SECTION 1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND THE COMPANY/UNDERTAKING

Product Identifier	
Product form	Clear, sterile aqueous solution provided as a 3 mL or 5 mL fill in a 5 ml USP Type I glass container with low extractable bromobutyl stopper and aluminum flip-off cap.
Product Name	**DefenCath®** (Taurolidine and Heparin Catheter Lock Solution)
Material Name	Taurolidine (1.3%), Citrate (3.5%) and Heparin (1,000 U/mL)
CAS No	19388-87-5
NDC No	72990-103-03; 72990-105-05
Chemical Formula of Active Ingredient	4,4'-Methylenebis(tetrahydro-1,2,4-sulfadiazine 1,1- dioxide); C7H16N4O4S2
Chemical Name of Active Ingredient(s)	Taurolidine and Heparin

Intended Use of the Product substance/mixture

Catheter lock solution that is instilled within the catheter lumen, for "locking" silicone or polyurethane catheters following hemodialysis treatment sessions in patients with kidney failure receiving chronic hemodialysis through a central venous catheter.

Name, Address, and Telephone of the Responsible Party Company

CorMedix, Inc.
300 Connell Drive, Suite 4200
Berkeley Heights, NJ 07922
908- 517-9500

Emergency Phone Number

CorMedix, Inc. Medical Information
1 844-424-6345

SECTION 2: HAZARDS IDENTIFICATION

Classification of the Substance or Mixture's Health Hazard

DefenCath is a non-hazardous aqueous antimicrobial and anticoagulant solution that was approved by the USA Food and Drug Administration in November of 2023, indicated to reduce the risk of catheter related bloodstream infections in adult patients with kidney failure receiving chronic hemodialysis through a central venous catheter. Taurolidine is the key anti-infective component and heparin is the key anticoagulant component of the DefenCath solution. At concentration of 1.35% and 1000 Units/mL, respectively, DefenCath poses little or no risk to human health.

Physical Hazard

Not classified

GHS Label elements, including precautionary statements

Non-hazardous aqueous mixture

Emergency Overview

Hazard Statements

DefenCath is found devoid of mutagenic/genotoxic risk. While exhibiting cytotoxic activities in *in vitro* systems, it showed little or no signs of mutagenic toxicity or genotoxicity in battery of *in vivo* mutagenic assays. According to ICH S2 (R1) guidance, while *in vitro* cytotoxicity were important in assessing toxic activity of agents, they alone were insufficient to predict actual clinical risk. It then follows that negative mutagenic results, as presented here, in appropriate *in vivo* assays with adequate justification for the endpoints as measured, and demonstration of exposure are sufficient to determine absence of significant genotoxic risk.

Appearance: Clear aqueous mixture

Physical State: Liquid

Odor: Odorless

Precautionary Statements

Prevention:
Obtain Special Instructions Before Use: Do not handle until all safety precautions have been read and understood.
Use personal protective equipment as required.

General Advice: If exposed or concerned, get medical attention/advice.

Storage: Store locked up.

Disposal: Dispose of contents/container to an approved waste disposal plant.

Hazard Not Otherwise Classified (HNOC): Not applicable

Other information: None known

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

Three or 5 mL vials of DefenCath composed of 1.35% of taurolidine, 3.5% citrate, and heparin 1000 Units/mL solution is not hazardous according to OSHA Hazard Communication Standard (29 CFR 1910.1200; Revision 3).

Synonym	4,4'-methylenebis (tetrahydro-1,2H,4-thiadiazine)1,1,1',1'-tetraoxide
Formula	C17H16N4O4S2

Chemical Name	CAS No	Weight %
Taurolidine	19388-87-5	1.3%

SECTION 4: FIRST AID MEASURES

Description of necessary first-aid measures

Eye Contact — In case of eye contact, immediately flush eyes with fresh water for at least 15 minutes while holding the eyelids open. Remove contact lenses if worn. Get medical attention if irritation persists.

Skin Contact — In case of contact, remove contaminated clothing. Immediately flush skin with copious amounts of water for at least 15 minutes. Obtain medical attention if skin reaction occurs.

Inhalation — In case of inhalation, remove to fresh air. If not breathing, provide artificial respiration. If breathing is difficult, administer oxygen. Seek medical attention immediately.

Ingestion — In case of accidental ingestion, wash out mouth with copious amounts of water. Seek medical attention immediately. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and delayed

Symptom — None anticipated from normal handling of this product. Based on clinical use, adverse events occurring in greater than or equal to 2% of patients in the Phase 3 study of DefenCath as a catheter lock solution were hemodialysis catheter malfunction, hemorrhage/bleeding, nausea, vomiting, dizziness, musculoskeletal chest pain, and thrombocytopenia. There are also clinical reports of mild transient change in taste (i.e. dysgeusia) and paresthesia.

Indication of any immediate medical attention and special treatment needed

Note to Physician — Treat symptomatically.

SECTION 5: FIRE-FIGHTING MEASURES

Suitable Extinguishing Media
Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Unsuitable Extinguishing Media	Not available

Specific hazards arising from the chemical Not available

Hazardous Combustion Products
Not available

Explosion data
Sensitivity to Mechanical Impact Not available
Sensitivity to Static Discharge Not available

Protective equipment and precautions for firefighters
As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear.

SECTION 6: ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures

Personal Precautions Wear appropriate personal protective equipment (see Section 8). Keep unnecessary personnel away. Ensure adequate ventilation, especially in confined areas.

Environmental Precautions Not available

Methods and material for containment and cleaning up

Methods for Containment Prevent further leakage or spillage if safe to do so.

Methods for Cleaning Up Pick up and transfer to properly labeled containers

SECTION 7: HANDLING AND STORAGE

Precautions for safe handling

Advice on Safe Handling Handle in accordance with good industrial hygiene and safety practice.

Conditions for storage, including any incompatibilities

Storage Conditions Store at room temperature 20-25ºC (68-77ºF).

Incompatible materials Not available

Specific End Use Pharmaceutical product used as catheter lock solution

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

Control parameters

Exposure Guidelines This product, as supplied, does not contain any hazardous materials with Occupational Exposure Limits (OEL) established by the region-specific regulatory bodies.

Appropriate engineering controls

Engineering Controls The health hazard risks of handling this material are dependent on factors, such as physical form and quantity. Site-specific risk assessments should be conducted to determine the appropriate exposure control measures. Good general ventilation should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits

have not been established, maintain airborne levels as low as reasonably achievable.

Individual protection measures, such as personal protective equipment

Eye/Face Protection	In laboratory, medical or industrial settings, safety glasses with side shields are highly recommended. The use of goggles or full face protection may be required depending on the industrial exposure setting. Contact a health and safety.
Skin and Body Protection	In laboratory, medical or industrial settings, gloves and lab coats are recommended. The use of additional personal protective equipment such as shoe coverings, gauntlets, and hood or head coverings may be necessary. Contact a health and safety professional for specific information.
Respiratory Protection	Respirators may be required for certain laboratory and manufacturing tasks if engineering controls do not maintain airborne concentrations below recommended exposure limits (where applicable) or to an acceptable level (where the exposure limits have not been established). Workplace risk assessments should be completed before specifying and implementing respirator usage. All respirators must conform to specifications for efficiency and performance indicated by OSHA Standard 29 CFR 1910.134.
General Hygiene Considerations	Always observe good personal hygiene measures, such as washing after handling the material and before eating, drinking, and/or smoking. Routinely wash work clothing and protective equipment.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Physical State	Liquid	Dosage	3 mL & 5 mL
Appearance	Aqueous	**Odor**	Odorless
Color	Clear	**Odor Threshold**	Not Available

Property	Values
pH	5.5 – 6.5
Melting Point/Freezing Point	Not available.
Boiling Point/Boiling Range	Not available.
Flash point	Not available.
Evaporation Rate	Not available.
Flammability (Solid, gas)	Not available.
Flammability, Limit in Air	Not available.
Upper Flammability Limit	Not available.
Lower Flammability Limit	Not available.
Vapor Pressure	Not available.
Vapor Density	Not available.
Specific Gravity	1.025 – 1.035 g/mL (25°C)
Water Solubility	Not available.
Solubility in Other Solvent	Not available.
Partition Coefficient	Not available.
Decomposition Temperature	Not available.
Kinematic Viscosity	1.2 cP
Explosive Properties	Not available.
Oxidizing Properties	Not available.

Other Information

Softening Point	Not available.
Molecular Weight (Taurolidine API)	284.5 g/mol
VOC Content %	Not available.
Density	Not available.
Bulk Density	Not available.

SECTION 10: STABILITY AND REACTIVITY

Reactivity	Not available
Chemical stability	The active component, taurolidine is unstable in biological fluid
Possibility of hazardous reactions	Not available
Hazardous Polymerization	Not available
Conditions to avoid	Not available
Incompatible materials	Not available
Hazardous decomposition products	Not available

SECTION 11: TOXICOLOGICAL INFORMATION

Studies were in compliance with OECD Guideline 474 and 489, the ICH S2 (R1) Guidance (1) and Biocompatibility conducted with ISO10993 Standard

Informational on toxicological effect

Symptoms	Up to date, no serious or unexpected adverse event has been reported with the use of DefenCath in the clinic, except for occasional mild transient change in taste, which resolves in a few minutes.
Mortality	In acute intravenous dose study in rats, no mortality related to Defencath were observed at up to 0.71 mL/Kg dose volume that represent 8.5 mg/Kg of taurolidine content. In contrast, lethality and mortality were reported at dose volume > 0.9 mL/Kg, representing an extreme dose component of 12 mg/Kg content. Despite the lethally reported at 0.9 mL/Kg in rats, it should be noted that there is marked margin of safety gap between rat dose and clinical dose that supports low risk adverse effect following normal clinical application or even when the whole 5 mL of DefenCath is accidental administered into the system see, table 1 below.

Delayed and immediate effects as well as chronic effects from short- and long-term exposure to DefenCath

Local Exposure	Moderate level of erythema and edema were observed with intra- cutaneous injection of DefenCath at 0.2 mL in rabbits. No immune-mediated hypersensitivity reactions were reported when administered subcutaneously with Freund's adjuvant in guinea pigs.
Acute Systemic Exposure	Well tolerated via intravenously injection at 0.71 mL/Kg in rabbits. A single bolus intravenous administration of DefenCath failed to evoke thrombocytopenia. A well-known adverse effect associated with heparin treatment.

Skin Corrosion/Irritation	Sites injected intra-cutaneously with diluted (25% and 10%) DefenCath does not showed a significantly greater biological reaction than the sites treated with the control article in rabbits. However, DefenCath prepared at 50% produced skin irritations at site of injection in rabbits.
Serious Eye Damage/Eye Irritation	No available data
Sensitization Cytotoxicity	No immune-mediated hypersensitivity reactions were observed when DefenCath is subcutaneously administered with Freund's adjuvant in guinea pigs. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) cytotoxicity, an *in vitro* assay showed DefenCath to lack mammalian cells culture (mouse fibroblast L929) cytotoxicity at the concentration of 0.06%, 0.02% and 0.1%. But considered to have cytotoxic potential at concentration ≥ 0.2%.
Mutagenicity/ Genotoxicity	While DefenCath is considered to have cytotoxic potential in MTT assay, no such signs were observed in Ames test, an *in vitro* mutagenic assay. Furthermore, determinant battery of *in vivo* mutagenic assays found DefenCath to be devoid of genotoxic risk. No evidence of genotoxicity were observed with intravenous administrations of the active component, taurolidine at either dose of 150, 300 or 600 mg/kg/day. Taurolidine failed to modify two independent critical endpoints in two tissues namely bone marrow for the formation of micronuclei in polychromatic erythrocytes (MnPCEs) and liver for the induction of hepatocytes DNA strand breaks (Comet assay) in rats.
Carcinogenicity	Up to date, no report of carcinogenic liability have been reported for the use of DefenCath To the contrary, cytotoxicity in tumorigenic cells has been reported for taurolidine, the active component DefenCath, potentially by causing cell cycle arrest and triggering induction of apoptosis.
Reproductive	No available
STOT- Single Exposure	Single doses of DefenCath up to 0.71 mL/Kg has been reported well tolerated when administered intravenously in rabbits or intraperitoneal in mouse. Additionally, no signs of thrombocytopenia reaction, typically associated with heparin treatment were observed with the single bolus intravenous dose in rats.
STOT- Single Repeat Exposure	14 day repeat intravenous volume of 0.71 mL/Kg DefenCath produced no signs of adverse systemic toxicity in rats. No apparent changes were observed in the toxicological end points, including body weights, clinical observations, hematology, clinical chemistry, coagulation parameters, organ/ relative organ weights and microscopic evaluation. Thrombocytopenia reaction, typically associated with heparin treatment were also absence.
Other Adverse Effect	The active component of DefenCath taurolidine's MTD was found to occur at 600mg/kg in rats. While the LD50 is ≧ 1000 mg/kg body weight in all species tested.
Aspiration hazard Extractable	Not available
and Leachable	Risk associated with leachable from catheter is unlikely as no marked difference were noted in catheter extractables (in either limited, semi or non- volatile agents) following use of DefenCath lock relative to physiological saline as defined by ISO10993.
Margins of Safety	Wide safety margins between rats and clinical dose suggest adverse effects in the clinic are unlikely, see table 1 below.

Table 1. Rat dose levels and clinical safety margin

		Taurolidine	Citrate	Heparin
Rat Dose Level	0.90 ml/kg	12 mg/kg	31.5 mg/kg	900 U/kg
	human equivalent[a]	840 mg	2205 mg	63000 U
Safety Margin	Safety margin (5ml)	12.4	12.6	12.6
	Safety margin (20%)	62.2	63.0	63.0
Rat Dose Level	0.71 ml/kg	8.5 mg/kg	24.85 mg/kg	710 U/kg
	human equivalent[a]	595 mg	1739.5 mg	49700 U
Safety Margin	Safety margin (5ml)	8.8	9.9	9.9
	Safety margin (20%)	44.1	49.7	49.7
Clinical Dose	5 ml	67.5 mg	175 mg	5000 U
	20%	13.5 mg	35 mg	1000 U

[a] Assumes 70 kg human (Toxikon Report 10-6116-N16)

SECTION 12: ECOLOGICAL INFORMATION

Ecotoxicity
Not available.

Persistence and degradability
Not available

Bioaccumulation
Not available

Mobility
Not available

Other adverse effects
Not available.

SECTION 13: DISPOSAL CONSIDERATIONS

Waste treatment methods

Disposal of Wastes Disposal should be in accordance with applicable regional, national and local laws and regulations.

Contaminated Packaging Disposal should be in accordance with applicable regional, national and local laws and regulations. Do not reuse container.

US EPA Waste Number Not available

California Hazardous Waste Codes Not available

This product does not contain substances that are listed with the State of California as hazardous waste.

SECTION 14: TRANSPORT INFORMATION

DOT Not regulated

IATA Not regulated

SECTION 15: REGULATORY INFORMATION

US Federal Regulations

SARA 313
Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372.

SARA 311/312 Hazard Categories

Acute Health Hazard	No
Chronic Health Hazard	No
Fire Hazard	No
Sudden Release of Pressure Hazard	No
Reactive Hazard	No

CWA (Clean Water Act)
This product does not contain any substances regulated as pollutants pursuant to the Clean Water Act (40 CFR 122.21 and 40 CFR 122.42).

CERCLA
This material, as supplied, does not contain any substances regulated as hazardous substances under the Comprehensive Environmental Response Compensation and Liability Act (CERCLA) (40 CFR 302) or the Superfund Amendments and Reauthorization Act (SARA) (40 CFR 355). There may be specific reporting requirements at the local, regional, or state level pertaining to releases of this material.

US State Regulations

California Proposition 65
No component is on the Prop 65 list.

U.S. State Right-to-Know Regulations
This product does not contain any substances regulated by state right-to-know regulations.

U.S. EPA Label Information
EPA Pesticide Registration Number Not applicable.

SECTION 16: OTHER INFORMATION

Originally Prepared by	Advanced Clinical
Issue Date	05/16/2019
Revision Date	11/13/2024
Revision Note	Rev 01 (Version 1)

Disclaimer
The information provided on this SDS is correct to the best of our knowledge and while it is provided in good faith, it is without warranty of any kind, expressed or implied. The information contained herein is designated only as guidance for safe handling, storage and use of the substance and is not a specification nor does it guarantee any specific properties. Only competent personnel, within a controlled environment should handle all chemicals. CorMedix not to be held liable for any loss, injury or damage from contact with the product

End of Safety Data Sheet