Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Hexiprep 2.0% w/v / 70.0% v/v Impregnated Pad

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One mL of solution contains 20mg chlorhexidine digluconate and 0.7 mL of isopropyl alcohol

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Impregnated Pad

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

The medicinal product is to be used for disinfection of the skin prior to invasive medical procedures that do not require a clean air environment.

4.2 Posology and method of administration

Posology
HEXI PREP may be used on all age groups and patient populations.

Paediatric Population

However, HEXI PREP should be used with care in newborn babies, especially those born prematurely (see also section 4.4, Special warnings and precautions for use).

One sachet is used containing a pad impregnated with 1.5mL or 3mL of the HEXI PREP alcoholic solution.

Method of Administration
For cutaneous use.

The choice of HEXI PREP sachet will depend on the size of the area to be disinfected, the invasive procedure and the clinician's preference.

Sachet Volume / Impregnated Pad Size	Maximum Coverage Area	For procedures such as:
1.5mL (10 cm x 10cm)	10cm x 13cm	• blood culture collection, • peripheral cannulation, • peripheral arterial line cannulation, • simple biopsy, • routine venepunctures • dialysis / fistula / graft site cleansing.
3.0mL (20cm x 10cm)	15cm x 15cm	• blood culture collection, • peripheral cannulation, • peripheral arterial line cannulation, • midline and central venous catheter (CVC) insertions and maintenance, • simple biopsy, • routine venepunctures, • dialysis fistula / graft site cleansing, peritoneal dialysis site cleansing

		• implantable device placement

Where required as part of sterile procedure (e.g. central line insertion), tear the sachet open and remove the impregnated pad with sterile tweezers onto a sterile tray. Contact with the outer face of the sachet by sterile gloves should be avoided as it is non-sterile.

For both non-sterile and sterile procedures, the user should wear gloves during application. Keep the impregnated pad folded and press firmly against the skin on the intended area and wipe back and forth for a total of 30 seconds. Allow to airdry completely. It is recommended that HEXI PREP solution remains on the skin post-procedure to provide continued antimicrobial activity. If removal is necessary, remove with soap and water or alcohol.

4.3 Contraindications

The medicinal product is contra-indicated where patients have shown previous hypersensitivity to chlorhexidine or isopropyl alcohol.

4.4 Special warnings and precautions for use

The solution is flammable. Do not use with electrocautery procedures or other ignition sources until dry.

Remove any soaked materials, drapes or gowns before proceeding with the intervention. 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 Hexiprep, care must be taken to ensure no excess product is present prior to application of the dressing

For external use only on intact skin.

Hexiprep 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. Hexiprep 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).

Hexiprep 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 Hexiprep 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 Hexiprep 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 alcoholic 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 Hexiprep should be stopped.

<u>Anaphylactic reactions during anaesthesia</u>
Chlorhexidine-containing products are known causes of anaphylactic reactions during anaesthesia. The symptoms of anaphylactic reactions might be masked in an anaesthetised 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 reactions should be considered.

When chlorhexidine-related 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

Paediatric population
The use of chlorhexidine solutions, both alcohol based and aqueous, for skin antisepsis prior to invasive medical 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 digluconate is negligible. HEXI PREP can be used during pregnancy.

Lactation
No effects on the breastfed newborn/infant are anticipated since the systemic exposure of breast-feeding woman to chlorhexidine digluconate is negligible. HEXI PREP can be used during lactation.

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

4.7 Effects on ability to drive and use machines

HEXI PREP 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: 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, chemical burn, 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 reactions potentially associated with solutions of chlorhexidine digluconate / isopropyl alcohol 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 Hexiprep is contraindicated 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 for continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:
HPRA Pharmacovigilance
Earlsfort Terrace
IRL – Dublin 2
Tel: +353 1 6764971
Fax: +353 1 3762517
Website: www.hpra.ie
Email: medsafety@hpra.ie

4.9 Overdose

There are no reports of overdose with this product.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: D08A C52 (Chlorhexidine, combinations).

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

Chlorhexidine digluconate is a cationic biguanide.
Bisbiguanide antiseptics exert their lethal effect upon bacterial cells through non-specific interaction with acidic phospholipids of the cell membranes.

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

Spectrum of antibacterial activity

Chlorhexidine has bactericidal or bacteriostatic activity against a wide range of Gram-positive and Gram-negative bacteria. It is relatively ineffective against mycobacteria and it is inactive against bacterial spores.

Isopropyl alcohol (at 70% v/v) has bactericidal activity against a wide range of Gram-positive and Gram-negative bacteria including mycobacteria, but is inactive against bacterial spores.

Clinical Efficacy
In a clinical trial that compared the bacterial load on skin at three sites (clavicle, inguinal and cubital fossa) after application of HEXI PREP or placebo, HEXI PREP was shown to be superior to placebo in reducing the bacterial load at the immediate time point (i.e. 1-10 minutes after application of the allocated treatment).
Efficacy of HEXI PREP vs Placebo at 1-10 minutes after application in Study GH001

Anatomical Site	Population (N per treatment)	Reduction in Log_{10} CFU/cm^2 (Least Squares		Difference of Least Squares Mean	Standard Error	p-value

		Mean)		(HEXI PREP -Placebo)		
		HEXI PREP Sites	**Placebo Sites**			
Clavicle	Intention to Treat (N=20)	2.613	0.968	1.645	0.2969	<0.0001
	Per Protocol (N=20)	2.606	0.962	1.644	0.2953	<0.0001
Cubital	Intention to Treat (N=20)	2.781	0.525	2.255	0.3003	<0.0001
	Per Protocol (N=20)	2.774	0.518	2.256	0.2987	<0.0001
Inguinal	Intention to Treat (N=20)	2.144	-0.286	2.431	0.2970	<0.0001
	Per Protocol (N=20)	2.031	-0.294	2.325	0.3045	<0.0001

The effect of HEXI PREP on individual bacterial species was not determined in this study.

5.2 Pharmacokinetic properties

There is little absorption of isopropyl alcohol or chlorhexidine digluconate 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

18 months

6.4 Special precautions for storage

Flammable. Store below 25°C.

The impregnated pad 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 pad material is non-woven (100% Polyethylene terephthalate [PET]) impregnated pad with HEXI PREP solution, packaged in a Transofoil (polyethylene) sachet. Two pack sizes are available:

- 10cm x 10cm pad (1.5mL). Available in cartons of 100
- 20cm x 10cm pad (3.0mL). Available in cartons of 50

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

GAMA Healthcare Ireland Limited, 1st Floor, Penrose 1, Penrose Dock, Cork, Ireland.

8 MARKETING AUTHORISATION NUMBER

PA23120/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16th April 2021

10 DATE OF REVISION OF THE TEXT

August 2024