reduction in the rate of PBCs compared to the use of Tego connector plus Curos cap in hemodialysis patients with catheters. See Table 3 below.

Table 3. Randomized Clinical Study Results Primary Analysis:
PBC rates of ClearGuard HD vs. Tego+Curos on a Per-Event Basis

Variable	Result
PBC Rate, ClearGuard HD	0.28 per 1,000 CVC-days
PBC Rate, Tego+Curos	0.75 per 1,000 CVC-days
Incidence Rate Ratio (IRR)	0.37
Reduction in PBC Rate	63%
P value	0.0001

The exploratory ad-hoc CLABSI analysis was conducted to explore the possible reduction of a more clinically meaningful outcome than PBC rates. However, this analysis was not pre-specified in the protocol and may have limitations (see Note below).
For a PBC to be classified as a CLABSI in this study per the NHSN surveillance definition, it must have been a Laboratory-Confirmed Bloodstream Infection (LCBI)2 as follows: LCBI1) a recognized pathogen (an organism not included on the NHSN common commensal list) identified from one or more blood specimens obtained by blood culture microbiologic testing and the organism(s) identified in the blood must not be related to an infection at another site (as indicated by the "vascular access" box being checked as the suspected source of the PBC on the Dialysis Event (DE) form)3, OR an LCBI2) the same NHSN common commensal identified by blood culture microbiologic testing from two or more blood specimens drawn on the same day, the organism(s) identified in blood must not be related to an infection at another site (as indicated by the "vascular access" box being checked as the suspected source of the PBC on the DE form), and the subject had at least one of the following symptoms: fever, chills, or hypotension (as indicated on the DE form). Also, the CLABSI analysis was conducted on a per-subject basis (i.e., censored the patient after the first CLABSI event to prevent potentially double counting the same infection). All cultures were processed by a single clinical laboratory. Note: CLABSI was defined as a positive blood culture (PBC) not related to an alternative source of infection per the National Healthcare Safety Network (NHSN) surveillance definition. Alternative sources were excluded if dialysis sites attributed the PBC to vascular access on the dialysis event form. The actual reduction in CLABSI rates may be less substantial as the evaluation for alternative PBC sources was not pre-specified, nor standardized between patients and clinical sites, and supplemental data evaluating for alternative sources were not available for review.
The CLABSI analysis demonstrated that using ClearGuard HD Antimicrobial Barrier Caps resulted in a reduction in the rate of CLABSIs compared to the control (Table 4).

Table 4. Randomized Clinical Study Results Exploratory Analysis:
CLABSI Rates of ClearGuard HD vs. Tego+Curos on a Per-Subject Basis

Variable	Result
CLABSI Rate, ClearGuard HD	0.17 per 1,000 CVC-days
CLABSI Rate, Tego+Curos	0.50 per 1,000 CVC-days
Incidence Rate Ratio (IRR)	0.34
Reduction in CLABSI Rate	66%

There was no formal safety endpoint associated with this clinical study. There were no device-associated adverse events reported via the FDA's medical device reporting (MDR) during this study or in a previous study4.

CONCLUSIONS

Results of design verification and validation testing demonstrate that 1) the ClearGuard HD Antimicrobial Barrier Cap is safe for its intended use as an end cap for hemodialysis catheters and 2) the chlorhexidine antimicrobial agent effectively reduces the number of microorganisms in hemodialysis catheter hubs following three years of real time ambient aging. The risk assessment results, together with the results of design verification and validation testing presented in this submission, confirm that the ClearGuard HD Antimicrobial Barrier Cap raised no new questions of safety or effectiveness compared to the predicate device. The ClearGuard HD Antimicrobial Barrier Cap has, therefore, been shown to be substantially equivalent to a legally marketed device for the purpose of 510(k) clearance. The post-market clinical study demonstrated a reduction in the rate of CLABSIs with use of the device, thus supporting the expanded indications for use.

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IFU0000385 REV 03 (11/22)

ClearGuard™ HD

STERILE R Rx only MD

2 2 STERILIZE PHT DEHP LATEX

www.icumed.com/symbols-glossary

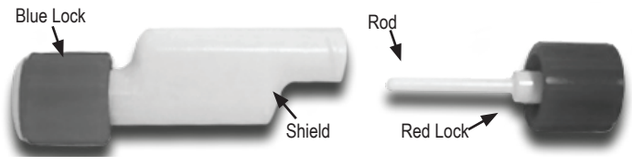

Figure 1 One ClearGuard HD Cap Removed from the Shield

DESCRIPTION

The ClearGuard™ HD Antimicrobial Barrier Cap (also referred to as the ClearGuard HD cap) is a cap for use with hemodialysis catheters. It has the antimicrobial agent chlorhexidine acetate on the rod and lock ring threads.
Each package contains two ClearGuard HD caps assembled in a shield (Figure 1). The total amount of chlorhexidine acetate on a pair of devices is not more than 2.53 mg, and the maximum amount that is available to be released to the patient is 0.6 mg per device pair.

INTENDED USE / INDICATIONS FOR USE

ClearGuard HD Antimicrobial Barrier Cap is indicated for use with hemodialysis catheter hubs.
Using in vitro methods, the antimicrobial treatment on the ClearGuard HD Antimicrobial Barrier Cap has been shown to be effective at reducing microbial colonization in hemodialysis catheter hubs against the following microorganisms: Enterococcus faecium (VRE), Enterococcus faecalis (VRE), Acinetobacter baumannii, Escherichia coli, Staphylococcus aureus (MRSA), Staphylococcus aureus, Staphylococcus epidermidis (MRSE), Pseudomonas aeruginosa, Candida albicans and Candida parapsilosis and has not been shown to be effective against Candida paratropicalis and Klebsiella pneumoniae.
Using post-market clinical surveillance data, use of the ClearGuard HD Antimicrobial Barrier Cap has been shown to reduce the incidence of central-line associated bloodstream infections (CLABSI) in hemodialysis patients with catheters. Note: CLABSI was defined as a positive blood culture (PBC) not related to an alternative source of infection per the National Healthcare Safety Network (NHSN) surveillance definition. Alternative sources were excluded if dialysis sites attributed the PBC to vascular access on the dialysis event form. The actual reduction in CLABSI rates may be less substantial as the evaluation for alternative PBC sources was not pre-specified, nor standardized between patients and clinical sites, and supplemental data evaluating for alternative sources were not available for review.
The subject device is not intended to be used for the treatment of existing infections. The antimicrobial is only present within the hub of the catheter and does not migrate to distal portions of the catheter.

CONTRAINDICATIONS

Do not use the ClearGuard HD cap for the following:

- Patients who are allergic to chlorhexidine.
- Patients who are allergic to nylon or polypropylene.
- Catheters that are dimensionally incompatible with the ClearGuard HD caps.

- Catheters with hubs that allow the ClearGuard HD rod to extend beyond the hub within reach of the extension line pinch clamp.
- Catheters that have antimicrobial agents eluting from their inner lumens.

WARNINGS

- Do not use if the package has been opened or is damaged, or if the expiration date has passed.
- Do not reuse any component of the ClearGuard HD cap. The ClearGuard HD cap is intended for single use only and should never be re-used. Reuse or reprocessing including resterilization may compromise the device integrity and may also create a risk of contamination of the device and/or cause recipient infection.
- Do not close extension line pinch clamp on ClearGuard HD rod.
- The ClearGuard HD cap has not been evaluated for safety in Magnetic Resonance Imaging (MRI).
- Do not allow the ClearGuard HD rod or luer to contact non-sterile items; touching the rod or luer with non-sterile items may lead to a bloodstream infection.
- Do not touch the rod with gloved hands.
- The ClearGuard HD cap should be discarded if the rod contacts non-sterile items or gloved hands.

CAUTIONS

- This product contains chlorhexidine acetate.
- Carefully read and follow all instructions prior to use.
- Federal (U.S.A.) law restricts this device to sale by or on the order of a physician.
- Only qualified dialysis center personnel or healthcare practitioners should place, manipulate or remove the ClearGuard HD caps.

PRECAUTIONS

- Follow universal precautions when inserting and maintaining the ClearGuard HD caps.
- Do not allow the ClearGuard HD rod to contact non-sterile items.
- Take care not to damage the ClearGuard HD cap during placement.

POTENTIAL COMPLICATIONS

- Allergic/anaphylactic/pyrogenic reaction
- Injury/pain/death
- Device failure (device cracking, breaking, leaking, splitting or disconnecting potentially requiring device intervention, removal or replacement)
- Embolism (air or device)
- Incompatibility with administered fluids or sanitizing agent.
- Incompatibility with connecting device/difficulty connecting
- Infection (local, bacteremia, endocarditis, sepsis)
- Sensitization
- Toxicity

PLACING A ClearGuard HD END CAP ON A HEMODIALYSIS CATHETER

1. Use the standard facility or industry recommended aseptic technique when accessing the catheter. A mask is to be worn by the caregiver and patient covering the nose and mouth. The caregiver's hands are to be cleaned and gloved.
   PRECAUTION: Use aseptic technique to avoid contaminating the end cap and catheter.
2. Use the standard facility and industry recommended practices to flush the catheter and to instill locking solution into the catheter prior to placing the ClearGuard HD cap. Ensure that the catheter extension tubing pinch clamp is closed, that the lock solution completely fills the extension tube and catheter hub, and the syringe remains attached to the catheter.
3. Remove the pair of ClearGuard HD caps that are contained in a shield from the foil pouch.
4. While holding the shield and a catheter hub in one hand, remove the syringe from the hub and discard syringe. Do not allow the hub to touch non-sterile surfaces.
5. Remove a single ClearGuard HD cap (red or blue), by rotating the lock ring counter-clockwise, taking care to only handle the lock ring; do not touch the rod.
   WARNING: Do not allow the ClearGuard HD rod or luer to contact non-sterile items; touching the rod or luer with non- sterile items may lead to a bloodstream infection. Discard the ClearGuard HD cap if the rod or luer contacts non-sterile items or gloved hands.
6. Carefully insert the ClearGuard HD rod into the catheter hub and, using a simultaneous push and twist motion, tighten by rotating clockwise.
   NOTE: As the ClearGuard HD rod enters the hub, it will displace some of the lock solution; this is desirable as it can wet the antimicrobial on the ClearGuard HD cap threads.
7. Repeat with the other ClearGuard HD cap and dispose of the shield and foil pouch.

REMOVING THE ClearGuard HD CAP FROM A HEMODIALYSIS CATHETER

1. Use the standard facility or industry recommended aseptic technique when accessing the catheter. A mask is to be worn by the caregiver and patient covering the nose and mouth. The caregiver's hands are to be cleaned and gloved.
   PRECAUTION: Use aseptic technique to avoid contaminating the cap and catheter.
2. Use the facility's standard cap and hub cleaning procedures.
3. Ensure that the extension tubing pinch clamp is closed.
4. Carefully support catheter hub with one hand and, using other hand, loosen ClearGuard HD cap by rotating counter-clockwise.
5. Remove the ClearGuard HD cap and dispose of the used device in accordance with facility protocol (see DEVICE DISPOSAL, below). The caps must be discarded after removal.
   PRECAUTION: Caps must never be reused or reconnected to the catheter hub once removed or contamination of the catheter may occur.
6. Attach sterile syringe to catheter and aspirate the lock solution from the catheter using your facility's standard practices.
   WARNING: After removing the ClearGuard HD cap from the catheter, aspirate a minimum of 5 mL of fluid from the catheter. This will prevent lock solution and antimicrobial agent from entering the bloodstream.
7. Use the catheter using standard facility and industry recommended practices.

MAXIMUM USE TIME

The recommended maximum use time is three days.

STERILITY & PACKAGING

The ClearGuard HD cap is provided sterile in a single sterile barrier foil package and is gamma sterilized. The device should be stored at room temperature and protected from UV exposure and moisture.

DEVICE DISPOSAL

ClearGuard HD caps that have been in contact with body fluids are a potential biohazard. Handle and dispose of the device and its components with acceptable medical practice and applicable local, state, and federal laws and regulations.

SAFETY AND EFFECTIVENESS DATA

The ClearGuard HD caps have been found to be safe and effective for their intended use. The ClearGuard HD caps have been subjected to biocompatibility testing in compliance with EN ISO 10993-1 and found to be non-hemolytic, non-cytotoxic, non-irritating, non-sensitizing, non-mutagenic, non-toxic and non- pyrogenic under intended use conditions. They have also been found to be sterile with a SAL ≤ 10-6. The ClearGuard caps have also met their requirements for luers, chemical resistance, assembly and disassembly torque and attachment strength.
The ClearGuard HD end cap effectiveness has been assessed using the following in vitro test method:

- Heparin lock solution, which was inoculated with microorganism strains that are known to cause catheter related blood stream infections, was injected into the hub region of a catheter.
- Equal numbers of ClearGuard HD end caps and uncoated control devices were then placed on the test catheter systems and allowed to remain in place for two to three days.
- For both the ClearGuard HD end cap and the uncoated control device, the number of surviving microorganisms were determined.
- The ClearGuard HD end cap was deemed to be effective against a microorganism if it produced at least a 4 log10 reduction (99.99% reduction), when compared to uncoated control device.
- Please see indications for use for a summary of results.
- The ClearGuard HD cap safety and effectiveness has been assessed in a post market clinical trial.

CLINICAL TRIAL RESULTS

A 13-month, prospective, cluster-randomized, multi-arm, unblinded clinical study with a control was conducted at 40 dialysis facilities throughout the United States only. Facilities were pair-matched and randomly assigned to treatment or control group. The treatment group received the ClearGuard HD Antimicrobial Barrier Cap and the control group received the Tego™ Connector with the Curos™ Disinfecting Cap. The primary study endpoint was PBC rate. There were no other primary study endpoints but an ad hoc exploratory analysis of CLABSI was also conducted. 1,671 subjects participated in the study during the primary and exploratory analyses, accruing approximately 183,000 CVC-days in the primary
analysis1. The subject enrollment is shown in Table 1 and the subject demographics are shown in Table 2

Table 1. Subject Enrollment During the Intervention Period

Stage	Investigation Device Arm (ClearGuard HD)	Control Device Arm (Tego+Curos)	Total in Both Arms
Subjects enrolled	951	960	1911
Subjects excluded for history of heparin allergy	9	0	9
Subjects receiving treatment	942	960	1902
Subjects excluded due to treatment ≤21 days	116	115	231
Subjects in primary and exploratory analyses	826	845	1671

Table 2. Subject Demographics During the Intervention Period

Characteristic	All	Treatment Group	Control Group	P-Value
No. of Facilities	40	20	20	
No. of CVC Subjects	1671	826	845	
Age, y	62.8 ± 14.9	63.7 ± 14.4	62.0 ± 15.3	0.02
Gender (% Male)	856 (51)	421 (51)	435 (51)	0.8
Race Caucasion African American Hispanic Other Missing	 778 (47) 621 (37) 171 (10) 98 (6) 3 (0)	 414 (50) 267 (32) 83 (10) 60 (7) 2 (0)	 364 (43) 354 (42) 88 (10) 38 (5) 1 (0)	 <0.001
Diabetes	998 (60)	477 (58)	521 (62)	0.1
Dialysis vintage, y	1.7 ± 3.2	1.6 ± 3.3	1.8 ± 3.2	0.2

Note: Values for categorical variables are given as number (percentage); values for continuous variables, as mean ± standard deviation.

As is standard policy at the participating facilities, blood culture results were reported into the electronic health record in automated fashion and to the National Healthcare Safety Network (NHSN) Dialysis Event (DE) Form, from which they were abstracted for analysis. The pre-specified primary study endpoint was PBC rate. This study demonstrated that use of the ClearGuard HD Antimicrobial Barrier Caps resulted in a statistically significant