DEFENCATH®
Taurolidine and Heparin
Catheter Lock Solution

Limited
Population

DefenCath® for Reducing the Incidence of CRBSIs in Adult Patients With Kidney Failure Undergoing Chronic HD-CVC

CRBSI=catheter-related bloodstream infection; CVC=central venous catheter; HD=hemodialysis.

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.

Please see Important Safety Information on slides 8-9 and accompanying full Prescribing Information at this presentation.

Introduction and Objectives

- To review the unmet need in CRBSI management in patients with kidney failure receiving HD through a CVC
- To introduce DefenCath (taurolidine and heparin), the first and only US Food and Drug Administration (FDA)-approved catheter lock solution (CLS) for reducing the incidence of CRBSIs in adult patients with kidney failure receiving chronic HD through a CVC
- To discuss the approval of DefenCath through the Limited Population for Antibacterial and Antifungal Drugs (LPAD) pathway
- To review results from LOCK-IT-100, the pivotal Phase 3 trial for DefenCath

CRBSI=catheter-related bloodstream infection; CVC=central venous catheter; HD=hemodialysis.

Unmet Need in CRBSI Management in the HD-CVC Population

CRBSI=catheter-related bloodstream infection; CVC=central venous catheter; HD=hemodialysis.

The Chronic HD-CVC Population Is at Persistent Risk for CRBSIs

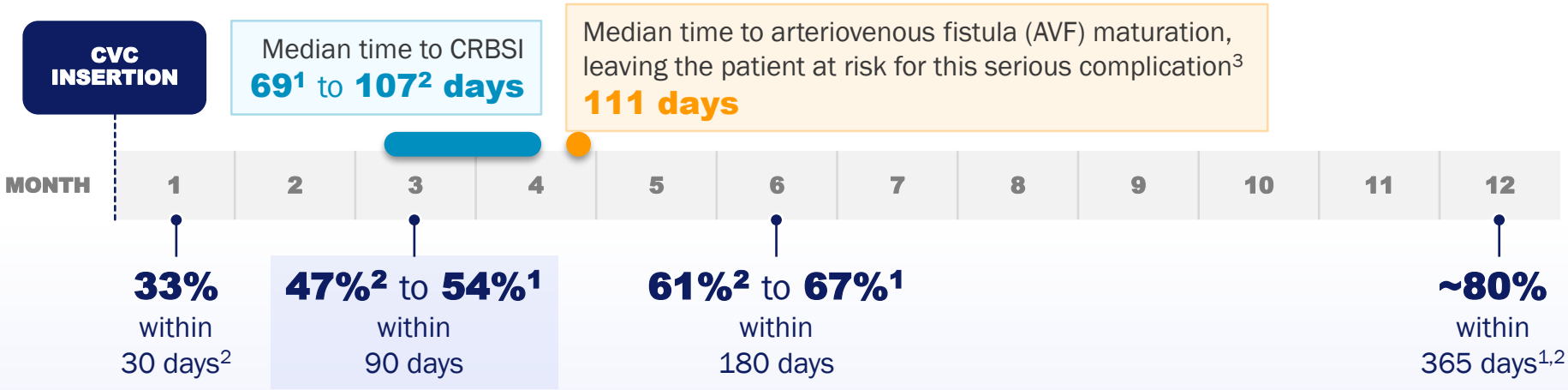
Image for illustration purposes only. Not an actual patient.

- Despite health system protocols to prevent infections, **patients with kidney failure receiving HD through a CVC are particularly vulnerable to CRBSIs**

CRBSI=catheter-related bloodstream infection; CVC=central venous catheter; HD=hemodialysis.

Reference: Janum S, Zingg W, Classen V, Afshari A. *Crit Care*. 2013;17(4)238.

About Two-thirds of CRBSIs Occur Within the First 6 Months of CVC Insertion in Patients With Kidney Failure Receiving HD



PERCENTAGE OF CRBSIs OCCURRING BY TIMEPOINT

Any time spent with a CVC puts patients at risk for developing a CRBSI

CRBSI=catheter-related bloodstream infection; CVC=central venous catheter; HD=hemodialysis.

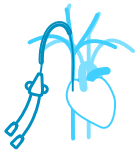
References: 1. Massey K, et al. CRBSI incidence and associated mortality risk: analysis of merged United States Renal Data System-Medicare claims. Poster presented at: the American Society of Nephrology Kidney Week 2021; November 4-7, 2021; San Diego, CA. **2.** Massey K, et al. Rapid incidence and emergence of CRBSIs among CVC-dependent HD patients. Poster presented at: the American Society of Nephrology Kidney Week 2022; November 3-6, 2022; Orlando, FL. **3.** Woodside KJ, et al. *Am J Kidney Dis*. 2018;71(6):793-801.

Given the Substantial Burden Associated with CRBSIs, Preventing CRBSIs Should Be a Priority

Recommendations for Prevention of Infections[1-3]

Education and training of healthcare personnel

Hand hygiene and aseptic technique



Appropriate CVC insertion, maintenance, and removal

Antimicrobial/antibiotic CLS may be considered

CLS=catheter lock solution; CRBSI=catheter-related bloodstream infection; CVC=central venous catheter.

References: 1. Joint Commission. Preventing central line-associated bloodstream infections. Accessed January 17, 2023. https://www.jointcommission.org/-/media/tjc/documents/resources/hai/clabsi_monographpdf.pdf **2**. Buetti N, et al. *Infect Control Hosp Epidemiol*. 2022;43(5):553-569. **3.** CDC. Guidelines for the Prevention of Intravascular Catheter-Related Infections (2011). Accessed January 9, 2024. https://www.cdc.gov/infectioncontrol/guidelines/bsi/recommendations.html#rec12

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Introducing DefenCath
The First and Only FDA-Approved Antimicrobial CLS

INDICATIONS AND USAGE

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Limitations of Use

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Not actual size.

CLS=catheter lock solution; CRBSI=catheter-related bloodstream infection; CVC=central venous catheter; FDA=US Food and Drug Administration; HD=hemodialysis

Reference: DefenCath [prescribing information]. Berkeley Heights, NJ: CorMedix Inc; 2023.

Please see Important Safety Information on slides 8-9 and accompanying full Prescribing Information at this presentation.

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.

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.

Continued

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.

CLS=catheter lock solution; FDA=US Food and Drug Administration.

Approved Under LPAD Pathway

- DefenCath® (taurolidine and heparin) was approved by the FDA in November 2023 under the Limited Population for Antibacterial and Antifungal Drugs (LPAD) pathway[1]
  - Drugs approved under the LPAD pathway are antibacterial or antifungal drugs approved to treat serious or life-threatening infections in a limited population of patients with unmet needs[2]
  - Approval of drugs under the LPAD pathway is based on a benefit-risk assessment that more flexibly considers the severity, rarity, or prevalence of the infection the drug is intended to treat and the lack of alternatives available for the patient population[2]

FDA=US Food and Drug Administration.

References: 1. US Food and Drug Administration. FDA approves new drug under special pathway for patients receiving hemodialysis. Accessed January 2, 2024. https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-new-drug-under-special-pathway-patients-receiving-hemodialysis **2.** US Food and Drug Administration. Limited population pathway for antibacterial and antifungal drugs – the LPAD pathway. Accessed January 2, 2024. https://www.fda.gov/drugs/development-resources/limited-population-pathway-antibacterial-and-antifungal-drugs-lpad-pathway

Mechanism of Action

- DefenCath® (taurolidine and heparin) contains a combination of **taurolidine**, a thiadiazinane with both antibacterial and antifungal activity, and **heparin**, an anticoagulant
- **Mechanism of action of taurolidine and its metabolites is nonspecific**
  - Causes damage to microbial cell walls
  - Inhibits adherence of microorganisms to biologic surfaces
- Taurolidine shown to have *in vitro* activity against most isolates of the following microorganisms*:

GRAM-POSITIVE	GRAM-NEGATIVE	FUNGI
• *Staphylococcus aureus* (including MSSA and MRSA)	• *Escherichia coli*	• *Candida albicans*
• *Staphylococcus epidermidis*	• *Klebsiella pneumoniae*	• *Candida glabrata*
• *Enterococcus faecalis*	• *Pseudomonas aeruginosa*	
	• *Serratia marcescens*	

- Time kill studies showed that taurolidine is bactericidal (>3 $\log_{10}$ CFU reduction) at 1x to 4x minimum inhibitory concentration (MIC). Frequency of resistant mutants was $<10^{-9}$ at 2x and 4x MIC for 2 strains each of *E coli*, *S aureus*, *E faecalis*, *Enterococcus faecium,* and *P aeruginosa*

***Per *in vitro* studies with unknown clinical significance**

CFU=colony forming unit; MRSA=methicillin-resistant *S aureus*; MSSA=methicillin-sensitive *S aureus*.

Reference: DefenCath [prescribing information]. Berkeley Heights, NJ: CorMedix Inc; 2023.

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LOCK-IT-100: A Pivotal Phase 3 Clinical Trial*

- The efficacy and safety of DefenCath for reducing the incidence of CRBSI in patients with kidney failure receiving chronic HD through a CVC was evaluated in LOCK-IT-100 (NCT02651428), a randomized, double-blind, active-controlled, multicenter trial
- Enrollment was not limited to patients with specific types of HD catheters

806 patients were randomized 1:1 to a CLS

DefenCath
(taurolidine USP 13.5 mg/mL, and heparin 1000 USP units/mL)

Heparin
(heparin sodium USP 1000 units/mL, benzyl alcohol 9.45 mg/mL, and sodium chloride 9.0 mg/mL)

DefenCath or heparin was instilled into central venous HD catheters at the end of all dialysis sessions and was withdrawn prior to the initiation of the next dialysis session

*FDA approval of DefenCath was supported by results from LOCK-IT-100

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LOCK-IT-100: Patient Demographics

Demographics[1]	Study Population N=806
Median age, years	63
Range, years	21-94
Male, %	58
Race, %	
White	63
Black or African-American	30
Patients receiving HD 3 times weekly, %	98
Patients with catheter implanted within 3 months prior to randomization, %	48
Patients with diabetes at baseline, %	70
Mean body mass index, kg/m^2	30

HD=hemodialysis.

References: 1. DefenCath [prescribing information]. Berkeley Heights, NJ: CorMedix Inc.; 2023. **2.** 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;18(11):1446-1455.

CAC Adjudication of CRBSIs

A CLINICAL ADJUDICATION COMMITTEE (CAC) ASSESSED CASES OF CRBSI

CAC definition of CRBSI included ≥1 positive blood 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

*Other than for coagulase-negative staphylococci, which required a confirmatory culture.

CRBSI=catheter-related bloodstream infection.

Reference: DefenCath [prescribing information]. Berkeley Heights, NJ: CorMedix Inc.; 2023.

Reduction of CRBSI Risk by 71%

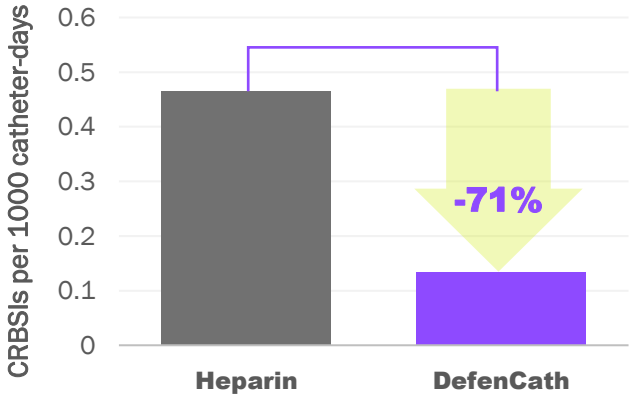
Primary Endpoint Results

CAC-ADJUDICATED CRBSI IN PATIENTS WITH KIDNEY FAILURE WHO RECEIVED ≥1 DOSE OF ALLOCATED STUDY CLS

	DefenCath N=397	Heparin N=398
CAC-adjudicated CRBSI	9 (2.3%)	32 (8.0%)
Event rate per 1000 catheter-days (95% CI)	0.13 (0.07, 0.26)	0.46 (0.33, 0.66)
Risk reduction (95% CI)*	71% (38%, 86%)	
Log-rank test P-value	0.0006	

*Based on 1 – Hazard Ratio

PATIENTS IN THE DEFENCATH GROUP HAD A LOWER INCIDENCE OF CRBSI EVENTS COMPARED WITH PATIENTS IN THE CONTROL GROUP



CAC=clinical adjudication committee; CLS=catheter lock solution; CRBSI=catheter-related bloodstream infection.
Reference: DefenCath [prescribing information]. Berkeley Heights, NJ: CorMedix Inc.; 2023.

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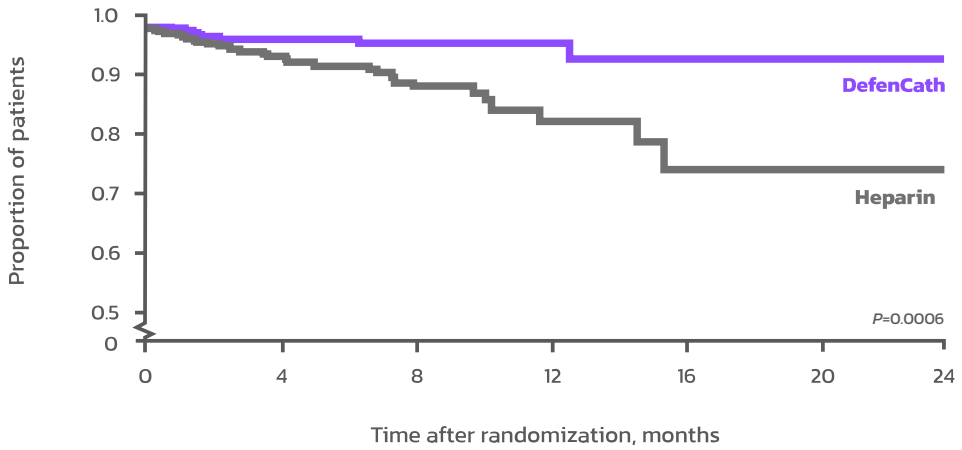
Time to CRBSI Occurrence

Primary Endpoint Results

Time to CRBSI was statistically significantly in favor of DefenCath (Taurolidine and Heparin) (*P*=0.0006)*

*Log-rank test P-value

CRBSI over time: Proportion of patients **without** CRBSIs



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

CRBSI=catheter-related bloodstream infection.

Reference: 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;18(11):1446-1455.

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Loss of Catheter Patency*

Secondary Endpoint Results[1]

	DefenCath N=398 N (%)	Heparin N=399 N (%)
Loss of Catheter Patency	63 (16)	48 (12)
Use of a Thrombolytic Agent[a]	46 (12)	33 (8)
Catheter Removal[b]	28 (7)	26 (7)
Catheter Removal without Thrombolytic Agent Use	17 (4)	15 (4)

[a]11 subjects in each arm had catheter removal following thrombolytic agent use and are included under both categories of use of a thrombolytic agent and catheter removal.
[b]Catheter removal refers to catheters removed due to loss of catheter patency. Overall, a total of 236 patients in the DEFENCATH arm and 225 patients in the heparin arm had a catheter removal for any reason, including loss of catheter patency.

- **Loss of catheter patency requiring catheter removal was comparable between heparin and DefenCath groups (7% of patients in each group)[1]**
- **No statistically significant difference in time to catheter removal for any reason[2]**

*Loss of catheter patency defined as requiring use of a thrombolytic agent to resolve catheter thrombosis or removal of the catheter due to malfunction/dysfunction.

References: 1. DefenCath [prescribing information]. Berkeley Heights, NJ: CorMedix Inc.; 2023. **2.** 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;18(11):1446-1455.

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.

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Common Adverse Reactions

In LOCK-IT-100, common adverse reactions were reported in 79% (314/398) of patients using DefenCath as a CLS and 79% (315/399) of patients using heparin

No overall differences in safety or effectiveness were observed between patients aged ≥65 years and younger adult patients

Adverse Reactions Occurring in ≥2% of Patients Receiving DefenCath in LOCK-IT-100	DefenCath N=398 n (%)	Heparin N=399 n (%)
Product issues		
Hemodialysis catheter malfunction	68 (17)	47 (12)
Blood and lymphatic system disorders		
Hemorrhage/bleeding	27 (7)	34 (9)
Thrombocytopenia	7 (2)	4 (1)
Gastrointestinal disorders		
Nausea	28 (7)	44 (11)
Vomiting	24 (6)	32 (8)
Nervous system disorders		
Dizziness	22 (6)	16 (4)
Musculoskeletal and connective tissue disorders		
Musculoskeletal chest pain	11 (3)	7 (2)

CLS=catheter lock solution.

Reference: DefenCath [prescribing information]. Berkeley Heights, NJ: CorMedix Inc.; 2023.

Serious Adverse Reactions

	DefenCath N=398 n (%)	Heparin N=399 n (%)
Serious adverse reactions	159 (40)	167 (42)
Adverse reactions leading to death	18 (5)	21 (5)
Adverse reactions leading to discontinuation of study drug	69 (17)	72 (18)

- **Other clinically significant adverse reactions** that occurred in <1% of patients receiving DefenCath in LOCK-IT-100: hypocalcemia and dysgeusia

Reference: DefenCath [prescribing information]. Berkeley Heights, NJ: CorMedix Inc.; 2023.

Summary

- Patients with kidney failure receiving chronic HD through a CVC are at high risk for CRBSIs[1]
- DefenCath is the first and only FDA-approved antimicrobial CLS indicated to reduce the incidence of CRBSIs in adult patients with kidney failure receiving chronic HD through a CVC[2]
  - DefenCath was approved by the FDA under the Limited Population for Antibacterial and Antifungal Drugs (LPAD) pathway. This drug is indicated for use in a limited and specific population of patients[3,4]
- In LOCK-IT-100, the pivotal Phase 3 trial, DefenCath reduced CRBSI risk by 71% compared with heparin in HD-CVC patients[2]
- Loss of catheter patency and adverse reactions were comparable between the DefenCath and heparin groups[2]

CLS=catheter lock solution; CRBSI=catheter-related bloodstream infection; CVC=central venous catheter, FDA=US Food and Drug Administration; HD=hemodialysis.

References: 1. Rajagopalan K, et al. Presented at: the American Society of Nephrology Kidney Week 2021; November 4-7, 2021; San Diego, CA. **2.** DefenCath [prescribing information]. Berkeley Heights, NJ: CorMedix Inc.; 2023. **3.** US Food and Drug Administration. FDA approves new drug under special pathway for patients receiving hemodialysis. Accessed January 2, 2024. https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-new-drug-under-special-pathway-patients-receiving-hemodialysis **4.** US Food and Drug Administration. Limited population pathway for antibacterial and antifungal drugs – the LPAD pathway. Accessed January 2, 2024. https://www.fda.gov/drugs/development-resources/limited-population-pathway-antibacterial-and-antifungal-drugs-lpad-pathway

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Thank you

CorMedix™

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