PROFESSIONAL INFORMATION

SCHEDULING STATUS **S0**

1 NAME OF THE MEDICINE

BETADINE® FIRST AID CREAM 5 % *w/w* (Topical cream)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 g of cream contains povidone-iodine 50 mg (5 % *w/w*), equivalent to 5 mg available iodine.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

A homogeneous reddish-brown viscous cream, free from lumps. For topical administration.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

BETADINE® FIRST AID CREAM is indicated for the acute treatment and prevention of infections in minor wounds, cuts, abrasions and burns.

4.2 Posology and method of administration

For topical use only.

Posology

The cream can be applied once or twice daily for up to 7 consecutive days.

Method of administration

The skin should be cleaned and dried before application.

Apply the following amount of cream to the affected area (once or twice daily for up to 7 days):

- Children from 2 – 6 years: Apply 1 – 2 small pea sized amounts each day.

- Children from 6 – 8 years: Apply 2 small pea sized amounts twice a day.
- Children from 9 – 13 years: Apply 3 small pea sized amounts twice a day.
- Children from 13 – 18 years: Apply 5 small pea sized amounts twice a day.
- Adults: Apply 8 – 9 small pea sized amounts twice a day.

The affected area may then be covered with a dressing or bandage if required.

Special populations

There is no adjustment of dose required in elderly population.

Paediatric population

Not to be used in children under 2 years of age or children of very low weight (1500 grams)

4.3 Contraindications

- Hypersensitivity to iodine or povidone or any other of the excipients listed in section 6.1.
- Hyperthyroidism or other acute thyroid diseases (especially nodular colloidal goitre, endemic goitre, Hashimoto's thyroiditis).
- Before and after radioiodine therapy for hyperthyroidism, until a lasting cure has been obtained.
- It should not be used for 4 weeks prior to radioiodine scintigraphy or radioiodine treatment of thyroid carcinoma.
- Children under 2 years of age or children of very low weight (1500 grams).
- Not to be used on patients on concurrent lithium therapy.

4.4 Special warnings and precautions for use

Patients with goitre, thyroid nodules, or other non-acute thyroid diseases are at risk of developing thyroid hyperfunction (hyperthyroidism) from the administration of large amounts of iodine. In this patient population, BETADINE® FIRST AID CREAM should not cover for a long period and large area of the skin (e.g., not to more than 10 % of the total body surface

and for not longer than 7 days) unless strictly indicated. Even after the end of the treatment (up to 3 months) one should look for the early symptoms of possible hyperthyroidism and if necessary the thyroid function should be monitored.

It should not be used prior to or after radioiodine scintigraphy or radioiodine treatment of thyroid carcinoma.

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

For external use only.

Prolonged exposure to the cream may cause allergy and contact dermatitis or rarely, severe skin reactions. In instances of local irritation or sensitivity, discontinue use.

Changes in the international and local antimicrobial resistance patterns should be a consideration. Principles of antibiotics stewardship should be adhered to.

4.5 Interaction with other medicines and other forms of interaction

The PVP-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 mercury, silver, hydrogen peroxide, and taurolidine may interact with povidone-iodine and should not be used concomitantly. Simultaneous use with mercury products may lead to the formation of a substance, which can damage the skin.

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 discolorations in the areas involved.

Effects on diagnostic tests

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 BETADINE® FIRST AID CREAM may interfere with thyroid function tests or radioiodine therapy. During the use of BETADINE® FIRST AID CREAM the iodine uptake of the thyroid can be lowered; this can lead to interference with various investigations (thyroid scintigraphy, determination of PBI (protein-bound iodine), radioiodine diagnostics) and can make a planned treatment of the thyroid with iodine (radioiodine therapy) impossible. After the end of the treatment an appropriate interval should be allowed before a new scintigram is carried out.

4.6 Fertility, pregnancy and lactation

During pregnancy and lactation, BETADINE® FIRST AID CREAM should only be used if strictly indicated and its use should be kept to the absolute minimum, since absorbed iodine can pass through the placenta and be secreted in breast milk.

Pregnancy

Povidone-iodine use may induce transient hypothyroidism with elevation of TSH (thyroid stimulating hormone) in the foetus or in the newborn. A check of the child's thyroid function may be necessary.

Breastfeeding

Iodine is excreted in breast milk and is present in higher concentrations in the breast milk compared to those in the serum.

Also, any oral ingestion of the cream by the infant must be avoided, therefore, breastfeeding women should ensure they do not apply BETADINE® FIRST AID CREAM to the breast when they are breastfeeding.

Fertility

No data is available.

4.7 Effects on ability to drive and use machines

BETADINE® FIRST AID CREAM has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The following adverse reactions have been reported with BETADINE® FIRST AID CREAM either during clinical trials or during post-marketing experience:

Very common (≥ 1/10), Common (≥ 1/100, < 1/10), Uncommon

(≥ 1/1 000, < 1/100), Rare (≥ 1/10 000, < 1/1 000), Very rare (<1/10 000) and

Not known (cannot be estimated from the available data).

Immune system disorders

Rare: Hypersensitivity

Very rare: Anaphylactic reaction

Endocrine disorders

Very rare: Hyperthyroidism (sometimes with symptoms such as tachycardia or restlessness) *

Not known: Hypothyroidism ****

Metabolism and nutrition disorders

Not known: Electrolyte imbalance **, metabolic acidosis **

Skin and subcutaneous tissue disorders

Rare: Contact dermatitis (with symptoms such as erythema, small blisters and pruritus), angioedema

Renal and urinary disorders

Not known: Acute renal failure**, Blood osmolarity abnormal **

Injury, poisoning and procedural complications

Not known: Chemical burn of skin ***

* In patients with a history of thyroid disease (see Section 4.4) following a notable uptake of iodine e.g. 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)

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

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

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

Excess iodine can produce goitre and hypothyroidism or hyperthyroidism. Systemic absorption of iodine after repeated application of povidone-iodine to large areas of wounds or burns or deliberate or accidental ingestion of large quantities of povidone-iodine may lead to a number of overdose effects: metallic taste in mouth, increased salivation, burning or pain in the throat or mouth, irritation and swelling of the eyes, pulmonary oedema, skin reactions, gastrointestinal upset and diarrhoea, metabolic acidosis, hypernatraemia, renal impairment up to anuria and circulatory collapse.

Treatment

In the case of deliberate or accidental ingestion of large quantities of BETADINE® FIRST AID CREAM, symptomatic and supportive treatment should be provided with special attention to electrolyte balance and renal and thyroid function.

5 PHARMACOLOGICAL PROPERTIES

A.14.1 Antibacterial and antiseptic agents (dermatological)

5.1 Pharmacodynamic properties

Povidone-iodine is a complex of the polymer polyvinylpyrrolidone with iodine (povidone-iodine) which, after application, continues to deliver iodine over a period of time. Elemental iodine (I_2) has long been known as a highly effective microbicidal agent that rapidly kills bacteria, viruses, fungi and some protozoa *in vitro*. Two mechanisms are involved: free iodine rapidly causes microbial killing, whereas iodine bound to the polymer serves as a reservoir. As the preparation comes in contact with the skin and mucous membranes, more and more iodine dissociates from the polymer. The free iodine reacts with oxidisable –SH or –OH groups of the amino acids in the enzymes and structural proteins of microorganisms thereby inactivating and killing these enzymes and proteins. Most vegetative microorganisms are killed in less than a minute *in vitro*, with many destroyed within 15 to 30 seconds. During this process, iodine is decolourised; thus, the intensity of brown colouration serves as indicator of its effectiveness. Repeated dosing may be required upon discolouration. Resistance has not been reported.

5.2 Pharmacokinetic properties

Absorption

In normal individuals, topical application results in very little systemic iodine absorption; with vaginal administration, however, iodine absorption is rapid and serum concentrations of total iodine and inorganic iodide are increased significantly. BETADINE® FIRST AID CREAM is intended for topical application to the skin and wounds.

Povidone (PVP)

Absorption, and in particular renal elimination, of povidone depend on the (mean) molecular weight (of the mixture). For molecular weights of more than 35,000 to 50,000, retention must be expected.

Iodine

The behaviour of absorbed iodine or iodide in the organisms is largely similar to that of iodine taken up by other routes. The volume of distribution corresponds to approximately 38 % of body weight in kg.

Elimination is almost exclusively by renal route with a clearance of 15 to 60 ml plasma/min depending on serum iodine level and creatinine clearance

5.3 Preclinical safety data

Acute toxicity

In experimental animal investigations (mouse, rat, rabbit, dog), acutely toxic effects were found after systemic administration (oral, i.p., i.v.) only with excessively high doses that are of no significance for the local use of povidone-iodine.

Chronic toxicity

Subchronic and chronic tests for toxicity were carried out on rats, among other animals, in the form of the admixture of povidone-iodine (10 % available iodine) into the feed in dosages of between 75 and 750 mg povidone-iodine per day and kg body weight for up to 12 weeks. After the povidone-iodine addition was stopped, only the practically completely reversible and dose-dependent rises in PBI (protein-bound iodine) in the serum and non-specific histopathologic changes in the thyroid gland were observed. Similar changes also occurred in the control group, which received potassium iodide in iodine-equivalent amounts instead of povidone-iodine.

Mutagenic and tumour-inducing potential

No carcinogenicity studies have been conducted; no information is therefore available.

Reproductive toxicity

Because of the ability of iodine to pass through the placenta and the sensitivity of the foetus to pharmacologic doses of iodine, no larger amounts of iodine should be administered during pregnancy. The use of povidone-iodine in obstetrics may lead to a significant rise in serum iodine concentration in the mother and to transient hypofunction of the thyroid gland with elevation of TSH (thyroid-stimulating hormone) concentration in the neonate. Moreover, iodide is concentrated in the milk, as compared with the serum.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cetostearyl alcohol, glycerol, liquid paraffin, macrogol stearate, polysorbate 60, potassium iodate, purified water, sodium hydroxide, sorbitan stearate, white soft paraffin.

6.2 Incompatibilities

BETADINE® FIRST AID CREAM should not be used together with alkali, hydrogen peroxide, taurolidine, tannic acid, silver 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

BETADINE® FIRST AID CREAM is supplied in internal lacquered aluminium tubes containing 15 g or 40 g of product. The tubes are closed with polypropylene or heterophasic copolymer screw caps.

The tubes are enclosed in printed cartons.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

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

27/14.1/0062

9 DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

24 November 1992

10 DATE OF REVISION OF THE TEXT

08 September 2022

® = **BETADINE** is a registered trademark