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SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Betadine Topical Spray

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Povidone-iodine 2.5 %

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dry Powder Spray

Spray for application on skin.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

As antiseptic for prevention and treatment of infections associated with burns, cuts and scrapes, and for preventive treatment of wounds at risk of infection, e.g. after placement of a suture for wound treatment or after surgery.

4.2. Posology and route of administration

Posology

The dose is proportionate to the size of the area to be treated.

Spray once or multiple times daily on the area to be treated until this is visibly covered with the golden-brown coloured povidone-iodine powder.

In the event the Betadine Topical Spray becomes discoloured, it may be reapplied.

New-borns and infants under 6 months

Betadine Topical Spray may only be used in new-borns and infants up to the age of 6 months after a thorough risk-benefit analysis has been carried out by the doctor, and applied only to a very limited extent (see Section 4.4 Special Warnings and Precautions for Use).

Route of administration

Betadine Topical Spray is intended for external use.

Betadine Topical Spray forms a dry film on the treated area and can be washed off easily.

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

Duration of administration

Betadine Topical Spray should continue to be administered for as long as there is evidence of an infection or a clear risk of infection. Should an infection recur after treatment with Betadine Topical Spray has been discontinued, then treatment may be reinitiated at any time.

4.3. Contraindications

- Hypersensitivity to the active ingredient or to one of the other excipients listed under Section 6.1.
- Hyperthyroidism or other manifesting thyroid diseases.
- Dermatitis herpetiformis (Dühring's disease).
- Use in conjunction with products containing mercury (see Section 4.5).
- Use in conjunction with octenidine-based antiseptics (see Section 4.5).
- Before and after radioactive iodine therapy (until the treatment is concluded).
- Before radioactive iodine scintigraphy for thyroid testing.
- Before radioactive iodine treatment for thyroid cancer.

4.4. Special Warnings and Precautions for Use

Due to the texture and sensitivity of the skin of new-borns and infants up to the age of 6 months to iodine, povidone-iodine may only be used after strict diagnosis, as the risk of hyperthyroidism (particularly if larger quantities are applied) cannot be completely excluded. If applicable, the thyroid function (e.g. T₄ and TSH values) should be monitored (see also Section 4.6 Fertility, Pregnancy and Lactation). Infants and small children must be prevented from ingesting povidone iodine.

In the case of latent thyroid function disorder (particularly in elderly patients and patients with goitre or thyroid nodules) Betadine Topical Spray should only be used over an extended period (more than 14 days) or over a large surface area (more than 10% of the surface of the body) after a thorough risk-benefit analysis, to avoid the risk of subsequent hyperthyroidism. It is necessary, to be vigilant in these patients for early symptoms of hyperthyroidism and, if applicable, to monitor thyroid function, even after the treatment has been discontinued (for up to 3 months).

Caution, do not inhale spray mist and do not spray into eyes or near the eye area.

Propellants are flammable. The spray mist can ignite. Caution is therefore advised in the vicinity of open flames. Do not undertake electrocautery until the spray mist has completely dissipated.

4.5. Interaction with other medicinal products and other forms of interaction

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

The use of Betadine Topical Spray in conjunction with taurolidine should be avoided, as taurolidine may metabolise to formic acid, which causes intense burning.

Povidone-iodine may not be used in conjunction with products containing mercury, as 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 discolorations (see Section 4.3).

The povidone-iodine complex is active at a pH value between 2.0 and 7.0. It is anticipated that povidone-iodine may react with protein and various other organic substances such as blood and pus constituents for example, which may impair its efficacy; this can be compensated for 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 larger quantities of iodine may be absorbed.

Influence on diagnostic tests

The use of Betadine Topical Spray can reduce iodine uptake by the thyroid; this can lead to problems during various tests (thyroid scintigraphy, PBI (protein-bound iodine) determination and radioactive iodine diagnostics), and can make planned radioactive iodine therapy impossible. An interval of 1-2 weeks after discontinuation of povidone-iodine treatment should be observed (see 4.3 Contraindications).

Due to the oxidising effect of povidone-iodine, various diagnostic agents can deliver false-positive results (including toluidine and guaiacum resin for determining haemoglobin or glucose in stools or urine).

4.6. Fertility, Pregnancy and Lactation

Povidone-iodine is not teratogenic.

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

Iodine passes through the placental barrier and into the breast milk. In addition, iodine is present in higher concentrations in breast milk compared with the serum. Accidental oral intake of Betadine Topical Spray by the infant as the result of contact with the treated area of the body of the breastfeeding mother must be avoided.

4.7. Effects on ability to drive and use machines

Betadine Topical Spray has no impact or only negligible impact on the ability to drive and use machines.

4.8. Undesirable Effects

The following frequencies are used as a basis to evaluate undesirable effects:

Very common ($\geq 1/10$)

Common ($\geq 1/100$, $< 1/10$)

Uncommon ($\geq 1/1,000$, $< 1/100$)

Rare ($\geq 1/10,000$, $< 1/1,000$)

Very rare ($< 1/10,000$)

Unknown (frequency cannot be estimated on the basis of the available data)

The undesirable effects are listed within each frequency group in order of decreasing severity.

Immune system disorders

Rare: Hypersensitivity

Very rare: Anaphylactic reaction frequently accompanied by hypotension, dizziness, nausea and possible respiratory distress

Endocrine disorders

Very rare: Iodine-induced hyperthyroidism in predisposed individuals (sometimes accompanied by the symptoms of tachycardia or anxiety; see also Section 4.3 Contraindications and 4.9 Overdose) ¹⁾

Unknown: Hypothyroidism ²⁾

Metabolism and nutrition disorders

Unknown: Electrolyte imbalance ³⁾, metabolic acidosis ³⁾

Skin and Subcutaneous Cell Tissue Disorders

Rare: Hypersensitivity reactions of the skin (for example delayed contact allergy reactions, which may manifest in the form of, for example, pruritus, erythema, blisters or similar.)

Very rare: Angioedema

Renal and urinary disorders

Unknown: acute kidney failure ³⁾, anomalous osmolarity of the blood ³⁾

- 1) In patients with a thyroid function disorder in their medical history (see in particular Warnings and Precautions for Use) after intake of a substantial quantity of iodine e. g. during application of povidone-iodine over a large surface area during the treatment of wounds and burns over an extended period
- 2) Hypothyroidism after longer-term or excessive use of povidone-iodine
- 3) May also occur after intake of a significant quantity of povidine-iodine (e.g. wound treatment)

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.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form

<https://sideeffects.health.gov.il/>

4.9. Overdose

Symptoms of an overdose

Symptoms of intoxication have been reported in the literature in relation to an intake exceeding 10 g povidone-iodine. These symptoms are: abdominal pain and cramping, nausea, vomiting, diarrhoea, dehydration, hypotension with tendency to collapse, glottic oedema, tendency to bleed (mucous membranes, kidneys), cyanosis, kidney damage culminating in anuria, paraesthesia, fever and pulmonary oedema.

Prolonged, excessive intake of iodine may result in symptoms of hyperthyroidism, tachycardia, anxiety, tremor, or headache.

Therapy for overdose:

Immediate administration of foodstuffs containing starch and protein (for example, corn-starch stirred into water or milk), if necessary gastric lavage with 5% sodium thiosulphate solution (or 10 ml 10% sodium thiosulphate solution i.v.) at 3-hourly intervals. After absorption has already taken place, toxic serum-iodine levels can be reduced by means of peritoneal dialysis or haemodialysis.

Furthermore, the thyroid function must be subject to careful clinical monitoring to facilitate exclusion or early detection of possible hyperthyroidism.

Further treatment is determined based on any other presenting symptoms such as metabolic acidosis and renal function disorders for example.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Antiseptics, ATC Code: D08AG02

Povidone-iodine is a polyvinylpyrrolidone polymer-iodine complex (povidone-iodine). The microbicidal action is based on the fraction of free, non-complex-bound iodine released from the povidone-iodine complex in an equilibrium reaction. In this way, the povidone-iodine complex constitutes an iodine depot, which releases elementary iodine over a prolonged period, thereby guaranteeing a constant concentration of active free iodine.

As a result of binding with the povidone complex, the iodine largely loses the topical irritant properties of alcohol-based iodine preparations and can be well tolerated on skin, mucous membranes and wounds.

The free iodine reacts with oxidisable SH or OH groups of the amino acids in enzymes and structural proteins of microorganisms, which are consequently inactivated and destroyed. During this process the iodine becomes discoloured; the intensity of the brown colouring is therefore an indicator of its efficacy. In the event of discolouration, the product should be reapplied.

This relatively unspecific principle of action explains the comprehensive efficacy of povidone-iodine against a broad spectrum of human-pathogenic microorganisms: Gram-positive, Gram-negative bacteria, *Gardnerella vag.*, mycoplasma, *Treponema pallidum*, chlamydia; fungi (*Candida* for example); viruses (including herpes and HIV); protozoa (trichomonads for example) as well as spores.

Resistances, even the forming of secondary resistances during longer-term use, should not be suspected because of the mode of action.

5.2. Pharmacokinetic properties

After the administration of Betadine Topical Spray, the possibility of iodine absorption must be considered, depending on the nature and duration of administration as well as the quantity applied.

Substantial intake of iodine may occur as the result of long-term application of Betadine Topical Spray on extensive wound and burn surfaces and mucous membranes. A consequent elevation of iodine levels in the blood is, in general, 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 thyroid hormone status.

Povidone:

The absorption and particularly the renal elimination of povidone are dependent on the (average) molecular weight (of the compound). Retention, particularly in the reticulohistiocytic system, is to be anticipated with a molecular weight above 35,000 to 50,000 Dalton. However, thesaurismosis and other changes such as those occurring after intravenous or subcutaneous administration of other medicinal products containing povidone are not evident for povidone-iodine.

Iodine:

The behaviour of absorbed iodine or iodide in the body corresponds largely to that of iodine taken in from another source. The volume of distribution corresponds to approximately 38% of the body weight in kg, the biological half-life after vaginal application is indicated as approximately two days. The normal level for total iodine in the serum is 3.8 to 6,0 µg/dl, and 0.01 to 0.5 µg/dl in the case of inorganic iodine. Elimination takes place almost exclusively via the kidneys, with a clearance of 15 to 60 ml plasma/min depending on the serum-iodine level and creatinine clearance (normal value: 100-300 µg iodide per g creatinine).

5.3. Preclinical Safety Data

Data from preclinical safety pharmacology studies, toxicity in repeated used, and genotoxicity or carcinogenic potential did not generate any particular advice on risks with regard to use on humans. As there is long-standing clinical experience with iodine, no long-term carcinogenicity studies were conducted on animals. Animal studies did not indicate any teratogenic effects.

During subchronic and chronic toxicity tests on rats, among other animals, after administration of the povidone-iodine was discontinued, only largely reversible and dose-dependent increases of PBI (protein-bound iodine in the serum) and unspecific, histopathological changes in the thyroid were observed.

6. PHARMACEUTICAL PARTICULARS

6.1. List of the other excipients

Isopropyl myristate, n-Pentane, Gas Propellant (mixture of propane, butane and isobutane).

6.2. Incompatibilities

Povidone-iodine is incompatible with reducing agents, alkaloid salts, tannic acid, salicylic acid, silver, mercury and bismuth salts, taurolidine, hydrogen peroxide, and octenidine (see also Section 4.5 Interactions with other medicinal products and other forms of interaction).

6.3. Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4. Special precautions for storage

Easily flammable. Store below 25°C.

Do not expose to temperatures above 50°C.

Keep away from potential sources of inflammation.

6.5. Nature and contents of the container

Pressurized aerosol aluminium can with inside lacquer, spray valve and spray head, weighing 30 g or 80 g.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other advice on handling

Shake the spray can well before use, hold upright and spray from a distance of 15 cm on the area to be treated. (See 4.2 Posology and route of administration).

Due to the oxidative effect of the povidone-iodine, metals may become corroded; plastics are generally resistant to povidone-iodine. In some cases, mostly reversible discolouration may occur.

Betadine Topical Spray can be easily removed from textiles and other materials with warm water and soap, and, in stubborn cases, by using ammonia (ammonia solution) or sodium thiosulphate (fixing salt).

Unused medicinal product or waste material must be disposed of in accordance with national requirements.

7. REGISTRATION HOLDER

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Registration number: 160-94-35157

Manufacturer: Mundipharma Ltd. Nicosia Cyprus.