DEFENCATH®
Taurolidine and Heparin Catheter Lock Solution

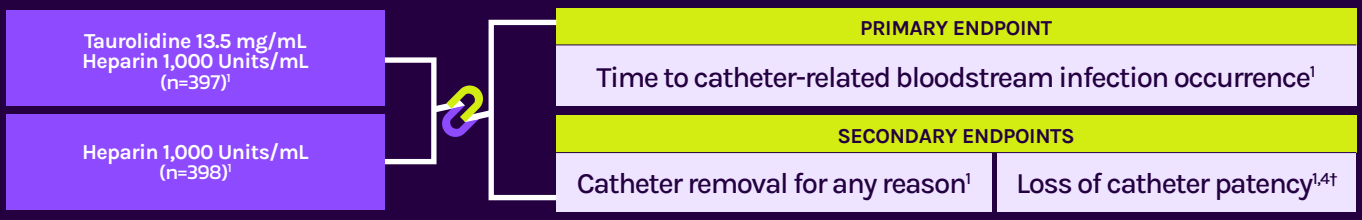
Limited Population

LOCK-IT-100 Trial:

Taurolidine/Heparin Lock Solution and Catheter-Related Bloodstream Infection in Hemodialysis: A Randomized, Double-Blind, Active-Control, Multicenter, Phase 3 Study

Anil K Agarwal, Prabir Roy-Chaudhury, Phoebe Mounts, Elizabeth Hurlburt, Antony Pfaffle, Eugene C Poggio. *Clinical Journal of the American Society of Nephrology*. 2023 Nov 1;18(11):1446-1455. doi:10.2215/CJN.0000000000000278

STUDY DESIGN



Please see additional study design under "Study Design" and "Patient Population".
†Defined as requiring use of a thrombolytic agent to resolve catheter thrombosis or removal of the catheter due to malfunction/dysfunction.[2]

INDICATIONS AND USAGE

LIMITED POPULATION: DefenCath® is indicated to reduce the incidence of catheter-related bloodstream infections (CRBSI) in adult patients with kidney failure receiving chronic hemodialysis (HD) through a central venous catheter (CVC). This drug is indicated for use in a limited and specific population of patients.

Limitations of Use

The safety and effectiveness of DefenCath have not been established for use in populations other than adult patients with kidney failure receiving chronic HD through a CVC.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DefenCath is contraindicated in patients with:

- Known heparin-induced thrombocytopenia (HIT).
- Known hypersensitivity to taurolidine, heparin or the citrate excipient (components of DefenCath), or pork products.

Please see additional Important Safety Information throughout and the full Prescribing Information.

DEFENCATH® Taurolidine and Heparin Catheter Lock Solution | Limited Population

Patient Population

Baseline demographic and disease characteristics of participants in the LOCK IT-100 study[1]

Characteristic	DefenCath (n=403)	Heparin (n=403)
Age, mean (SD), years	61 (14)	61 (14)
Age category, years, n (%)		
<65 years	239 (59)	236 (59)
≥65 to <75 years	99 (25)	95 (24)
≥75	65 (16)	72 (18)
Female, n (%)	184 (46)	154 (38)
Race, n (%)		
American Indian or Alaska Native	3 (1)	2 (<1)
Asian	15 (4)	18 (4)
Black	126 (31)	112 (28)
Native Hawaiian or other Pacific Islander	10 (2)	4 (1)
White	248 (62)	262 (65)
Others	1 (0.2)	5 (1)
Ethnicity, n (%)		
Not Hispanic or Latino	226 (56)	214 (53)
Hispanic or Latino	177 (44)	189 (47)
BMI, mean (SD), kg/m²[a]	29.7 (7.9)	29.2 (10.3)
Diabetes, n (%)	278 (69)	277 (69)
Time since first dialysis, months[b]		
Mean (SD)	21.2 (37.5)	19.8 (37.0)
Minimum, maximum	0.2, 280.2	0.1, 254.8
Time receiving dialysis, n (%)		
≤30 days	35 (9)	31 (8)
1-12 months	237 (59)	246 (61)
>12 months	131 (33)	126 (31)
Catheter location, n (%)		
Jugular vein	371 (92)	365 (91)
Subclavian vein	30 (7)	31 (8)
Others[c]	2 (<1)	6 (1)

BMI, body mass index; SD, standard deviation.

[a]Taurolidine/heparin, n=401; heparin, n=402.
[b]Taurolidine/heparin, n=403; heparin, n= 402.
[c]The classification of participants as others was due to site staff data entry errors. Catheter location (jugular or subclavian) for these participants was confirmed after data entry and documented in study records.

IMPORTANT SAFETY INFORMATION

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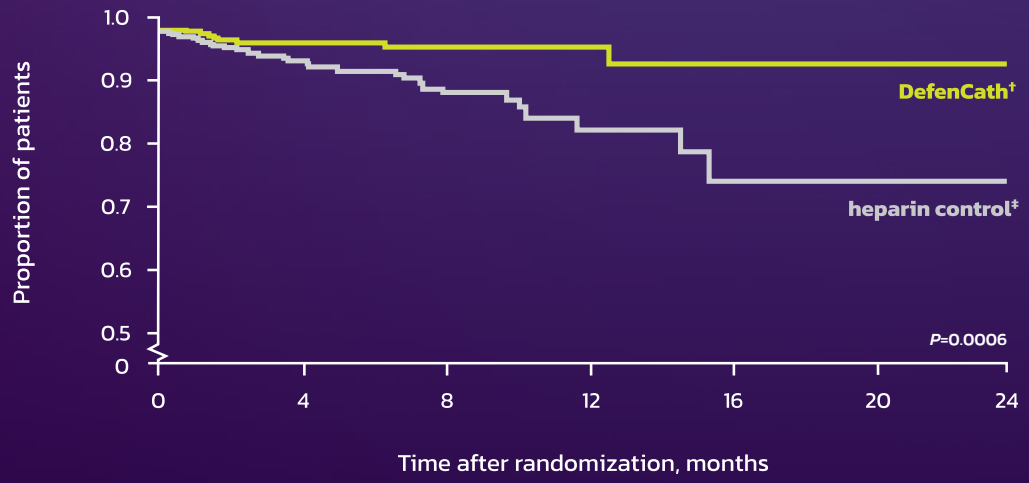
In adult participants receiving chronic hemodialysis (HD) through a central venous catheter (CVC),

Significant reduction in catheter-related bloodstream infection (CRBSI) occurrence was demonstrated in this trial[1]

PRIMARY ENDPOINT

Time to CRBSI occurrence

CRBSI over time: Proportion of patients **without** CRBSIs[1]



Patients at risk, n							
DefenCath	397	215	104	37	9	2	2
heparin control	398	218	103	41	14	4	1

Risk reduction of CRBSI occurrence

- **DefenCath reduced the risk of CRBSIs by 71%** compared to heparin, the standard of care[3] (95% CI,[§] 38-86%; *P*=0.0006)[1,2]
- CRBSI rates = event rate per 1000 catheter-days (95% CI) was 0.13 (0.07, 0.26) for DefenCath and 0.46 (0.33, 0.66) for heparin[2]
- 3.5x fewer CRBSI events were seen for patients on DefenCath vs heparin control (2.3% (9/397) vs 8.0% (32/398))[2]

†DefenCath contains 13.5 mg/mL of taurolidine and 1,000 USP Units/mL of heparin, as a sterile, non-pyrogenic, pre-mixed, preservative-free, clear, aqueous solution of taurolidine and heparin with a pH of 5.5-6.5.[2]
‡Control composition: heparin sodium 1,000 USP Units/mL, benzyl alcohol 9.45 mg/mL and sodium chloride 9.0 mg/mL.[2]
§Based on 1 – Hazard Ratio.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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SECONDARY ENDPOINTS

Time to catheter removal for any reason and loss of catheter patency was similar for both DefenCath and heparin control[1,2,4]

IMPORTANT SAFETY INFORMATION (Cont'd)

WARNINGS AND PRECAUTIONS

Heparin-Induced Thrombocytopenia (HIT): HIT was reported in patients using heparin, a component of DefenCath, as a catheter lock solution. If HIT occurs, discontinue DefenCath and institute appropriate supportive measures.

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Adverse reactions were similar between DefenCath and heparin control[1]

Summary of Treatment-Emergent Adverse Events (TEAEs) (safety population)[1]

Participants with events	DefenCath (n=398) n (%)	Heparin (n=399) n (%)
Any TEAE	314 (79)	315 (79)
Mild	91 (23)	80 (20)
Moderate	112 (28)	102 (26)
Severe	89 (22)	112 (28)
Life-threatening	22 (6)	21 (5)
Serious TEAE	159 (40)	167 (42)
Drug-related TEAE	17 (4)	13 (3)
TEAE leading to early withdrawal from the study	4 (1)	5 (1)
TEAE (cardiac) with an outcome of death	5 (1)	5 (1)
Serious TEAE related to study drug[a]	1 (0.3)	0
Serious TEAEs occurring in ≥2% of participants in either study arm		
Pneumonia	12 (3)	21 (5)
Fluid overload	14 (4)	12 (3)
Sepsis	9 (2)	14 (4)
Acute myocardial infarction	5 (1)	13 (3)
Cardiac failure, congestive	12 (3)	7 (2)
Hyperkalemia	10 (3)	8 (2)
Hypertension	4 (1)	10 (3)
Respiratory failure	7 (2)	9 (2)
Device-related infection	6 (2)	8 (2)

[a]Includes one event of device malfunction that was considered possibly related to the study drug by the investigator. There were no serious treatment-emergent adverse events with a probable or definite relationship to the study drug.

Overall, rates of TEAEs, serious TEAEs, and discontinuations due to TEAEs were similar or comparable across treatment groups/arms[1]

Please see the full Prescribing Information for additional details on safety and risks associated with DefenCath.

These findings support the use of taurolidine/heparin in chronic hemodialysis adult patients through a CVC to reduce incidence of CRBSIs.[1]

IMPORTANT SAFETY INFORMATION (Cont'd)

WARNINGS AND PRECAUTIONS (Cont'd)

- **Drug Hypersensitivity:** Drug hypersensitivity reactions have been reported in patients using heparin, a component of DefenCath, as a catheter lock solution. If a hypersensitivity reaction occurs, discontinue DefenCath and institute appropriate supportive measures.

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Study Design

LOCK-IT-100 was the largest study of catheter lock solutions ever conducted in the US to date[1]

The study population reflected hemodialysis patients in the United States[1]:

Key Inclusion Criteria[1]

- Ages ≥18 years
- Underwent hemodialysis ≥2 times per week in an outpatient HD unit
- Catheters were required to be in place for ≥14 days
- Catheters had to have been used successfully to dialyze the participant ≥2 times prior to enrollment

Key Exclusion Criteria[1]

- Treatment with antibiotics ≤14 days of enrollment
- Catheter exit-site infection
- Thrombolytic treatment (i.e., tissue plasminogen activator [tPA]) in the patient's current catheter ≤30 days of randomization, or
- Systemic immunosuppression (e.g., patients actively on immunosuppressants), or
- Malignancy with life expectancy ≤6 months

CRBSI definition

The clinical adjudication committee (CAC) definition for CRBSI included one positive blood culture (other than for coagulase-negative staphylococci, which required a confirmatory culture) from a peripheral site or either the arterial or venous catheter hub or the arterial or venous dialysis blood line and the patient had to have signs and symptoms of infection and no other apparent source of bloodstream infection.

IMPORTANT SAFETY INFORMATION (Cont'd)

ADVERSE REACTIONS

The most frequently reported adverse reactions occurring in ≥2% of patients using DefenCath as a CLS were hemodialysis catheter malfunction, hemorrhage/bleeding, nausea, vomiting, dizziness, musculoskeletal chest pain, and thrombocytopenia.

To report SUSPECTED ADVERSE REACTIONS, contact CorMedix Inc at 1-844-424-6345 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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DEFENCATH®
Taurolidine and Heparin Catheter Lock Solution

Limited Population

Reduce the risk of CRBSIs

To read the published article, scan the QR code.

Not actual size.

IMPORTANT SAFETY INFORMATION (Cont'd)

WARNINGS AND PRECAUTIONS

- **Heparin-Induced Thrombocytopenia (HIT):** HIT was reported in patients using heparin, a component of DefenCath, as a catheter lock solution. If HIT occurs, discontinue DefenCath and institute appropriate supportive measures.
- **Drug Hypersensitivity:** Drug hypersensitivity reactions have been reported in patients using heparin, a component of DefenCath, as a catheter lock solution. If a hypersensitivity reaction occurs, discontinue DefenCath and institute appropriate supportive measures.

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References: 1. Agarwal AK, Roy-Chaudhury P, Mounts P, Hurlburt E, Pfaffle A, Poggio EC. 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. doi: 10.2215/CJN.0000000000000278 **2.** DefenCath® (taurolidine and heparin) catheter lock solution Prescribing Information, CorMedix, Berkeley Heights, New Jersey. **3.** Arechabala MC, Catoni MI, Claro JC, et al. Antimicrobial lock solutions for preventing catheter-related infections in haemodialysis. *Cochrane Database Syst Rev.* 2018;(4):CD010597.doi.org/10.1002/14651858.CD010597.pub2 **4.** Agarwal AK, Roy-Chaudhury P, Mounts P, Hurlburt E, Pfaffle A, Poggio EC. Supplemental Material. *Clin J Am Soc Nephrol.* 2023;18(Suppl):1-10.

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