1. NAME OF THE MEDICINAL PRODUCT

ChloraPrep with Tint 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.
Orange 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

Posology
ChloraPrep with Tint may be used on all age groups and patient populations.

Paediatric population
However, ChloraPrep with Tint 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 3 ml, 10.5 ml or 26 ml of the ChloraPrep with Tint alcoholic solution.

Method of administration
Cutaneous use

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

Applicator	Coverage Area (cm x cm)	For Procedures such as:
3 ml 	**15 x 15**	- Midline & Central Venous Catheter (CVC) insertion and maintenance - Peritoneal dialysis site cleansing
10.5 ml  26 ml 	**25 x 30** **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 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 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 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 with Tint remain on the skin post-procedure to provide continued antimicrobial activity. The tint will slowly fade from the skin. If removal is necessary, remove with soap and water or alcohol.

4.3 Contraindications

Known hypersensitivity to ChloraPrep with Tint 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 with Tint, 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 with Tint 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 with Tint 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 mucous membranes. It should therefore be kept away from these areas.

ChloraPrep with Tint must not come into contact with the eye. Serious cases of persistent corneal injury, potentially requiring corneal transplant, were reported following accidental ocular exposure to chlorhexidine containing medicinal products despite taking eye protective measures due to migration of solution beyond the intended surgical preparation area. Extreme care must be taken during application to ensure that ChloraPrep with Tint does not migrate beyond its intended application site into the eyes. Particular care should be taken in anaesthetised patients, who are unable to immediately report ocular exposure. If ChloraPrep with Tint comes into contact with the eyes, wash out promptly and thoroughly with water. An ophthalmologist's advice should be sought.

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 with Tint should be stopped.

Anaphylactic reactions during anaesthesia
Chlorhexidine-containing products are known causes of anaphylactic reactions during anaesthesia.
The symptoms of anaphylactic reactions might be masked in an anesthetized patient e.g. a significant portion of skin may be covered or patient unable to communicate early symptoms.
If symptoms of an anaphylactic reaction are detected during anaesthesia (e.g. abrupt fall in blood pressure, hives, angioedema), chlorhexidine-related allergic reaction should be considered.
When chlorhexidine-related allergic reaction during anaesthesia is suspected, other products containing chlorhexidine used during anaesthesia (e.g. IV lines) should be removed. Special precaution should be taken to avoid patient exposure to any other product containing chlorhexidine during the course of the treatment.

<u>Paediatric population</u>
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.

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 with Tint 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 with Tint 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 with Tint has no or negligible 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, isopropyl alcohol and Sunset Yellow (E110) 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.

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.
Cases of anaphylactic reactions have been reported during anaesthesia.

Eye disorders
Frequency not known: Eye irritation, pain, hyperaemia, corneal erosion, epithelium defect/corneal injury, significant permanent visual impairment*.

*Cases of severe corneal erosion and permanent significant visual impairment due to inadvertent ocular exposure have been reported post-marketing, leading to some patients requiring corneal transplant (see section 4.4).

Description of selected adverse reactions
There have been isolated spontaneous reports of generalised allergic reactions potentially associated with ChloraPrep solution and have been reported during anaesthesia. In some cases the patient may have had a pre-existing sensitivity to chlorhexidine (see Section 4.4).

This product may cause a severe allergic reaction. Symptoms may include wheezing/difficulty breathing, shock, facial swelling, hives, or rash. Use of ChloraPrep with Tint is contra-indicated where patients have shown previous hypersensitivity to chlorhexidine or isopropyl alcohol (see Section 4.3). If hypersensitivity or an allergic reaction occurs, stop use and seek medical help right away.

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 Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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.

Mechanism 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.

Pharmacodynamic effects
ChloraPrep with Tint 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 efficacy and safety
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 with Tint 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 with Tint 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 with Tint 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

Absorption
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

Sunset Yellow (E110)

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 dyed pledget and glass ampoule containing the sterile antiseptic solution. The 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 3 ml, 10.5 ml and 26 ml fill volumes.

Pack Size:

3 ml:	1 applicator or 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

Becton Dickinson UK Ltd
1030 Eskdale Road, Winnersh
Wokingham RG41 5TS
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

PL 05920/0003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27/11/2014

10. DATE OF REVISION OF THE TEXT

14/06/2024