PROFESSIONAL INFORMATION

SCHEDULING STATUS S0

1 NAME OF THE MEDICINE

BETADINE® ANTISEPTIC 10 % *w/v* SOLUTION

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of BETADINE® ANTISEPTIC SOLUTION contains 100 mg povidone-iodine (10 % *w/v*).

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Antiseptic solution.

For topical administration.

Reddish-brown, clear solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Disinfection of minor wounds (cut and abrasions), ulcers and burns
- Pre-operative disinfection of skin
- Hygienic hand disinfection
- Skin disinfection
- Surgical hand disinfection

4.2 Posology and method of administration

It is recommended for up to 14 consecutive days (up to 5 ml) of use up to twice a day for adults and once a day for children aged 2 years or older.

Disinfection of minor wounds (cut and abrasions), ulcers and burns

Clean the wound area and apply undiluted (3 to 5 ml), once (children) or twice (adults) daily until the wound or burn has healed up to a maximum of 14 consecutive days. If necessary, a non-occlusive dressing can be applied.

Solutions of iodine applied to the skin should not be covered with occlusive dressings, wash off excess solution before using occlusive dressings.

Pre-operative disinfection of skin

Apply to area undiluted and allow to dry.

Hygienic hand disinfection

Apply 3 to 5 ml undiluted, onto the hands and rub into hands and around the fingers. Leave on for about a minute before washing off.

Surgical hand disinfection

Apply 3 to 5 ml undiluted, onto the hands and rub into hands and around the fingers. Leave on for about 5 minutes before washing off.

Skin disinfection

Skin with low density of sebaceous glands (keeping skin moist):

- Prior to punctures and injections: Apply undiluted and leave on for about 1 minute.
- Prior to punctures of joints, cavities and hollow organs; before surgical interventions: Apply undiluted and leave on for about 1 minute.

Skin with high density of sebaceous glands (keeping skin moist):

- Before all operations/interventions: Apply undiluted and leave on for about 10 minutes.

To be used for a maximum of 14 days.

Method of administration

Topical

4.3 Contraindications

- Hypersensitivity to the povidone-iodine, iodine or to any of the excipients listed in section 6.1.
- Thyroid dysfunction or goitre (in particular nodular colloid goitre, endemic goitre and Hashimoto's thyroiditis).
- Not to be used on patients on concurrent lithium therapy.
- During radioiodine scintigraphy or radioiodine treatment of thyroid carcinoma. An interval of at least 1-2 weeks is required prior to or after radioiodine investigations/treatments (see section 4.5).
- Products containing mercury, should not be used concomitantly due to formation of a substance which can damage the skin.
- Children below the age of 2 years.

4.4 Special warnings and precautions for use

In instance of skin irritation, contact dermatitis or hypersensitivity discontinue use.

In pre-operative preparation, avoid pooling beneath the patient. Prolonged exposure to wet solution may cause irritation or rarely, severe skin reactions. Chemical burns of skin due to pooling may occur.

Do not heat prior to application.

Special caution is needed when regular applications to broken skin are made to patients with pre-existing renal insufficiency.

Special caution is needed in pregnant and breastfeeding women (see section 4.6).

Do not use on large open wounds.

Povidone-iodine may permanently discolour white gold jewellery and it is recommended that this type of jewellery be removed before using Betadine® Antiseptic Solution.

For external use only.

4.5 Interaction with other medicines and other forms of interaction

The povidone-iodine complex is effective at pH values of between 2,0 and 7,0. It has to be expected that the complex will react with protein and other unsaturated organic compounds, leading to impairment of its effectiveness.

The concomitant use of wound-treatment preparations containing enzymatic components leads to a weakening effect of both substances.

Products containing silver, hydrogen peroxide and taurolidine may interact with povidone-iodine and cause mutual reduction of effects.

Povidone-iodine products when used concomitantly or immediately after application of octenidine-containing antiseptics in the same or adjacent sites may lead to transient dark discolouration in the areas involved.

Due to the oxidative effect of povidone-iodine preparations various diagnostic agents can show false-positive lab results (e.g., tests with toluidine or gum guaiac for the determination of haemoglobin or glucose in the stool or the urine).

Absorption of iodine from povidone-iodine may lower the iodine uptake of the thyroid. This can lead to interference with various investigations (thyroid scintigraphy, determination of protein-bound iodine (PBI), radioiodine diagnostics) and can interfere with treatment of the thyroid with iodine (radioiodine therapy). After the end of the treatment, an appropriate interval should be allowed before a new scintigram is carried out (see section 4.3).

4.6 Fertility, pregnancy and lactation

Povidone-iodine passes into the placenta and is secreted in breast milk. Thyroid function disorders including congenital hypothyroidism have been reported in the offspring of mothers who have received Iodine.

Povidone-iodine use should be avoided in pregnancy and breastfeeding.

4.7 Effects on ability to drive and use machines

Betadine® Antiseptic Solution has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Immune system disorders

Less frequent: Hypersensitivity, anaphylactic reactions.

Endocrine disorders

Less frequent: Hyperthyroidism (sometimes with symptoms such as tachycardia or restlessness) *

Frequency unknown: Hypothyroidism ***

Metabolism and nutrition disorders

Frequency unknown: Electrolyte imbalance **, metabolic acidosis **

Renal and urinary disorders

Frequency unknown: Acute renal failure**, blood osmolarity abnormal **

Skin and subcutaneous tissue disorders

Less frequent: Contact dermatitis (with symptoms such as erythema, small blisters and pruritis), angioedema

Injury poisoning and procedural complications

Frequency unknown: Chemical burn of skin****

* In patients with a history of thyroid disease following long-term use of povidone-iodine solution for the treatment of wounds and burns over extensive areas of the skin

** May occur following uptake of large amounts of povidone-iodine (e.g. in the treatment of burns)

*** Hypothyroidism following prolonged or extensive use of povidone-iodine

*** *May occur due to “pooling” beneath the patient in pre-operative preparation

Reporting suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reactions Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8

Alternatively report to: ZADrugSafety@mundipharma.co.za

4.9 Overdose

Acute iodine toxicity is manifested by abdominal symptoms, anuria, circulatory collapse, pulmonary oedema and metabolic abnormalities.

Systemic toxicity may result in renal impairment (including anuria), tachycardia, hypotension, circulatory failure, oedema of glottis resulting in asphyxia, or pulmonary oedema, seizures, fever and metabolic acidosis. Hyperthyroidism or hypothyroidism may also develop.

Treatment is symptomatic and supportive.

For severe hypotension, intravenous fluid should be administered; vasopressors should be added if necessary.

Endotracheal intubation may be required if caustic injury to the upper airway results in significant swelling and oedema.

Vomiting should not be induced. Patient should be maintained in a position to keep the airways open and prevent aspiration (in case of vomiting).

If the patient is not vomiting and can tolerate oral feeding, then ingestion of starchy food (e.g. potato, flour, starch, bread) may help convert iodine to less toxic iodide.

Haemodialysis effectively clears iodine and should be employed in severe cases of iodine poisoning particularly if renal failure is present. Continuous venous haemodiafiltration is less effective than haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

A.13.1 Antiseptics, disinfectants and cleansing agents

5.1 Pharmacodynamic properties

Mechanism of action

Povidone-iodine is a complex of elemental iodine (I_2, the active moiety) and the synthetic polymer povidone, PVP, which acts as a sustained release reservoir of iodine (PVP does not have any intrinsic antibacterial activity) and also enables easier contact of iodine to cell membranes. As povidone-iodine comes in contact with the skin and mucous membranes, iodine dissociates from the povidone-iodine polymer complex; it is the free iodine that rapidly causes microbicidal activity, whereas iodine bound to the polymer serves as an iodine reservoir. This gradual release of iodine reduces the drawbacks associated with the presence of elemental iodine and maintains its highly effective microbiocidal activity. The free iodine

rapidly penetrates microorganisms and attacks the key groups of proteins, amino acids, nucleotides and unsaturated fatty acids. It reacts with thiol, sulfhydryl and hydroxyl groups of the amino acids in the enzymes and structural proteins of the microorganisms thereby oxidising them.

Pharmacodynamic effects

Povidone-iodine is a broad-spectrum antimicrobial agent; its antimicrobial effects have been demonstrated *in vitro* against several different microorganisms including numerous strains of bacteria (both gram-negative and gram-positive), viruses (enveloped and non-enveloped), yeasts, moulds, fungi and protozoa.

Povidone-iodine action appears to be non-specific, causing irreversible damage to the microorganism with no tendency to induce resistance. In addition, no development of resistance has been observed for povidone- iodine, during > 60 years of extensive use in hospitals, dental and medical practices. Antibiotic resistance has no influence on the sensitivity to povidone- iodine.

5.2 Pharmacokinetic properties

Absorption

Studies *in vivo* indicate that the skin absorbs iodine and the amount absorbed is dependent on the type of skin (e.g. healthy or damaged) and also on the duration and the surface area of the application. Limited amounts of iodine are absorbed through an intact skin; enhanced absorption occurs through denuded skin, ulcers, mucosal surfaces with high, absorptive capacity (vagina), or large areas of intact skin.

A negligible amount of povidone (~ 35 KDa) could be absorbed into the systemic circulation.

Distribution

Absorbed iodine/iodide is distributed throughout the body via the circulatory system. A portion (approximately 30 %) is removed by the thyroid for hormonal synthesis. Iodine is also

distributed (despite to a minor extent) to different organs including liver, blood and thyroid gland after 24 hours.

Iodine crosses the placenta and is excreted in breast milk.

Povidone does not pass the blood brain barrier or cross the placenta.

Biotransformation

Iodine is reduced to iodide and is concentrated from the blood stream into the thyroid follicular cell through the action of the sodium/iodide symporter (NIS). The thyroid stimulating hormone (TSH) stimulates iodide transport from the blood into thyroid cells, oxidation of iodide to iodine, and iodine binding to tyrosine.

The metabolism of povidone is minimal (< 0, 3%).

Excretion

Iodine, unless utilised in the thyroid, is excreted mainly via urine. The excretion of povidone is mainly via urine and in a small amount also via bile.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid monohydrate, disodium hydrogen phosphate anhydrous, glycerol, macrogol lauryl ether 9, potassium iodate, purified water, sodium hydroxide.

6.2 Incompatibilities

The activity of povidone-iodine is reduced in the presence of alkali, hydrogen peroxide, taurolidine, tannic acid, acetylsalicylic acid, all silver, bismuth and mercury salts.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 30 °C.

6.5 Nature and contents of container

Green coloured, high-density polyethylene container fitted with a transparent low-density polyethylene insert and white high-density polyethylene cap. One container is packed into a cardboard carton.

Pack sizes: 15 ml, 30 ml, 120 ml,125 ml, 250ml, 500 ml and 1000 ml.

6.6 Special precautions for disposal

N/A

7 HOLDER OF CERTIFICATE OF REGISTRATION

Mundipharma (Pty) Ltd

Block D, Grosvenor Square

Park Lane, Century City

Cape Town, 7441

South Africa

8 REGISTRATION NUMBER

56/13.1/0372

9 DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

19 March 2024

10 DATE OF REVISION OF THE TEXT

19 March 2024

® = Betadine is a registered trademark