SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product – Betaiodine 10% solution for external use

2. Qualitative and quantitative composition

1 ml of the solution contains povidone-iodine 100 mg
For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Solution for external use.
A brown colored liquid having a characteristic iodine odor.

4. Clinical particulars

4.1 Therapeutic indications

• Disinfection of the skin before injections, blood sampling, biopsy, blood transfusion, infusion therapy
• Antiseptic treatment of the skin and mucous membranes, for example, before surgical interventions
• Aseptic wound care
• Bacterial and fungal skin infections
• Complete or partial preoperative skin disinfection (preoperative disinfectant preparation of the patient, "disinfectant baths").

4.2 Posology and method of administration

Posology
Betaiodine solution can be used undiluted or diluted with water as a 10% (1:10) or 1% (1:100) solution, depending on the area to be disinfected.
The diluted solution should be prepared immediately before use.
The drug should be left on the skin for 1-2 minutes before injection, blood sampling, biopsy, blood transfusion, infusion therapy or before any other surgical intervention on intact skin.
For aseptic treatment of wounds, burns, for disinfection of mucous membranes, for bacterial and fungal infections of the skin, you can use a 10% solution (dissolving Betaiodine with water in a ratio of 1:10).
For preoperative "disinfectant baths" a 1% solution of Betaiodine (1:100) is used. The entire surface of the body should be evenly treated with a 1% solution and, after a 2-minute exposure, wash off the solution with warm water.
During preoperative disinfection of the skin, it is necessary to ensure that excess solution does not accumulate under the patient. Prolonged contact with the solution may cause skin irritation and, in rare cases, severe skin reactions. The accumulations of the solution under the patient can cause a chemical burn (see section 4.4).

Children and adolescents
The use of Betaiodine solution is not recommended for children under 2 years of age. The drug is contraindicated in newborns and children under 1 year of age (see section 4.3).

Method of administration
Betaiodine solution is intended only for external use on the skin and mucous membranes in undiluted or diluted form.

4.3 Contraindications

• hypersensitivity to the active substance or to any of the excipients listed in section 6.1
• dysfunction of the thyroid gland
• kidney failure
• dermatitis herpetiformis Duhring
• after stopping the use of povidone-iodine, a certain interval of time (1-2 weeks) should be observed before and after the use of radioactive iodine for scintigraphy and treatment of thyroid carcinoma (see section 4.5)
• combined use with drugs containing mercury, due to the formation of substances. which can cause skin damage
• lithium therapy
• pregnancy and lactation
• children under 1 year old.

4.4 Special warnings and precautions for use

The use of the drug in pregnant and lactating women requires special care and a benefit/risk assessment. Povidone-iodine should only be used when absolutely necessary (see section 4.6).
During preoperative preparation of the patient, it is necessary to ensure that excess solution does not accumulate under the patient. Prolonged contact with the solution may cause skin irritation and, in rare cases, severe skin reactions. The accumulations of the solution under the patient can cause a chemical burn. In case of skin irritation, contact dermatitis or hypersensitivity, the drug should be discontinued.
The drug should not be heated before use.
Betaiodine should not be used before or after radioactive iodine scintigraphy or radioactive iodine treatment of thyroid carcinoma (see section 4.3).
The oxidizing action of povidone-iodine can cause corrosion of metals, while plastic and synthetic materials are usually not sensitive to povidone-iodine. Povidone-iodine may cause permanent discoloration of certain fabrics, such as clothing.
Betaiodine is easily removed from textiles and other materials with warm soapy water. Stains that are difficult to remove should be treated with a solution of ammonia or sodium thiosulfate.
Avoid getting the drug in the eyes. In case of contact with eyes, hold eyelids open and flush eyes with plenty of water for 10-15 minutes. The patient should consult an ophthalmologist.
Degradation of the solution occurs in the light and at temperatures above 40°C.

Children and adolescents
Betaiodine solution is not recommended for children aged 1-2 years (see section 4.2) and its use is contraindicated in children under 1 year of age (see section 4.3).

4.5 Interaction with other medicinal products and other forms of interaction

The povidone-iodine complex is effective in the pH range of 2.0 - 7.0. Probably, the drug can react with proteins and other unsaturated organic complexes, which will lead to a deterioration in its effectiveness.
The combined use of povidone-iodine and enzyme preparations for the treatment of wounds leads to a mutual decrease in effectiveness. Preparations containing silver, hydrogen peroxide, as well as antiseptics and wound preparations containing taurolidine, can interact with povidone-iodine, resulting in a mutual deterioration in their effectiveness, therefore they should not be used simultaneously.
Povidone-iodine should not be used in combination with mercury preparations due to the risk of formation of alkaline mercury iodide (see section 4.3).

The use of povidone-iodine for a long time, especially on large surfaces, should be avoided in patients receiving treatment with drugs containing lithium. Betaiodine solution cannot be used in combination with preparations containing alkaline substances and tannic acid.
Avoid contact with jewelry, especially silver items (see section 6.2).
The use of povidone-iodine at the same time or immediately after the use of antiseptics containing octenidine on the same or adjacent skin areas may lead to the formation of dark spots on the treated surface.
The oxidizing effect of preparations containing povidone-iodine can lead to false positive results in various diagnostic tests (for example, measurement of hemoglobin and glucose in feces and urine using toluidine and guaiac resins).
Absorption of iodine from povidone-iodine solution may reduce the uptake of iodine by the thyroid gland, which may affect the results of certain tests and procedures (thyroid scintigraphy, determination of protein-bound iodine, diagnostic procedures with the use of radioactive iodine), and therefore, planning the treatment of thyroid diseases with iodine preparations may become impossible. After stopping the use of povidone-iodine, a certain period of time (at least 1-2 weeks) should be maintained before the next scintigraphy.

4.6 Fertility, pregnancy and breastfeeding

Pregnancy and breastfeeding
Iodine, after dissociation from povidone-iodine, freely crosses the placenta and is secreted in breast milk. It was reported about the development of congenital hypothyroidism in children whose mothers received iodine therapy.
The drug is contraindicated during pregnancy and breastfeeding.

4.7 Effects on ability to drive and use machines

Betaiodine solution does not affect the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions are listed below by system organ class and frequency.
Very common (> 1/10),
Common (≥ 1/100 - < 1/10),
Uncommon (≥ 1/1,000 - < 1/100),
Rare (≥ 1/10,000 - < 1/1,000),
Not known (cannot be estimated from the available data):

Immune system disorders	
Rare	hypersensitivity
Very rare	anaphylactic reaction
Endocrine disorders	
Very rare	hyperthyroidism
Not known	hyperthyroidism (sometimes accompanied by symptoms such as tachycardia and restlessness)
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 on the skin, itching)
Very rare	angioedema
Renal and urinary disorders	

Not known	acute renal failure change in blood osmolarity kidney dysfunction
Injuries, intoxications and complications of manipulations	
Not known	chemical burn of the skin

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. Healthcare professionals are asked to report any suspected adverse reactions via Arpimed "LLC" by going to www.arpimed.com and fill out the appropriate form ″Report an adverse reaction or inefficiency of drug″. Hotline number: (+374 55) 05 79 86. And by using Scientific Centre of Drug and Medical Technology Expertise after academician E. Gabrielyan ″CJSC ″, going to the site: www.pharm.am in ″Report about adverse effect of medicine″ section and fill out the ″Report of adverse reaction or manufacturing problem of medicinal product″.
Hotline numbers: +37410200505; +37496220505.

4.9 Overdose

Symptoms
Symptoms of iodine poisoning: disorders of the gastrointestinal tract, anuria, vascular collapse, pulmonary edema, metabolic disorders.
Systemic toxicity can lead to renal failure (including anuria), tachycardia, hypotension, circulatory failure, glottic edema leading to asphyxia, pulmonary edema, convulsions, fever, and metabolic acidosis.
Hyperthyroidism or hypothyroidism may also develop.
If thyroid function is impaired, povidone-iodine treatment should be discontinued.

Treatment
Symptomatic and supportive therapy is carried out.
In severe hypotension, intravenous fluid should be given; if necessary, vasopressors should be added.
Endotracheal intubation may be required if corrosive involvement of the upper airways results in significant edema and swelling.
You should not induce vomiting. The patient should be in such a position that the airways are free and protected from aspiration (in case of vomiting).
If the patient is not vomiting and can take food by mouth, starchy foods (eg, potatoes, flour, starch, bread) may help convert iodine to less toxic iodide.
If there is no evidence of bowel perforation, gastric lavage with a starch solution through a nasogastric tube can be used (gastric effluent will turn dark blue-violet, and this color can be used as a guide in determining when to stop lavage).
Hemodialysis effectively clears iodine and should be used in severe cases of iodine poisoning, especially in kidney failure. Continuous veno-venous hemofiltration is less effective than hemodialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiseptics and disinfectants. Iodine products
ATC code: D08AG02
Mechanism of action
Povidone-iodine is a complex of a synthetic polymer polyvinylpyrrolidone (povidone) with elemental iodine (I2 active ingredient), which serves as a depot for permanent release of iodine

from the complex (polyvinylpyrrolidone has no own antibacterial activity), as well as facilitates iodine contact with cell membranes. After application to the surface of the skin or mucous membranes, iodine is released from the polymeric complex for some time. Elemental iodine (I2) is a highly effective microbicide agent and the polymer serves as an iodine depot. This gradual release of iodine compensates for the disadvantages associated with the presence of elemental iodine and maintains its highly effective microbiocidal efficacy. Free iodine rapidly penetrates microorganisms and attacks key groups of proteins, amino acids, nucleotides and unsaturated fatty acids. It reacts with the thiol, sulfhydryl and hydroxyl groups of amino acids in enzymes and structural proteins of microorganisms, thereby oxidising them.

Pharmacodynamic effects

Povidone-iodine has a rapid antibacterial (including Gram positive and Gram negative bacteria), antifungal and virucidal action (enveloped and non-enveloped viruses).

Resistance to povidone-iodine has not been observed for over 60 years of intensive use in hospitals, dental and medical practices.

In addition, antibiotic resistance has no effect on the sensitivity to povidone-iodine.

5.2 Pharmacokinetic properties

The pharmacokinetics of povidone-iodine are affected by the dissociation of povidone and iodine and its subsequent reduction to iodide in the body. Different dosage forms and different routes of administration may affect the absorption of povidone iodine, and the extent of systemic absorption depends on the site and conditions of use (area, healthy skin surface, damaged skin surface, mucous membranes, wounds, body cavities).

Absorption.

The results of in vivo studies show that iodine is able to be absorbed through the skin, and the extent of absorption depends on the skin condition (e.g. damaged or healthy skin) as well as on the duration of application and the surface to which iodine is applied. A limited amount of iodine is absorbed through intact skin.

- Increased absorption of iodine occurs on damaged skin, ulcers, mucous membranes, which are characterized by significant absorption of iodine (vagina), or when applied to large surfaces of intact skin.

Only a small amount of povidone (~35 kDa) is detected in the systemic circulation.

Distribution

Regardless of the route of administration, absorbed iodine/iodide is distributed throughout the body through the circulatory system. Part of it (about 30%) is removed by the thyroid gland during hormonal synthesis.

After 24 hours, iodine is also distributed (albeit to a small extent) to various organs, including the liver, blood, and thyroid gland. Iodine crosses the placenta and is excreted in breast milk. (see section 4.6).

After topical, oral or vaginal application, povidone is absorbed to a small extent and does not penetrate the blood-brain barrier and the placenta.

Biotransformation

Iodine is reduced to iodide and concentrated from the bloodstream in the follicular cells of the thyroid gland by the sodium iodide symporter (NIS). Thyrotropic hormone (TSH), stimulates iodine transport from the blood to thyroid cells, iodide oxidation to iodine and iodine binding to tyrosine. The metabolism of povidone is minimal (<0.3%).

Excretion

Iodine, if not absorbed in the thyroid gland, is mainly excreted by the kidneys. Renal clearance of iodine (Cl) is 872.4 ± 119.3 ml/hour with an elimination rate constant (k) of 0.0996 ± 0.009/hour and a half-life of 6.22 hours. Povidone is mainly excreted by the kidneys and in small amounts also with the bile.

5.3 Preclinical safety data

Iodine is an essential element that is necessary for the synthesis of thyroid hormones, and therefore plays an important role in energy metabolism and many other physiological processes. Iodine is ingested through food such as sea fish, seaweed, dairy products, eggs, poultry, and meat. Oral LD50 for mice, rats and guinea pigs is 40-100 g/kg, and intraperitoneal LD50 for mice is 12-15/kg (average molecular weight of povidone 10-30 kDa).
Acute, subchronic and chronic toxicity studies with povidone iodine have revealed toxicity following systemic administration at relatively high doses, so toxicity is not clinically significant.
Genotoxicity
Several in vitro genotoxicity studies have suggested that povidone-iodine may exhibit mutagenic effects, while other studies have shown negative results, including separate in vivo studies. Given the toxicity of povidone-iodine in in vitro test systems, a wealth of evidence suggests that povidone iodine is not genotoxic. No long-term animal studies have been performed to assess the carcinogenic potential of povidone-iodine.
Reproductive and developmental toxicity
Developmental toxicity studies in rabbits showed that a low molecular weight povidone-iodine complex (16 - 75 g/kg/day) caused a dose-dependent decrease in maternal weight gain, and the average weight of the embryo and placenta was lower than in control animals. Embryotoxicity has been demonstrated when povidone-iodine is applied to the vaginal opening of mice. Due to the ability of iodine to pass through the placenta and the sensitivity of the fetus to pharmacological doses of iodine, povidone-iodine should be used in pregnant women only after a thorough medical examination.

6 Pharmaceutical particulars

6.1 List of excipients

Sodium phosphate dibasic
Citric acid
Glycerin
Nonoxynol 9
Purified water

6.2 Incompatibilities

Povidone-iodine is incompatible with reducing agents, with alkaline substances, tannin acid, silver salts, and mercury, hydrogen peroxide, taurolidine (see sections 4.3 and 4.5).
Avoid contact with jewelry, especially items containing silver.

6.3 Shelf life

24 months unopened.
Shelf life 6 months from date of opening.

6.4 Special precautions for storage

Store at a temperature below 25°C, in a dry place, out of the reach of children, protected from light.

6.5 Nature and contents of container

30 ml of 10% for external use solution is filled into the green plastic bottle inserted together with the leaflet in cardboard box.
60 ml of 10% for external use solution is filled into the green plastic bottle inserted together with the leaflet in cardboard box.
100 ml of 10% for external use solution is filled into the green plastic bottle inserted together with the leaflet in cardboard box.
1 liter of 10% for external use solution are filled into white transparent plastic bottles, closed with caps.

6.6 Special precautions for disposal

Any unused product or waste should be disposed of in accordance with local regulations.

7. Marketing Authorisation Holder

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8. Date of first authorisation

27.12.2002

9. Date of revision of the text