed venoocclusive disease cases. The authors used these independent review committee assessments in the primary efficacy analysis. Key bias criteria evaluated were (1) random sequence generation of randomization; (2) lack of allocation concealment, (3) lack of blinding, (4) incomplete accounting of patients and outcome events, and (5) selective outcome reporting bias. The study was at low risk of bias for these key criteria, and no additional biases were identified.	2

Corbacioglu,S.: Defibrotide for prophylaxis of hepatic veno-occlusive disease in pediatric hematopoietic stem cell transplantation: Subanalysis data from an open-label, phase III, randomized trial. Blood Dec 03, 2015; Vol 126, Issue 23; p. 4310.		3
Richardson,P.G., et al: The use of defibrotide in blood and marrow transplantation. Blood Adv Jun 26, 2018; Vol 2, Issue 12; pp. 1495-1509.		4
Chalandon,Y., et al: Prevention of veno-occlusive disease with defibrotide after allogeneic stem cell transplantation. Biol Blood Marrow Transplant May 2004; Vol 10, Issue 5; pp. 347-354.		3
Qureshi,A.: Defibrotide in the prevention and treatment of veno-occlusive disease in autologous and allogeneic stem cell transplantation in children. Pediatric Blood and Cancer Apr 2008; Vol 50, Issue 4; pp. 831-832.		3
Picod,A., et al: Defibrotide for sinusoidal obstruction syndrome/veno-occlusive disease prophylaxis in high-risk adult patients: a single-center experience study. Biol Blood Marrow Transplant Jul 2018; Vol 24, Issue 7; pp. 1471-1475.		3

Dignan,F.: Prophylactic defibrotide in allogeneic stem cell transplantation: Minimal morbidity and zero mortality from veno-occlusive disease. Bone Marrow Transplantation Jul 2007; Vol 40, Issue 1; pp. 79-82.		3
Park,M., et al: Safety and effects of prophylactic defibrotide for sinusoidal obstruction syndrome in hematopoietic stem cell transplantation. Ann Transplant Jan 28, 2013; Vol 18, pp. 36-42.		3
Dignan,F.L., et al: BCSH/BSBMT guideline: diagnosis and management of veno-occlusive disease (sinusoidal obstruction syndrome) following haematopoietic stem cell transplantation. Br J Haematol. Nov 2013; Vol 163, Issue 4; pp. 444-457.		S
Bajwa,R.P.S., et al: Consensus Report by Pediatric Acute Lung Injury and Sepsis Investigators and Pediatric Blood and Marrow Transplantation Consortium Joint Working Committees: supportive care guidelines for management of veno-occlusive disease in children and adolescents, part 1: focus on investigations, prophylaxis, and specific treatment. Biol Blood Marrow Transplant Nov 2017; Vol 23, Issue 11; pp. 1817-1825.		4

Literature evaluation codes: S = Literature selected; 1 = Literature rejected = Topic not suitable for scope of content; 2 = Literature rejected = Does not add clinically significant new information; 3 = Literature rejected = Methodology flawed/Methodology limited and unacceptable; 4 = Other (review article, letter, commentary, or editorial)

CONTRIBUTORS:

*to meet requirement 3

PACKET PREPARATION	DISCLOSURES	EXPERT REVIEW	DISCLOSURES
Felicia Gelsey, MS	None		
Stacy LaClaire, PharmD	None		
Catherine Sabatos, PharmD	None		
		John D Roberts	None
		Jeffrey Klein	None
		Richard LoCicero	Incyte Corporation Local PI for REVEAL. Study is a multicenter, non-interventional, non-randomized, prospective, observational study in an adult population for patients who have been diagnosed with clinically overt PV and are being followed in either community or academic medical centers in the US who will be enrolled over a 12-month period and observed for 36 months.

ASSIGNMENT OF RATINGS:

*to meet requirement 4

	EFFICACY	STRENGTH OF RECOMMENDATION	COMMENTS	STRENGTH OF EVIDENCE
MICROMEDEX	Evidence Favors Efficacy	Class IIb: Recommended, in Some Cases		B
John D Roberts	Evidence is Inconclusive	Class IIb: Recommended, In Some Cases	One randomized trial reported only in abstract form showed a moderately reduced rate of venoocclusive disease of the liver in children undergoing hematopoietic stem cell transplantation. Enrollment was limited to children with additional risk factor(s) for veno-occlusive disease. Other, retrospective series are consistent with this finding. In the absence of any definitive reports, this information supports the use of defibrotide in some cases.	N/A

Jeffrey Klein	Evidence Favors Efficacy	Class IIa: Recommended, In Most Cases	The prophylactic use of Defibrotide to prevent veno-occlisive disease in pediatric patients who have received stem cell transplants seems to be very effective. The most effective dose needs to be analyzed further as well as the extent of hemorrhage as an adverse effect.	N/A
Richard LoCicero	Effective	Class I: Recommended	Defribotide has been shown in multiple clinical trials to be effective in reducing the risk of veno-occlusive disease of the liver in both children and adults undergoing hematopoietic stem cell transplantation. Evidence-based guidelines also support the use of defibrotide in this setting.	N/A