

## **PRESCRIBING INFORMATION**

**Betadine®**

### **TOPICAL PREPARATIONS**

**Mouthwash/Gargle**

**Ointment**

**Solution**

**Surgical Scrub**

### **ANTISEPTIC**

Purdue Pharma  
575 Granite Court  
Pickering, ON  
L1W 3W8

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## **PRESCRIBING INFORMATION**

### **NAME OF DRUG**

**Betadine®**

### **TOPICAL PREPARATIONS**

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Solution

Surgical Scrub

### **PHARMACOLOGICAL CLASSIFICATION**

Antiseptic

### **ACTIONS**

**Betadine®** is iodine complexed with povidone (polyvinyl-pyrrolidone). The compound is soluble in water forming a golden brown solution. Like iodine, the solution of the iodine complex is bactericidal, fungicidal, virucidal and trichomonacidal. However, unlike solutions of iodine, it is non-staining to natural fabrics. The antiseptic action of povidone-iodine is due to the available iodine present in the complex.

### **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<sub>2</sub>) 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 oxidizable -SH or -OH groups of the amino acids in the enzymes and structural proteins of microorganisms thereby inactivating 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 decolorized; thus, the intensity of brown coloration serves as indicator of its effectiveness.

Repeated dosing may be required upon discoloration. Resistance has not been reported.

### **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.

*Povidone:* 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 biological half-life after vaginal administration is approximately 2 days.

Elimination is almost exclusively by renal route.

### **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 solution.

### **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 nonspecific 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**

A mutagenic action for povidone-iodine can be ruled out. No carcinogenicity studies have been conducted; no information is, therefore, available.

**INDICATIONS**

**Mouthwash/Gargle:** As a mouth wash for routine use. Eliminates or reduces offensive mouth odours. As a gargle or mouth wash as primary or adjunctive therapy in infections of the mouth and throat such as aphthous stomatitis, Vincent's infection, pharyngitis, oral moniliasis, tonsillitis and following oral surgery and dental procedures.

**Ointment:** For the prevention of infection in burns, cuts abrasions, poison ivy rash and insect bites. The treatment of skin infections, including infections of varicose and decubitus ulcers.

**Solution:** Use full strength for pre- and post-operative skin and mucus membrane antisepsis, prophylaxis and treatment of wounds, lacerations and burns, trichomonal, monilial and non-specific vaginitis, cervicitis, oral infections, and dental procedures.

**Surgical Scrub:** Pre- and post-operative scrubbing or washing, pre- and post-operative use on patients, general use in physician's office.

**CONTRAINDICATIONS**

Not to be used in known hypersensitivity to iodine or povidone. Not to be used in hyperfunction of the thyroid (hyperthyroidism), other manifest thyroid diseases, as well as before and after

radioactive iodine therapy. It should not be used prior to radioiodine scintigraphy (thyroid gland) or radioiodine treatment of thyroid carcinoma.

### **SPECIAL WARNINGS AND PRECAUTIONS**

For topical use only. Avoid contact with eyes. If contact occurs, flush eyes with water. 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 (chemical burn of skin). In instances of skin irritation or contact dermatitis or hypersensitivity, discontinue use. Do not heat prior to application. Keep out of the reach of children.

Patients with goiter, thyroid nodules, or other thyroid diseases (thyroid disorder) are at risk of developing thyroid hyperfunction (hyperthyroidism) from the administration of large amounts of iodine. In this patient population, povidone-iodine solution should not be applied for an extended period of time and to large areas of the skin unless strictly indicated. Even after the end of the treatment one should look for the early symptoms of possible hyperthyroidism and if necessary the thyroid function should be monitored.

Newborns and small infants are at increased risk of developing hypothyroidism from the administration of large amounts of iodine. Because of the permeable nature of their skin and the increased sensitivity to iodine, the use of povidone-iodine should be kept to the absolute minimum in newborns and small infants. A check of the child’s thyroid function (e.g., T<sub>4</sub> levels

and TSH levels) may be necessary. Any possible oral ingestion of povidone-iodine by the infant must be absolutely avoided.

For information on use during pregnancy and lactation, see Pregnancy and Lactation.

Blue stains on starched linen will wash off with soap and water.

Drug Interactions and Other Forms of Interactions: 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 weakening of the effects of both substances. Products containing mercury, silver, hydrogen peroxide, and taurolidine may interact with povidone-iodine and should not be used concomitantly.

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.

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

Absorption of iodine from povidone iodine solution may interfere with thyroid function tests. During the use of povidone-iodine solution 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.

Pregnancy and Lactation: During pregnancy and lactation, povidone-iodine solution should only be used if strictly indicated and its use should be kept to the absolute minimum. Because of the ability of iodine to pass through the placenta and be secreted in breast milk, and because of the increased sensitivity of the fetus and newborn to iodine, no large amounts of povidone-iodine should be administered during pregnancy and lactation. Povidone-iodine use may induce transient hypothyroidism with elevation of TSH (thyroid stimulating hormone) in the fetus or in the newborn. A check of the child's thyroid function may be necessary. Any possible oral ingestion of the solution by the infant must be absolutely avoided.

### **ADVERSE EFFECTS**

Rarely, hypersensitive skin reactions may occur (e.g., delayed contact-allergic reactions (delayed type hypersensitivity reaction), which can appear in the form of pruritus, erythema, small blisters or similar manifestations).

Very rarely, acute, generalized, allergic reactions (anaphylactic reactions) with drop in blood pressure (blood pressure decreased) and/or dyspnea as well as cases of acute skin and mucosal swelling (angioedema) have been reported.

The long-term use of povidone-iodine solution for the treatment of wounds and burns over extensive areas of the skin can lead to a notable uptake of iodine. In isolated cases, patients with a history of thyroid disease can develop hyperfunction of the thyroid (iodine induced hyperthyroidism), sometimes with symptoms such as tachycardia or restlessness (see **SPECIAL WARNINGS AND PRECAUTIONS**).

Following uptake of large amounts of povidone-iodine (e.g., in the treatment of burns), the appearance of additional disorders of electrolyte imbalance and abnormal blood osmolarity, impairment of renal function with acute renal failure and metabolic acidosis have been described in the use of iodine-containing products.

### **OVERDOSE**

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

Treatment is symptomatic and supportive.

**DOSAGE AND ADMINISTRATION**

**Mouthwash/Gargle:** As a routine mouth wash: use full strength or dilute to taste. Effective up to dilution of 1 part **Betadine** with 2 parts water. As a gargle or mouth wash: use full strength for 30 seconds, hourly, or as directed by physician or dentist.

**Ointment:** Apply directly to affected area as needed. May be bandaged.

**Solution:** Apply full strength as often as needed as a paint or wet soak. Allow to dry before applying surgical drapes and avoid “pooling” beneath the patient. Prolonged exposure to the solution may cause irritation or rarely, severe skin reaction. In rare instance of local irritation or sensitivity, discontinue use.

**Surgical Scrub:**

A. Preoperative scrubbing by operating personnel: wet hands with water. Pour 5 mL on the palm of the hand and spread over both hands. Without adding more water, rub the scrub thoroughly over all areas for about 5 minutes. Use a soft brush, if desired. Clean thoroughly under fingernails. Add a little water to develop copious suds. Rinse thoroughly under running water. Complete the wash by scrubbing with another 5 mL if desired.

- B. Preoperative use on patients: wet the operative area with water. Apply scrub (1 mL is sufficient to cover an area of 125 to 200 cm<sup>2</sup>) and rub thoroughly for about 5 minutes. Then develop a lather and rinse off by aid of sterile gauze saturated with water. The area may then be painted with solution and allowed to dry.
- C. Use in physician's office: use for washing whenever a germicidal soap is required. For maximum degerming of the hands proceed as under (A). To prepare the patient's skin proceed as under (B).

### **SUPPLIED**

#### **Mouthwash/Gargle:**

Each mL of mahogany coloured solution contains: povidone-iodine USP 1% (0.1% available iodine) and alcohol 8%. pH: 4 to 6. Non-medicinal ingredients: Alcohol, eucalyptus oil, glycerine, menthol, methyl salicylate, sodium cyclamate, sodium hydroxide, water. Bottles of 250 mL. Protect from excessive heat. Check label for expiration date.

#### **Ointment:**

Each g contains: povidone-iodine USP 10% (1% available iodine) in a water-soluble polyethylene glycol ointment base. pH (5% solution): 3.5 to 4.5. Non-medicinal ingredients: Polyethylene glycol, sodium bicarbonate, water. Tubes of 20 g.

**Solution:** Each mL of mahogany coloured solution contains: povidone-iodine USP 10% (1% available iodine) with surfactant. pH 4.5 to 5.5. Non-medicinal ingredients: Citric acid, disodium hydrogen phosphate, glycerine, nonoxynol-9 (surfactant), sodium hydroxide, water. Plastic bottles of 100 and 500 mL.

**Surgical Scrub:** Each mL of mahogany coloured liquid contains: povidone-iodine USP 7.5% (0.75% available iodine) with sudsing agent. pH 4.5 to 5.5. Non-medicinal ingredients: Ammonium nonoxynol-4 sulfate (surfactant), lauric myristic diethanolamide, potassium iodate, sodium hydroxide, water. Plastic bottles of 500 mL.

**Storage Conditions:** Store at room temperature (15-25 °C).