PROFESSIONAL INFORMATION

SCHEDULING STATUS S0

1 NAME OF THE MEDICINE

BETADINE® WOUND SPRAY (Powder)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 g of BETADINE® WOUND SPRAY contains 25 mg povidone-iodine (2,5 % *w/w).* The amount of povidone iodine from a 3 second spray is equivalent to 73 mg.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Dry Powder (Cutaneous Spray), which is a fine brown powder after spraying.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

BETADINE® WOUND SPRAY is indicated for the prevention and treatment of skin infections in wounds, including ulcers, burns, cuts and abrasions and other minor injuries.

4.2 Posology and method of administration

Dosage/Administration

The dose is based on the size of the area to be treated. Spray for 3 seconds from a distance of 15 – 26 cm once or multiple times daily (every 3-4 hours) on the area to be treated until this is visibly covered with the golden-brown povidone-iodine powder. If the BETADINE® WOUND SPRAY becomes discoloured, it should be reapplied.

Paediatric Population

Not recommended for children below 2 years of age.

Method of administration

BETADINE® WOUND SPRAY is intended for external use only. BETADINE® WOUND SPRAY forms a dry film on the treated area and can be washed off easily.

Shake the spray can vigorously before use, hold upright and spray the area to be treated from a distance of 15 to 26 cm for 3 seconds. The propellant evaporates immediately, and the cold sensation experienced when the product is sprayed on very quickly disappears. If necessary, a dressing can then be applied on top.

Duration of treatment

BETADINE® WOUND SPRAY should continue to be administered for as long as there is evidence of infection or a clear risk of infection, for a maximum of 14 consecutive days. If an infection recurs after treatment with BETADINE® WOUND SPRAY has been discontinued, treatment may be reinitiated at any time.

4.3 Contraindications

- Hypersensitivity to the active ingredient or any of the excipients (see section 6.1)
- Hyperthyroidism or other manifest thyroid diseases
- Dermatitis herpetiformis (Duhring's disease)
- Use in conjunction with products containing mercury (see section 4.5)
- Use in conjunction with octenidine-based antiseptics (see section 4.5)
- Four weeks before, during and four weeks after radioiodine therapy for thyroid cancer or radioiodine scintigraphy thyroid testing (see section 4.4)
- Not to be used in patients on concurrent lithium therapy
- Children below the age of 1

4.4 Special warnings and precautions for use

Due to the skin texture and the sensitivity to iodine of newborns and infants up to the age of 2 years, povidone-iodine may only be used if strictly indicated, as the risk of hypothyroidism (particularly if larger quantities are applied) cannot be completely ruled out. If applicable, the thyroid function (e.g. T4 and TSH values) should be monitored (see section 4.6). Any oral ingestion of povidone-iodine by infants and small children must be avoided.

In the event of a latent thyroid function disorder (particularly in elderly patients) and in patients with a goitre or thyroid nodules, BETADINE® WOUND SPRAY should not be used for a prolonged period (more than 14 days) or over a large surface area (more than 10 % of the body surface area) given the risk of subsequent hyperthyroidism. Even after treatment has been discontinued (for up to 3 months), these patients should be carefully observed for early symptoms of hyperthyroidism, and thyroid function should be monitored where appropriate.

Povidone-iodine use could lead to transient skin discolouration at the application site caused by the drug products own colour.

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

Caution: do not inhale the spray mist and do not spray into or near the eyes. The propellants and n-pentane are flammable. The spray mist can ignite. Caution is therefore advised in the vicinity of naked flames. Do not undertake electrocautery until the spray mist has completely dissipated.

4.5 Interaction with other medicines and other forms of interaction

Concomitant use of povidone-iodine and hydrogen peroxide, enzymatic wound treatment agents or those containing silver or taurolidine, or antiseptics may lead to mutually reduced efficacy.

The use of BETADINE® WOUND SPRAY together with taurolidine should be avoided, since taurolidine may metabolise to formic acid, which causes intense burning.

Povidone-iodine may not be used together with products containing mercury, since caustic mercury iodide may form (see section 4.3).

Povidone-iodine may not be used in conjunction with octenidine-based antiseptics as this may result in temporary dark discolourations (see section 4.3).

The povidone-iodine complex is effective in a pH range of 2.0 - 7.0. It is anticipated that povidone-iodine may react with protein and various other organic substances such as blood or pus constituents, which may impair its efficacy; this can be offset with a higher dose of povidone-iodine.

Longer-term application, particularly over a large surface area, should be avoided in patients undergoing lithium therapy, as fairly large quantities of iodine may be absorbed.

Effects on diagnostic tests

The use of BETADINE® WOUND SPRAY can reduce iodine uptake by the thyroid; this can lead to problems during various tests (thyroid scintigraphy, PBI (protein-bound iodine) determination, radioiodine diagnostics), making any planned radioiodine therapy impossible. An interval of 4 weeks after discontinuation of treatment with povidone-iodine should be observed (see section 4.3).

As a result of the oxidising effect of povidone-iodine, various diagnostic agents can produce false-positive results (including toluidine and guaiac resin for determining haemoglobin or glucose in the stools or urine).

4.6 Fertility, pregnancy and lactation

Povidone-iodine is not teratogenic.

Use in pregnant women and during breastfeeding must be strictly indicated, and povidone-iodine used to an extremely limited extent. In pregnant or breastfeeding women, monitoring of thyroid function in the mother and/or the infant is indicated. Povidone-iodine may induce temporary hypothyroidism (elevated TSH).

Iodine crosses the placental barrier and is excreted in breast milk. Moreover, iodine is present in higher concentrations in the breast milk compared to those in the serum. The accidental oral ingestion of BETADINE® WOUND SPRAY by the infant as a result of contact with the treated area of the breastfeeding mother's body must be avoided.

Fertility

No data is available.

4.7 Effects on ability to drive and use machines

BETADINE® WOUND SPRAY has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Immune system disorders

Less frequent: Hypersensitivity, anaphylactic reaction

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 **

Skin and subcutaneous tissue disorders

Less frequent: Contact dermatitis (with symptoms such as urticaria, erythema, small blisters and pruritus), skin discolouration, angioedema

Renal and urinary disorders

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

** 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)*

**** 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

Signs and symptoms of overdose

In the case of deliberate or accidental ingestion of large quantities of povidone-iodine acute iodine toxicity is manifested by abdominal symptoms, anuria, circulatory collapse, oedema of glottis resulting in asphyxia, or 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

The overdose effects that can occur are due to iodine toxicity and often require specialised treatment in a hospital setting.

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 venovenous haemodiafiltration is less effective than haemodialysis. In case of thyroid dysfunction, treatment with povidone-iodine should be discontinued.

5 PHARMACOLOGICAL PROPERTIES

A.14.1 Antibacterial and antiseptic agents (dermatological)

5.1 Pharmacodynamic properties

Povidone-iodine is a polyvinylpyrrolidone polymer-iodine complex (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.

5.2 Pharmacokinetic properties

Absorption

After the administration of BETADINE® WOUND SPRAY, the possibility of iodine absorption should be considered, depending on the nature and duration of administration as well as the quantity applied. Appreciable iodine absorption can occur after the prolonged use of BETADINE® WOUND SPRAY on extensive wound and burn surfaces and mucous membranes. A consequent elevation of iodine levels in the blood is usually temporary (restitution within 7-14 days after discontinuation of the treatment). In a healthy thyroid gland, the increased availability of iodine does not lead to clinically relevant changes in the thyroid hormone status.

Distribution

See "Absorption".

Metabolism

See "Absorption".

Elimination

Povidone

The absorption and particularly the renal elimination of povidone depend on the (average) molecular weight (of the compound). Retention, particularly in the reticulohistiocytic system, can be expected above a molecular weight of 35,000 to 50,000 daltons.

Iodine

The behaviour of absorbed iodine or iodide in the body largely corresponds with that of iodine absorbed in other ways. The volume of distribution corresponds to approximately 38% of the body weight in kg, and the biological half-life after vaginal application is stated as approximately two days. The normal level for total iodine in the serum is 3.8 to 6.0 µg/dl, compared to 0.01 to 0.5 µg/dl for inorganic iodine.

Elimination takes place almost exclusively via the kidney, with a clearance of 15 to 60 ml plasma/min depending on the serum iodine level and creatinine clearance (normal range: 100-300 µg iodide per gram of creatinine).

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butane, isobutane, isopropyl myristate, n-pentane, propane.

6.2 Incompatibilities

Povidone-iodine is incompatible with reducing agents, alkaloid salts, tannic acid, salicylic acid, mercury and bismuth salts, taurolidine, hydrogen peroxide and octenidine.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 25 °C.

Highly flammable.

Keep away from sources of ignition.

Do not expose to temperatures above 50 °C (for example, do not leave to stand in the sun, in a hot car or immediately next to a radiator).

6.5 Nature and contents of container

Aluminium aerosol can with inside lacquer, fitted with a non-metering valve, high density polyethylene (HDPE) actuator with micromist insert, and a polypropylene (PP) cap.

Pack sizes: 30 g, 55 g and 80 g. Not all pack sizes are marketed.

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

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South Africa

8 REGISTRATION NUMBERS

51/14.1/0533

9 DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

7 June 2022

10 DATE OF REVISION OF THE TEXT

TBD

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