SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

PurPrep 8.3% w/w / 72.5% w/w cutaneous solution in single-dose container

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml solution contains 72.5 mg of iodinated povidone and 633 mg of isopropyl alcohol.

Each applicator with 10.5 ml solution contains 761 mg of iodinated povidone (72.5 mg/ml) and 6646 mg of isopropyl alcohol (633 mg/ml).

Each applicator with 26 ml solution contains 1884 mg of iodinated povidone (72.5 mg/ml) and 16456 mg of isopropyl alcohol (633 mg/ml).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cutaneous solution in single-dose container.

Dark yellow to brown solution provided in a single use applicator.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is to be used as antiseptic on intact skin prior to invasive medical procedures (including surgery) and has bactericidal and levurocidal activity (see section 5.1).

PurPrep is indicated in adults, adolescents, and children 1 year of age or older.

4.2 Posology and method of administration

Posology

PurPrep may be used on patient populations 1 year of age or older.

Single use applicator. With repeated application, there may be a potential for increased drug absorption, skin irritation and thyroid disorder (see section 4.4).

Paediatric population

PurPrep should not be used in children less than 1 year of age because of the potential for excessive skin irritation and increased drug absorption resulting in transient hypothyroidism (see section 4.3).

Elderly

PurPrep should only be applied after a careful consideration in elderly patients with thyroid disorder.

Method of administration

For cutaneous use.

1 PurPrep applicator contains either 10.5 ml or 26 ml cutaneous solution.

The appropriate PurPrep applicator should be chosen based on the invasive procedure being undertaken and the size of the area to be prepped to avoid excess of solution and the risk of product pooling.

Applicator	**Maximum Coverage Area (cm**	- **For Procedures such as**:
10.5 ml 	25 x 30	- 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.
 **26 ml**	50 x 50	

The applicator is removed from the wrapper and held with the sponge facing downward. In order to activate the 10.5 ml applicator, the wings are squeezed. For the 26 ml applicator, the lever is pressed. This will break the ampoule containing the antiseptic solution, which is released onto the sponge with a controlled flow. Wings or lever are pinched or pressed respectively **once only** to activate the applicator and release the antiseptic. Do not repeatedly pinch or pump in an attempt to accelerate the saturation of the sponge. The broken ampoule remains safely contained within the applicator. The sponge is pressed against the patient's skin in order to apply the antiseptic solution. Once the solution is visible on the skin, back and forth strokes

should be applied to prep the site for 30 seconds. The area covered should be allowed to air dry completely.

It is recommended that PurPrep 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

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1;
- Children less than 1 year of age;
- Patients with dermatitis herpetiformis;
- Patients with hyperthyroidism and other thyroid dysfunction.

4.4 Special warnings and precautions for use

The solution is flammable. PurPrep should be used in a well-ventilated area. Electrocautery procedures or other ignition sources must not be used until the skin is completely dry.

Any soaked materials, drapes or gowns should be removed before proceeding with the intervention. The solution must not be used in excessive quantities and must not 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 PurPrep, care must be taken to ensure no excess product is present prior to application of the dressing.

Single use applicator, for external use only and on intact skin.

PurPrep contains iodine as iodinated povidone. Iodine, as iodinated povidone, may induce hypersensitivity, including skin reaction and sensitisation. The prevalence of hypersensitivity to iodine, as iodinated povidone is not known but available literature suggests this is likely to be rare. PurPrep should not be administered to anyone with a potential history of hypersensitivity to iodine as the iodinated povidone 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.

PurPrep must not be used:

- on open skin wounds or as a general skin cleanser.
- on broken or damaged skin or mucous membranes.

In addition, direct contact with neural tissue or the middle ear must be avoided.

Use with caution in women who are breastfeeding due to the potential for transient hypothyroidism in the nursing newborn (see section 4.6).

It is important to ensure that the correct method of application is strictly followed (see section 4.2). Prolonged skin contact with alcohol containing solutions should be avoided unless necessary. When the solution has been applied in an over-vigorous manner to very fragile or sensitive skin or after repeated use, application-site reactions such as pruritus, erythema, rash, papules, and vesicles may occur (see section 4.8). At the first sign of local skin reaction, application of PurPrep should be stopped.

Anaphylactic reactions

If symptoms of an anaphylactic reaction are detected, application of PurPrep should be stopped immediately (see section 4.8).

Thyroid disorder and renal insufficiency

PurPrep should be used with caution in patients with thyroid disorder (i.e hyperthyroidism, mild nodular goitre) and patients with renal insufficiency due to prolonged time of elimination. Very rare cases of iodine-induced hyperthyroidism have been reported with products containing iodine as iodinated povidone.

With repeated application, there may be a potential for increased drug absorption, skin irritation and thyroid disorder (see sections 4.2 and 4.8).

If re-operation within a few days following application of PurPrep is necessary, the use of a preoperative antiseptic that does not contain iodine as iodinated povidone, or close monitoring of thyroid function, should be determined by the clinician.

Paediatric population

PurPrep should not be used on children less than 1 year of age because of the potential for excessive skin irritation and absorption of iodine (see section 4.3 and 4.8).

The use of alcohol-based antiseptic solutions on skin prior to invasive procedures has been associated with chemical burns in neonates (see section 4.8).

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.

It is expected that iodine, as iodinated povidone, reacts with proteins such as blood which may impair efficacy.

PurPrep solution must not be used concomitantly or immediately following disinfectants containing mercury due to the risk of chemical burns following the formation of mercury iodide.

PurPrep solution must not be used concomitantly or immediately after application of octenidine as transient dark discoloration can occur at the concerned area.

PurPrep solution should not be used with hydrogen peroxide or taurolidine, as oxidation can weaken the activity of the drug.

The concomitant application of PurPrep solution and silver-containing disinfectants or wound dressings can form silver iodine.

Absorption of iodine through the skin is minimal. Misuse, such as application to non-intact skin and/or repeated daily use can result in hypothyroidism of individuals receiving concomitant lithium therapy.

Effect on diagnostic tests:

During the application of iodine as iodinated povidone, uptake of radio-iodine by the thyroid gland may be reduced; this can lead to disturbances in thyroid scanning, PBI (protein-bound iodine) determination and radioiodine diagnostics and make planned radioiodine therapy impossible. A waiting period of at least 1-2 weeks should be observed after discontinuing the iodine as iodinated povidone treatment, before conducting a new thyroid scan.

4.6 Fertility, pregnancy and lactation

Pregnancy and Breastfeeding

During pregnancy and lactation, PurPrep, like all iodine preparations, should only be administered following a very careful assessment of the risk/benefit by the physician.

A moderate amount of data on pregnant women (between 300-1000 pregnancy outcomes) indicate no malformative or feto/ neonatal toxicity of 8.3% w/w iodine as iodinated povidone, and 72.5% w/w isopropyl alcohol.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

PurPrep should be used with caution in women who are pregnant or breast-feeding, since a minimal absorption of iodine to the mother's blood even through intact skin and excretion into human milk may occur.

After application of PurPrep, monitoring of thyroid function in the child may be indicated. In the case of hypothyroidism, consider early treatment with thyroid hormones until normalisation of thyroid function.

Further, oral absorption of PurPrep by the infant through contact with the treated part of the nursing mother's body must be avoided.

Fertility

The effects on human reproduction have not been studied.

4.7 Effects on ability to drive and use machines

PurPrep has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The following frequencies are used for the evaluation of adverse reactions:

Very common (≥1/10)

Common (≥1/100 to <1/10)

Uncommon (≥1/1,000 to <1/100)

Rare (≥1/10,000 to <1/1,000)

Very rare (<1/10,000)

Not known (cannot be estimated from data available)

System Organ Class	**Rare**	**Very Rare**	**Not Known**
Immune System Disorders	Hypersensitivities	Anaphylactic reactions	
Metabolic and Nutrition Disorders		Hyperthyroidism	Metabolic Acidosis Hypothyroidism Electrolyte imbalance
Skin and Subcutaneous Tissue Disorders	Erythema Skin irritation Pruritus Vesicles Rash Papules Contact dermatitis	Angioedema	Chemical burns Thermal burns Exfoliative dermatitis
Renal and Urinary Disorders			Renal insufficiency

Hyperthyroidism: in patients with a history of thyroid disease (see section 4.4), after prolonged use or application over large coverage areas.

Hypothyroidism: after prolonged use or application over large coverage areas, increase of the absorption of iodine through non-intact skin.

Electrolyte imbalance, renal insufficiency, metabolic acidosis: may occur after absorption of large amounts of iodine as iodinated povidone, due to application on large coverage areas.

Chemical burns: cases have been associated with the use of alcohol-based solutions, especially in neonates.

Application-site reactions such as pruritus, erythema, rash, papules, and vesicles may occur when the solution has been applied in an over-vigorous manner to very fragile or sensitive skin or after repeated use.

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

In case of accidental ingestion of large quantities of the medicinal product, institute symptomatic and supportive treatment with particular attention to the renal and thyroid function.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Dermatologicals; Antiseptics and Disinfectants

ATC code: D08AX and D08AG.

Mechanism of action

Iodine as iodinated povidone is an iodophor and a complex of povidone and iodine.

Iodine as iodinated povidone has potent broad-spectrum activity against bacteria, mycobacteria, fungi, viruses, and protozoa. The antimicrobial action of iodine as iodinated povidone occurs after iodine disassociates from the complex. Once in the free form, iodine rapidly penetrates microbial cell membranes and interacts with proteins, nucleotides, and fatty acids in the cytoplasm and cytoplasmic membrane. This interaction ultimately results in rapid cell death.

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.

Pharmacodynamics effects:

PurPrep is a sterile antiseptic solution containing a combination of 8.3% iodine as iodinated povidone, in 72.5% isopropyl alcohol, which is effective for both rapid and persistent reduction of bacterial load across various body regions for a broad spectrum of organisms. PurPrep has an antimicrobial persistence on the skin that has been documented at 96 hours post application. Isopropyl alcohol provides an immediate kill of transient and resident microorganisms on the stratum corneum and 8.3% iodine as iodinated povidone contributes to the persistent antimicrobial effect as iodine is released slowly from povidone.

Clinical efficacy and safety:

PurPrep combines 8.3% w/w iodine as iodinated povidone and 72.5% w/w isopropyl alcoho,l to provide a rapid, broad-spectrum antiseptic that exhibits immediate and persistent activity. Cutaneous application results in minimal dermal absorption and is

non-irritating. The rationale for development of a fixed combination product containing iodine as iodinated povidone and isopropyl alcohol was to produce a safe antiseptic with both rapid onset and persistent antimicrobial activity that can be used as an alternative for patients with a sensitivity to chlorhexidine.

PurPrep solution meets the criteria for chemical disinfectants and antiseptic products as established by European Standards with the exception of Aspergillus brasiliensis.

EN 13727 - bactericidal activity (Phase 2/Step 1)

EN 13624 - levurocidal activity (Phase 2/Step 1)

Table: *In vitro* microbiocidal effects

Strain	**Contact time**	**Conditions**	**Result log reduction**	**EN Criteria**
Enterococcus hirae	1 min	100% in clean 0.3 g/L bovine serum albumin and in tested in dirty conditions 0.3 g/L bovine albumin fraction V in TSC plus 3.0 mL/L erythrocytes	> 5.60	EN 13727
Pseudomonas aeruginosa	1 min	100% in clean 0.3 g/L bovine serum albumin and tested in dirty conditions 0.3 g/L bovine albumin fraction V in TSC plus 3.0 mL/L erythrocytes	> 5.61	EN 13727
Staphylococcus aureus	1 min	100% in clean 0.3 g/L bovine serum albumin and tested in dirty conditions 0.3 g/L bovine albumin fraction V in TSC plus 3.0 mL/L erythrocytes	> 5.56	EN 13727
Escherichia coli	1 min	100% in clean 0.3 g/L bovine serum albumin and tested in dirty condition 0.3 g/L bovine albumin fraction V in TSC plus 3.0 mL/L erythrocytes	> 5.54	EN 13727
Candida albicans	1 min	100% in clean 0.3 g/L bovine serum albumin and tested in dirty conditions 0.3 g/L bovine albumin fraction V in TSC plus 3.0 mL/L erythrocytes	> 4.81	EN 13624

5.2 Pharmacokinetic properties

Pharmacokinetic studies have not been conducted with the medicinal product.

Absorption

There is little absorption of isopropyl alcohol or iodine through intact skin.

After applying iodine as iodinated povidone, the possibility of iodine absorption must be considered. This depends upon the nature and duration of treatment as well as the amount applied. Following application to the intact skin, only very small amounts of iodine are absorbed. In people with a healthy thyroid gland, the increased availability of iodine does not lead to clinically relevant changes in thyroid - hormone status.

Little absorption of isopropyl alcohol occurs through intact skin, except on prolonged exposure. Preterm infants are at increased risk for percutaneous absorption of topically applied agents, which may cause damage to the underlying dermis and broader systemic effects. Reports in the literature recommend restricted use with regards to birth weight, gestational age and chronological age. Extreme caution is recommended for use of topical antiseptics, particularly alcohol-based preparations in extreme preterm infants. However, PurPrep is not indicated in children less than 1 year of age (see section 4.3).

Distribution and Elimination

Approximately 20% to 30% of ingested iodine is distributed to the thyroid in animals and humans. Serum and tissue (thyroid, liver, and kidney) iodine concentrations have also been shown to be significantly elevated in rats fed iodine-supplemented diets than in rats fed a control diet. If kidney function is normal, iodine is eliminated via the kidneys. Any increase in the blood iodine level is generally transient.

Isopropyl alcohol is readily distributed around the body due to its high level of water solubility, and 20-50% of the absorbed dose is excreted unchanged. In the liver, alcohol dehydrogenase oxidises most isopropyl alcohol to acetone, formate, and finally carbon dioxide. Acetone is slowly eliminated by the lung (40%) or kidney. Clinically insignificant excretion occurs in the stomach and saliva.

5.3 Preclinical safety data

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical.

Published nonclinical literature has demonstrated that iodine, as iodinated povidone, and isopropyl alcohol are well-established, safe and effective antimicrobial and bactericidal products. PurPrep has been investigated through the nonclinical program. It has been demonstrated through studies that PurPrep displays a potent antimicrobial activity on a large number of microorganisms.

Acute and chronic toxicity

The risk of iodine toxicity from a single application of iodine as iodinated povidone applied topically to intact skin is low.

No long-term, repeat-dose, preclinical studies measuring toxicity from iodine as iodinated povidone have been reported in the literature.

Genotoxicity

Studies have demonstrated no genotoxic effects.

Mutagenic and carcinogenic potential

No long-term studies in animals to evaluate the carcinogenic potential of iodine as iodinated povidone have been reported in the literature.

Reproduction and developmental toxicity

No information on reproductive or developmental effects from dermal exposure to iodine as iodinated povidone have been identified. Significant disruptions of reproductive function from dermal exposure unlikely.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Purified water

Methacrylic acid-methyl methacrylate copolymer (1:2)

Acrylates / octylacrylamide copolymer

Macrogol 400

2-amino-2-methyl-1-propanol (95%)

6.2 Incompatibilities

Iodine as iodinated povidone may react with organic matter such as proteins in blood. It should not be used with reducing agents, silver, mercury, taurolidine, disinfectants containing silver, octenidine, and used with caution with hydrogen peroxide.

Absorption of iodine from iodine as iodinated povidone, through either healthy or damaged skin, may interfere with thyroid functions tests. However, there is little absorption of iodine through intact skin.

6.3 Shelf life

3 years

After opening, the medicinal product should be used immediately.

6.4 Special precautions for storage

Flammable. Do not store above 30°C.

Store in the original package; 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 10.5 ml applicators consist of a latex-free round foam sponge attached to a plastic handle which holds a pledget and a type I glass ampoule containing the sterile antiseptic cutaneous solution. The 26 ml applicator consists of a latex-free square foam sponge attached to a plastic handle which holds a pledget and two type I glass ampoules containing the sterile antiseptic cutaneous solution. The 26 ml applicator includes two swabs. The sterile applicators are individually packaged in a film.

The medicinal product is available as 10.5 ml and 26 ml fill volumes.

The packaging consists of a lidding material sealed to a polymeric film creating a “pouch-like" packet surrounding the applicator. The final packaged applicator is sterilised using ethylene oxide.

Pack sizes:

1 applicator containing 10.5 ml cutaneous solution.

Multipacks containing 25 applicators each containing 10.5 ml cutaneous solution.

1 applicator containing 26 ml cutaneous solution.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

This medicinal product is for single use only.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Becton Dickinson UK Ltd,

1030 Eskdale Road, Winnersh,
Wokingham, RG41, 5TS,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 05920/0007

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09/05/2024

10 DATE OF REVISION OF THE TEXT

09/05/2024