Chloragard® Technology Information

Introduction and Rationale for Antimicrobial Catheters:

Infection is the leading complication associated with intravascular devices, and there is a strong need to develop products to help prevent complications and increase safety for patients and providers. The National Nosocomial Infection Surveillance System (NNIS) tracks central line-associated bloodstream infection (BSI) rates in adult and pediatric intensive care units from 300 participating hospitals. This report serves as a benchmark for other hospitals to use in comparing their rates with the national rates. Approximately 90% of catheter-related bloodstream infections (CRBSIs) occur with central lines.[7] Mortality attributable to CRBSIs has been reported to be between 4% to 20% with prolonged hospitalization (a mean stay of 7 days) and increased hospital costs. Peripherally Inserted Central Catheters (PICCs) are associated with similar rates of CRBSI as Central Venous Catheters (CVCs), placed in internal jugular or subclavian veins (2 to 5 per 1,000 catheter days).[8]

Vascular catheter infections develop for many reasons. They begin when a catheter becomes colonized by microorganisms entering through one or both of two routes: 1) colonization of the outside surface of the catheter or 2) colonization of the inside surface of the catheter. This colonization may be caused by any of five sources: environmental contamination, skin organisms, post-placement subcutaneous tract infection, intraluminal contamination or hematogenous seeding.[9]

Introduction and Rationale for Antithrombogenic Catheters:

Clinically symptomatic and detectable catheter-related venous thrombosis rates associated with peripherally inserted central venous catheters range from 3.4% to as high as 20%.[11] However, when diagnostic methods (ultrasound, contrast injection etc.) are used to assess for asymptomatic venous thrombosis, the incidence dramatically increases up to 58%.[11] Occlusive and/or thrombotic events of peripherally inserted central venous catheters, described as inability to infuse solutions or withdraw blood, has an incidence of 7 to 25%.[5]

Catheter-related thrombus can be distinguished as either intraluminal, with clots occurring inside the lumen of the catheter, or extraluminal, with clots outside of the catheter and within the blood vessel (vein thrombosis). Formation of clot in the catheter lumen can lead to loss of its patency. If left untreated, extraluminal clot can cause complete occlusion of the blood vessel and can lead to a serious clinical condition called deep vein thrombosis (DVT). The introduction of a venous catheter into the bloodstream triggers host responses to the presence of a foreign body. These host/biomaterial interactions occur on the external surface of the catheter, the internal surface of the venous wall, and the luminal surface of the catheter. The interactions of blood components, primarily proteins, platelets, and white blood cells in contact with the catheter material occur in a sequence of events. Within seconds of the catheter's exposure to the blood, protein adsorption and contact activation occur, followed by platelet adhesion, complement activation, and leukocyte adhesion minutes to hours later. The adhered bacteria, platelets and White Blood Cells (WBCs) become enmeshed within layers of fibrin forming a sheath on the surface of the catheter.

Product Description:

The Arrow® PICC with Chloragard® Technology is a peripherally inserted central venous catheter manufactured with medical grade, radiopaque polyurethane. It has a non-tapered catheter body with a Blue FlexTip®, designed to be softer than a cut tip. It has a contour design to enhance maneuverability and minimize vessel trauma. The Blue FlexTip also provides visual confirmation of an intact catheter upon removal. The catheters are available in usable lengths of 40 to 55 cm and are indicated for pressure injectability.

The Arrow PICC with Chloragard Technology is processed with an external surface treatment that uses the antimicrobial chlorhexidine acetate on the catheter body and juncture hub nose, as well as an internal lumen impregnation utilizing an antimicrobial combination of chlorhexidine acetate and chlorhexidine base for the catheter body, juncture hub, extension line(s) and extension line hub(s). A maximum total amount of chlorhexidine content applied to various French sizes and lengths of catheters could range up to 20.5 mg.

The Arrow PICC with Chloragard Technology kit includes essential tools required to:

- Access patients' vasculature
- Promote compliance for reducing risk with an ergonomic, comprehensive design
- Protect patients from five sources of bloodstream infections
- Reduce instances of catheter surface thrombus accumulation and luminal occlusions
- Comply with current evidence-based guidelines for infection reduction and safety

Technology Sheet

Characterization of Chlorhexidine:

Chlorhexidine is characterized as having a broad antimicrobial activity spectrum, including bacteriostatic and bactericidal effects on gram positive bacteria, gram negative bacteria and fungi.[3,4,6,10] Chlorhexidine also has been shown to be effective against viruses with a lipid component in their coats or with an outer envelope,[1,2,12] but these properties have not been evaluated with this product. The antithrombogenic effect of the Chlorag+ard Technology on the Arrow PICC appears to be a function of thrombin inhibition by Chlorhexidine via intrinsic and common pathways of blood coagulation, causing delayed blood clotting response and thrombus accumulation on catheter surface.

Whether chlorhexidine is bacteriostatic or bactericidal depends largely on the concentration of the agent, its pH and the susceptibility of specific organisms. Optimum stability ($C_{26}H_{38}C_{l2}N_{10}O_4$) is demonstrated between pH levels of 5.5 and 7.0, which are consistent with pH levels of body surfaces and tissues.[3,13]

Chlorhexidine is a cationic compound. Its positively charged molecules are strongly attracted to the negative charges present on microbial surfaces. The outer membrane of gram negative bacteria, cell wall of gram positive bacteria or cytoplasmic membrane of yeasts then becomes weakened from increased permeability caused by chlorhexidine being adsorbed onto the cell surface. Chlorhexidine exhibits bacteriostatic effects at low concentrations due to the release of substances characterized by low molecular weights (i.e., phosphorus and potassium ions) from the cell. This damage is enough to inhibit bacterial cell function. Bactericidal activity of chlorhexidine occurs at higher concentrations by causing precipitation of proteins and nucleic acids.[3]

Chlorhexidine is poorly absorbed from the gastrointestinal tract. In human and animal studies, the average plasma level peaked at 0.206 µg/g in humans 30 minutes after ingesting 300 mg of chlorhexidine. Excretion occurred primarily through the feces (about 90%), and less than 1% was excreted in urine. Chlorhexidine is metabolized in the same manner as most other foreign substances. The majority will be excreted without being metabolized.[3]

Preclinical biocompatibility studies support the conclusion that there is a negligible risk of adverse effects from the Antimicrobial/Antithrombogenic PICC products with Chlorag+ard Technology.

Indications for Use:

The Arrow PICC with Chlorag+ard Technology is indicated for short-term or long-term peripheral access to the central venous system for intravenous therapy, blood sampling, infusion, pressure injection of contrast media, and allows for central venous pressure monitoring. The maximum pressure of pressure injector equipment used with the Arrow PICC with Chlorag+ard Technology may not exceed 300 psi. Chlorag+ard Technology on the external surface of the catheter body as well as the entire fluid pathway of the catheter has been shown to be effective in reducing microbial colonization and thrombus accumulation on catheter surfaces. Antimicrobial and antithrombogenic effectiveness were evaluated using *in vitro* and *in vivo* test methods, and no correlation between these test methods and clinical outcome has currently been ascertained. It is not intended to be used for the treatment of existing infections or vein thrombosis.

Contraindications:

Clinical assessment of the patient must be completed to ensure no contraindications exist. The Arrow PICC with Chlorag+ard Technology is contraindicated in the following areas:

- Patients with known hypersensitivity to chlorhexidine
- In presence of device related infections
- In presence of previous or current thrombosis in the intended vessel or along the catheterized vessel pathway.

Warning:

Remove catheter immediately if adverse reactions occur after catheter placement.

NOTE: Perform sensitivity testing to confirm allergy to catheter antimicrobial agents if adverse reaction occurs.

Refer to enclosed product Instructions for Use (IFU) for additional Warnings and Precautions.

Hypersensitivity Potential:

Benefits of the use of this catheter should be weighed against any possible risk. Hypersensitivity reactions are a concern with antimicrobial catheters and can be serious and even life-threatening. Since antimicrobial catheters were introduced into the market, there have been some reports of hypersensitivity occurrences outside the United States. This hypersensitivity potential has been reported to occur more frequently in Japan.

Pre-Clinical Evaluations:

The Arrow PICC with Chlorag+ard Technology has demonstrated reduction in colonization by gram-positive and gram-negative bacteria, and yeast in *in vitro* and *in vivo* studies for up to 30 days for external surface and *in vitro* studies for up to 30 days for fluid pathway.[10] In addition, this PICC has also demonstrated reduction in thrombus accumulation on catheter surfaces for up to 30 days in *in vivo* testing. *In vitro* testing has exhibited reduction in platelet adhesion on catheter surface and catheter occlusion.[10]

Refer to enclosed product Instructions for Use (IFU) for specific indications, procedural technique(s) and potential complications associated with PICC insertion procedures.

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