ChloraPrep®
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

ChloraPrep® 2% w/v / 70% v/v cutaneous solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Chlorhexidine gluconate 20 mg/ml
Isopropyl alcohol 0.70 ml/ml
For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Cutaneous Solution.
Clear Solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

The medicinal product is to be used for disinfection of the skin prior to invasive medical procedures.

4.2 Posology and method of administration

For cutaneous use.

ChloraPrep may be used on all age groups and patient populations. However, ChloraPrep should be used with care in newborn babies, especially those born prematurely (see also section 4.4, Special warnings and precautions for use).

One applicator is used containing 0.67 ml, 1.5 ml, 3 ml, 10.5 ml or 26 ml of the ChloraPrep alcoholic solution.

The choice of applicator will depend on the invasive procedure being undertaken and the clinician's preference.

The applicator is removed from the wrapper and held with the sponge facing downward. The applicator is squeezed gently to break the ampoule containing the antiseptic solution, which is released onto the sponge in a controlled flow (for the 0.67 ml the barrel is squeezed; for the 26 ml applicator the lever is pressed). Pinch wings **once only** to activate the applicator and release the antiseptic. Do not repeatedly pinch or pump the wings in an attempt to accelerate the saturation of the foam. The broken ampoule remains safely contained within the applicator. The sponge is gently pressed against the patient's skin in order to apply the antiseptic solution. Once

Sepp 0.67 ml Applicator	**For Procedures such as:**
Coverage Area (cm x cm) 5 x 8 	- Routine venipuncture - Blood culture collection - Peripheral (arterial line) cannulation - Simple biopsy

1.5 ml Applicator	**Frepp 1.5 ml Applicator**	**For Procedures such as:**
Coverage Area (cm x cm) 10 x 13 	Coverage Area (cm x cm) 10 x 13 	- Routine venipuncture - Blood culture collection - Peripheral (arterial line) cannulation - Simple biopsy - Dialysis Fistula/Graft site cleansing

3 ml Applicator	**For Procedures such as:**
Coverage Area (cm x cm) 15 x 15 	- Midline & Central Venous Catheter (CVC) insertion and maintenance - Peritoneal dialysis site cleansing

10.5 ml Applicator	26 ml Applicator	For Procedures such as:
Coverage Area (cm x cm) 25 x 30 	Coverage Area (cm x cm) 50 x 50 	- Minor and major surgical procedures - Implantable device placement - Prosthetic device placement or removal - Midline, Peripheral Intravascular Central Catheter (PICC) & CVC insertion and maintenance - Cardiac catheterisation and Cardiac Cath Lab procedures - Interventional Radiology procedure

the solution is visible on the skin, use gentle back and forth strokes to prep the site for 30 seconds. The 26 ml applicator includes two swabs. Clean intact umbilicus with enclosed swabs when applicable. (Moisten swabs by pressing against solution-soaked sponge applicator.) The area covered should be allowed to air dry completely.

It is recommended that ChloraPrep remain on the skin post-procedure to provide continued antimicrobial activity. If removal is necessary, remove with soap and water or alcohol.

4.3 Contraindications
Known hypersensitivity to ChloraPrep or any of its components, especially in those with a history of possible chlorhexidine-related allergic reactions (see sections 4.4 and 4.8).

4.4 Special warnings and precautions for use
The solution is flammable. Do not use electrocautery procedures or other ignition sources until the skin is completely dry.

Remove any soaked materials, drapes or gowns before proceeding with the intervention. Do not use excessive quantities and do not allow the solution to pool in skin folds or under the patient or drip on sheets or other material in direct contact with the patient. Where occlusive dressings are to be applied to areas previously exposed to ChloraPrep, care must be taken to ensure no excess product is present prior to application of the dressing.

For external use only on intact skin.

ChloraPrep contains chlorhexidine. Chlorhexidine is known to induce hypersensitivity, including generalised allergic reactions and anaphylactic shock. The prevalence of chlorhexidine hypersensitivity is not known, but available literature suggests this is likely to be very rare. ChloraPrep should not be administered to anyone with a potential history of an allergic reaction to a chlorhexidine-containing compound (see sections 4.3 and 4.8).

The solution is an irritant to eyes and mucous membranes. It should therefore be kept away from these areas. If the solution comes in contact with the eyes, they should be washed promptly and thoroughly with water.

The use of chlorhexidine solutions, both alcohol based and aqueous, for skin antisepsis prior to invasive procedures has been associated with chemical burns in neonates. Based on available case reports and the published literature, this risk appears to be higher in preterm infants, especially those born before 32 weeks of gestation and within the first 2 weeks of life.

Do not use on open skin wounds. Do not use on broken or damaged skin. In addition, direct contact with neural tissue or the middle ear must be avoided.

Prolonged skin contact with alcohol containing solutions should be avoided.

It is important to ensure that the correct method of applications is strictly followed (see section 4.2 above). When the solution has been applied in an over-vigorous manner to very fragile or sensitive skin or after repeated use, local skin reaction may occur including: erythema or inflammation, itching, dry and/or flaky skin and local application site pain. At the first sign of local skin reaction application of ChloraPrep should be stopped.

4.5 Interaction with other medicinal products and other forms of interaction
Alcohol should not be brought into contact with some vaccines and skin test injections (patch tests). If in doubt, consult the vaccine manufacturer's literature.

4.6 Fertility, Pregnancy and Lactation
There are no studies with this product in pregnant or lactating women.

Pregnancy
No effects during pregnancy are anticipated, since systemic exposure to chlorhexidine gluconate is negligible. ChloraPrep can be used during pregnancy.

Breastfeeding
No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to chlorhexidine gluconate is negligible. ChloraPrep can be used during breast-feeding.

Fertility
The effects of chlorhexidine gluconate on human reproduction have not been studied.

4.7 Effects on ability to drive and use machines
ChloraPrep has no influence on the ability to drive and use machines.

4.8 Undesirable effects
Skin disorders:
Very rarely (<1/10,000) allergic or irritation skin reactions have been reported with chlorhexidine and isopropyl alcohol including: erythema, rash (e.g. erythematous, papular, or maculopapular), pruritus and blisters or application site vesicles. Other local symptoms have included skin burning sensation, pain and inflammation.

Frequency not known: dermatitis, eczema, urticaria, chemical burns in neonates.
At the first sign of local skin reaction the use of ChloraPrep should be discontinued.

Immune disorders: Frequency not known: Hypersensitivity including anaphylactic shock (see sections 4.3 and 4.4).

The most commonly reported adverse reactions reported are associated with application site reactions. These were noted to occur most often within the area of application of the solution (i.e. at the prep site) and very rarely spread. The adverse reactions were often self-limiting in nature or resolved following treatment with topical steroids and / or antihistamines. The most commonly reported reactions were non-serious in nature and included application site rash, application site erythema, application site vesicles, application site pain and application site pruritus. Frequency, type and severity of adverse reactions in children are expected to be the same as in adults.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose
There are no reports of overdose with this product.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Chlorhexidine, combinations, ATC code: D08A C52.

Mode of Action: Bisbiguanide antiseptics exert their lethal effect upon bacterial cells through non-specific interaction with acidic phospholipids of the cell membranes.

Chlorhexidine gluconate is a cationic biguanide. Its antimicrobial action is due to the disruption of the cell membrane and the precipitation of cell contents. It has a bactericidal or bacteriostatic action against a wide range of gram-positive and gram-negative bacteria. It is relatively ineffective against mycobacteria. It inhibits some viruses and is active against some fungi. It is inactive against bacterial spores. It has a superior residual property in comparison to currently available skin antiseptics. Chlorhexidine gluconate has a strong binding property to skin and has a residual property on the skin that has been documented at 48 hours. Chlorhexidine gluconate is not neutralised in the presence of organic matter.

Isopropyl alcohol is a rapidly bactericidal and a fast acting broad spectrum antiseptic, but is not considered persistent. Its mechanism of action appears to be denaturation of proteins.

ChloraPrep is a sterile antiseptic solution containing a combination of 2% Chlorhexidine gluconate in 70% Isopropyl alcohol, which is effective for both rapid and persistent reduction of bacterial load across various body regions for a broad spectrum of organisms. Isopropyl alcohol (70%) provides an immediate kill of transient and resident microorganisms on the stratum corneum and 2% Chlorhexidine gluconate binds to the superficial cell layers of the epidermis and provides a residual, or persistent, antimicrobial property that prevents regrowth of microorganisms.

Clinical studies with 2% Chlorhexidine gluconate in 70% Isopropyl alcohol have demonstrated that the combination offers equal or similar effectiveness in reducing skin bacterial load and more sustained antibacterial effects over longer periods after application, compared to the individual components alone, as well as to other commonly used antiseptics such as Povidone-iodine.

ChloraPrep meets the criteria for chemical disinfectants and antiseptic products as established by European Standards:

EN 1040 - basic bactericidal activity (Phase 1)
EN 1275 - basic yeasticidal activity (Phase 1)
EN 13727 - bactericidal activity (Phase 2/Step 1)
EN 13624 - fungicidal activity (Phase 2/Step 1)

ChloraPrep meets these EN criteria for bactericidal and fungicidal activity for the following organisms at contact times ranging from 5 to 15 minutes, with the exception of *Aspergillus brasiliensis*. Additional testing of ChloraPrep at full concentration against *Aspergillus brasiliensis* for exposure up to 60 minutes met EN 13624 criteria, as follows:

Table: *In vitro* microbiocidal effects

Strain	Contact time	Conditions	Result	EN Criteria
Pseudomonas aeruginosa	5 min	100%, 75%, 50%	> 5.69 log reduction	EN 1040
Staphylococcus aureus	5 min	100%, 75%, 50%	> 4.67 log reduction	EN 1040
Candida albicans	15 min	100%, 75%, 50%	> 4.25 log reduction	EN 1275
Enterococcus hirae	5 min	100%, 75%, 50% in clean 0.3 g/L bovine serum albumin	> 5.71 log reduction	EN 13727
Pseudomonas aeruginosa	5 min	100%, 75%, 50% in clean 0.3 g/L bovine serum albumin	> 5.55 log reduction	EN 13727
Staphylococcus aureus	5 min	100%, 75%, 50% in clean 0.3 g/L bovine serum albumin	> 5.78 log reduction	EN 13727
Candida albicans	15 min	100%, 75%, 50% in clean 0.3 g/L bovine serum albumin	> 4.17 log reduction	EN 13624
Aspergillus brasiliensis	60 min	100%	> 4.26 log reduction	EN 13624

5.2 Pharmacokinetic properties
There is little absorption of isopropyl alcohol or of chlorhexidine gluconate through intact skin.
Pharmacokinetic studies have not been conducted with the product.

5.3 Preclinical safety data
There are no preclinical data of relevance to the prescriber that are not already included elsewhere in the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Purified water

6.2 Incompatibilities
Chlorhexidine is incompatible with soap, hypochlorite bleach and other anionic agents. Hypochlorite bleaches may cause brown stains to develop in fabrics, which have previously been in contact with preparations containing chlorhexidine.

6.3 Shelf life
3 years

6.4 Special precautions for storage
Flammable. This medicinal product does not require any special temperature storage conditions.
Store in the original packaging; applicator is sterile unless seal is broken.
Avoid exposure of the container and contents to naked flames during use, storage and disposal.

6.5 Nature and contents of container
The applicators consist of a latex-free sponge attached to a plastic handle/barrel which holds a latex-free pledget and glass ampoule containing the sterile antiseptic solution. The Sepp 0.67 ml applicator consists of a latex-free foam tip attached to a plastic barrel which holds a glass ampoule containing the antiseptic solution. The Frepp 1.5 ml applicator consists of a latex-free rectangular foam sponge attached to a plastic barrel which holds a glass ampoule containing the antiseptic solution. The 1.5 ml, 3 ml and 10.5 ml applicators consist of a latex-free round foam sponge attached to a plastic barrel which holds a glass ampoule containing the antiseptic solution. The 26 ml applicator consists of a latex-free square foam sponge attached to a plastic barrel which holds two glass ampoules containing the antiseptic solution. The sterile applicators are individually packaged in a transparent film.

The medicinal product is available as 0.67 ml, 1.5 ml, 3 ml, 10.5 ml and 26 ml fill volumes.

Pack Size:

0.67 ml (Sepp®):	200 applicators
1.5 ml (Frepp®):	20 applicators
1.5 ml and 3 ml:	25 applicators
10.5 ml:	1 applicator or 25 applicators
26 ml:	1 applicator

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
This product is for single use only.

Any unused product or waste material should be discarded in accordance with local requirements. No additional environmental precautions for disposal are necessary.

7 MARKETING AUTHORISATION HOLDER

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