Taurolidine and Heparin (DEFENCATH) catheter lock solution in Patients Receiving Hemodialysis via Central Venous Catheter
National Drug Mini-monograph
SEPT 2024

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION

Description / MOA	Taurolidine and its metabolites cause damage to microbial cell walls in a non-specific manner.
Indication Under Review[1]	Taurolidine/Heparin (DEFENCATH) is indicated to reduce the incidence of catheter-related bloodstream infections (CRBSIs) in adult patient receiving chronic hemodialysis (HD) via a central venous catheter (CVC). DEFENCATH was approved under the Limited Population Pathway for Antimicrobial/Antifungal Drugs (LPAD)
Dosage Regimen	Taurolidine/Heparin catheter lock solution (CLS) is instilled into the catheter lumen after each dialysis session and removed/aspirated from the catheter prior to subsequent hemodialysis sessions. Taurolidine/heparin is not intended for systemic administration and should not be used as a catheter lock flush product
Dosage Forms Under Review	3mL CLS in a single use vial containing 40.5mg/3000 Units of taurolidine and heparin, respectively 5mL of CLS in a single use vial containing 67.5mg and 5000 Units of taurolidine and heparin, respectively

EFFICACY CONSIDERATIONS

Trial[2]	**LOCK-IT 100**
Design	Randomized, double blind, active comparator trial with time to CRBSI being the primary endpoint
Population	Adult patients (n=806) receiving intermittent HD (>/= 2 per week) via a permanent tunneled cuffed silicone or polyurethane CVC. Patients could not have received antibiotics, thrombolytics or be immunosuppressed and life expectancy was > 6 months
Intervention	The active or control CLS removed from the catheter lumen prior to HD and instilled after each HD session
Comparator	Taurolidine/heparin CLS vs. heparin CLS
Results	At interim analysis fewer taurolidine+heparin treated patients had fewer CRBSIs. Primary endpoint was analyzed with time to CRBSI with event rates of 0.14 vs. 0.49 CRBSI events per 1000 catheter days (P=0.003). Key secondary analysis was overall catheter removal rate with no statistical difference between groups.

SAFETY CONSIDERATIONS

Boxed Warnings	None
Contraindications	Known heparin induce thrombocytopenia (HIT) Known hypersensitivity to taurolidine, heparin or the citrate component of the drug or pork products
Other Warnings	HIT has been reported in patient using heparin, discontinue if HIT occurs and institute supportive care
Top 5 AEs[3]	Hemorrhage (7%), Nausea (7%), Vomiting (6%), Dizziness (6%), Thrombocytopenia (2%)
Drug Interactions	None reported

PLACE IN THERAPY

DRUG	VANF	CFU	FDA	GUIDELINES
Heparin CLS	Yes	No	Yes	N/A
Citrate 4% CLS	No	No	No	N/A
Taurolidine / Heparin (DEFENCATH)	TBD	No	Yes	TBD

VHA PLACE IN THERAPY		
	Potential Use in VHA	1. DEFENCATH had fewer CRBSIs than heparin alone, but this product has not been compared in head-to-head studies versus a 4% citrate solution which is routinely used and has inherent antimicrobial and antimicrobial properties. 2. Although taurolidine containing CLS have been reported in literature for almost 20 years, and studied in populations which would be off-label for DEFENCATH (e.g. Oncology, GI TPN requiring patients), VHA requests for this product to date have been infrequent. As such, potential for off-label use is difficult to predict.

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References

[1] Taurolidine/Heparin (DEFENCATH) catheter lock solution [prescribing-information.pdf (defencath.com)]. Berkeley Heights, NJ CorMedix Inc., Accessed AUG 2024

[2] Agarwal AK, et al., Taurolidine/Heparin Lock Solution and Catheter-Related Bloodstream Infection in Hemodialysis: A Randomized, Double-Blind, Active-Control, Phase 3 Study. Clin J Am Soc Nephrol. 2023 Nov 1;18(11):1446-1455. Epub 2023 Sep 6. PMID: 37678222;

[3] Taurolidine/heparin. In: MicroMedex In Depth Answers. Ann Arbor, MI CO. Merative corporation. Accessed AUG 2024