SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

BETADINE® VAGINAL DOUCHE

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Povidone-Iodine Ph. Eur. 10% w/v.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BETADINE® Vaginal Douche is indicated for vaginal infections (Intra-Vaginal use). It offers rapid relief of symptoms such as burning or irritation.

It is used as vaginal cleanser for the treatment of vaginitis (inflammation of the vagina) due to candidal, trichomonal, non-specific or mixed infections and for pre-operative disinfection of the vagina.
BETADINE® Vaginal Douche contains Povidone-Iodine, which is broad-spectrum germicide.

4.2 Posology and method of administration

Posology

Paediatric population

BETADINE® Vaginal Douche is contraindicated in pre-puberty children (see section 4.3).

Method of administration

For Intra-Vaginal use. Adults and the elderly.
Use once a day preferably in the morning for up 14 days (including days of the menstrual cycle) or as directed by the doctor.

- Add two measuring capfuls of the concentrate to the squeeze bottle.
- Fill the squeeze bottle with lukewarm water.
- Screw the applicator to the squeeze bottle and shake gently.
- Carefully insert the applicator high into the vagina without causing discomfort. Expel as much cleansing liquid as possible by gentle pressure on the sides of the squeeze bottle, allowing solution to run freely from the vagina.
- Remove the applicator from the vagina allowing air to enter the squeeze bottle, so that it regains its original shape.
- Re-insert the applicator into the vagina squeezing once again to cleanse the vagina thoroughly.
- Repeat until all the **BETADINE® Vaginal Douche** has been used.
- Finally rinse away the excess solution from around the vagina with a clean sponge or a flannel. Dry the vaginal area with a clean cloth or paper towel.
- Rinse clean the empty bottle and applicator in warm water and store for future use.

- If you forget to use your medication, use it as soon as you remember unless it's time for the next application. Then follow the original instructions for use.

BETADINE® Vaginal Douche is well tolerated. It can be removed with water and soap and stains neither the skin nor most fabrics. In most cases marks can be removed from nylon items with a dilute solution of ammonia.

4.3 Contraindications

Contraindicated in:

- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1 .
- Hyperfunction of the thyroid (hyperthyroidism), other manifest thyroid diseases esp. nodular colloidal goitre, endemic goitre, Hashimoto's thyroiditis, as well as before and after radioiodine therapy for hyperthyroidism, until a lasting cure has been obtained.
- Before, during and after radio-iodine administration (see section 4.5).
- Patients with goitre, thyroid nodules, or other thyroid diseases (especially elderly patients) are at risk of developing thyroid hyperfunction (hyperthyroidism) from the administration of large amounts of iodine.
- Not to be used in pre-puberty children.
- Not to be used in patients on concurrent lithium therapy.
- Products containing mercury, should not be used concomitantly due to formation of a substance which can damage the skin.

4.4 Special warnings and precautions for use

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

Avoid solutions containing a vaginal detergent if treating vaginal areas with povidone-iodine.

For vaginal use only. The course of treatment is usually free of any discomfort, but if redness or swelling develop discontinue use.

The product is spermicidal and should not be used when conception is desired.

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

Paediatric population
Keep out of the reach of children.

Special caution is needed in pregnant and breast-feeding patients. In such cases benefit/risk assessment should be performed and povidone-iodine should only be administered if clearly necessary (see section 4.6).

4.5 Interactions with other medicinal products 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 component leads to a weakening effect of both substances. Products containing mercury (see section 4.3), silver, hydrogen peroxide, and taurolidine may interact with povidone-iodine and cause mutual reduction of effects.

Povidone-iodine products when used before or after application of octenidine may lead to transient dark discolourations at the application site.

Due to 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 hemoglobin or glucose in the stool or the urine).

Absorption of iodine from povidone iodine products may lower the iodine uptake of the thyroid. This can lead to interference with various investigations (thyroid scintigraphy, determination of protein-bound iodine (PBI), radioiodine diagnostics) and can make a planned treatment of the thyroid with iodine (radioiodine therapy) impossible. After the end of the treatment, 4 weeks should be allowed before a new scintigram is carried out (see section 4.3).

4.6 Fertility, pregnancy and lactation

Povidone Iodine passes into the placenta and is secreted in breast milk. Thyroid function disorders including congenital hypothyroidism have been reported in the offspring of mothers who have received Iodine.
Povidone Iodine use should be avoided unless the potential benefit to the mother justifies the potential risk to the foetus and neonate or if a safer alternative is unavailable.

Fertility
There are limited human fertility data for Povidone iodine. No data are available on fertility outcomes.

4.7 Effects on ability to drive and use machines

BETADINE® Vaginal Douche has no influence on the ability to drive and use machines.

4.8 Undesirable effects

In single cases acute, generalized, allergic reactions with drop in blood pressure and/or shortness of breath (anaphylactic reactions) have been reported.

Following uptake of large amounts of Povidone-Iodine (e.g., in the treatment of burns), the appearance of additional disorders of electrolyte and serum osmolarity, impairment of renal function with acute renal failure and metabolic acidosis have been described

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

If local irritation, redness or swelling develops, discontinue treatment. Iodine is absorbed from the vagina and following prolonged use thyroid dysfunction may develop. The product may be spermicidal and should not be used when conception is desired.

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 to:
ADR Reporting Website:
www.medicinesauthority.gov.mt/adrportal

4.9 Overdose

Excess iodine can produce goitre and hypothyroidism or hyperthyroidism.

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.

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

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. If no signs of bowel perforation are present, irrigation of the stomach with starch solution via nasogastric tube may be utilized (gastric effluent will turn dark blue-purple and the colour can be used as a guide in determining when lavage can be terminated).

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

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 oxidizable –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 coloration serves as indicator of its effectiveness. Repeated dosing may be required upon discoloration. 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. This product is intended for topical application to the vagina.

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, biological half-life after vaginal administration has been described with approximately 2 days.

Elimination

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

A mutagenic action for Povidone-Iodine can be ruled out. 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 absorbed 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**

Nonoxinol 9, Fleuroma Bouquet 477, Purified Water.

6.2 **Incompatibilities**

The activity of Povidone-Iodine is reduced in the presence of alkali, hydrogen peroxide, taurolidine, tannic acid, acetylsalicylic acid, all silver, bismuth and mercury salts

Compatibility with barrier contraceptives has not been established. Therefore, this product should not be used with such methods of contraception as their reliability may be affected.

6.3 **Shelf life**

3 years.

6.4 **Special precautions for storage**

Store at or below 25°C.

6.5 Nature and contents of container

Supplied in turquoise polyethylene containers with a transparent polyethylene inserts and white high density polyethylene cap. It is also available as **BETADINE® Vaginal Douche Kit,** which contains and an empty squeeze bottle and a vaginal applicator both product are enclosed in printed carton.

Pack size: 125ml, 250ml, 500ml.

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. Marketing Authorisation Holder

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8. Marketing Authorisation Number

MA 197/00107

9. Date of First Authorisation/Renewal of Authorisation

Date of first authorization: 26th May 2006

Date of latest renewal: 21st August 2012

10. Date of (Partial) Revision of the Text

02/2023

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