SUMMARY OF PRODUCT CHARACTERISTICS

1. TRADE NAME OF THE MEDICINAL PRODUCT

BETADINE ® 200 mg pessaries

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pessary contains 200 mg of povidone, iodine (equivalent to 20 mg of available iodine).

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

* pessary

Dark - brown to red, bullet shape pessary.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Betadine pessaries are indicated for acute and chronic vaginal infections (vaginitis) due to mixed infections, non-specific infections, and mycotic (Candida albicans) infections, especially after antibiotic or steroid therapy and Trichomonas vaginalis infections.

4.2. Posology and method of administration

Once a day, at bedtime, in lying position, insert previously wetted vaginal pessary deeply into the vagina. Usual therapy lasts 14 days and may be continued up to 3 weeks if needed. Treatment may start in any time of menstrual cycle, including the days of menstrual bleedings. Since licking out couldn't be always prevented, sanitary pads, but not tampons are recommended.

4.3. Contraindication

Betadine pessaries are contraindicated in case of:

- Hypersensitivity to Povidone Iodine or iodides;
- Hyperthyroidism;
- Dermatitis herpetiformis –Duhring;
- Before and after radioiodotherapy.

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4.4. Special warnings and special precautions for use

Regular or prolonged use should be avoided in patients with lithium therapy, renal failure and thyroid disease.
Povidone Iodine is not recommended for use in patients with renal failure due to its potential for hazards of metabolic acidosis and nephrotoxicity.
Povidone Iodine is not recommended for use in patients with hepatic failure.
Betadine pessaries are for vaginal use only.
If signs of local intolerance occur (irritation, sensitivity), the therapy should be discontinuated and physician should be consulted if needed.

Special notes
Brown coloration of Povidone Iodine indicates the efficacy of preparation. Decoloration of preparation signifies diminishing of its activity.
Concomitant administration of Povidone Iodine may perturb thyroid scintigraphycs. A period of 1-2 weeks without Povidone Iodine treatment is necessary before thyroid scintigraphic.

4.5. Interaction with other medicaments and other forms of interaction

Povidone iodine pessaries should not be used with preparations containing chlorhexidine, Ag-sulfadiazine, alkalis and mercury, hidrogen-peroksid, taurolidin because partial inactivation may occur.
In patients treated with Lithium concomitant administration of povidone iodine, exhibits synergistic hypothireotic effect.

4.6. Pregnancy and lactation

The potential exists for possible abnormalities in development and for possible congenital hypothyroidism and/or goiter in infants maternally exposed to PVP-Iodine.
Iodine is concentrated in breast milk, reaching breast milk total Iodine concentrations up to 8-times higher than maternal serum levels; use during pregnancy or while nursing except with physician approval is not recommended.
Iodine-induced alterations in thyroid function may occur in newborn infants after prenatal and perinatal exposure to Povidone-Iodine.

4.7. Effects on ability to drive and use machines

Povidone Iodine does not affect driving ability or operating machinery.

4.8. Undesirable effects

The adverse effects of Betadine pessaries are rare.
Most common are local irritation, itching, and burning.
Cases of hypothyroidism and hyperthyroidism are reported.
Extensive and long-term treatment of Povidone Iodine may cause neutropenia.
The product may be spermicidal and should not be used when conception is desired.

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4.9. Overdose

Overdosage of Betadine pessaries is manifested with symptoms associated with iodine toxicity

(fever, diarrhea, metabolic acidosis and abnormal thyroid function).
In case of manifest Iodine-induced hyperthyroidism due to iodine therapy, thyreostatic therapy, plasmaferesa or thyroidectomy may be necessary.

5. PHARMACOLOGICAL PROPERTIES

Pharmaco-therapeutical group: Gynecological antiinfective and antiseptic
ATC code: G01AX11

5.1. Pharmacodynamic properties

Povidone Iodine is known to be a powerful broad-spectrum germicidal agent effective against a wide range of bacteria, viruses, fungi, protozoa, and spores.
PVP Iodine acts against bacteria (Gram positive and Gram negative) including Eschericia coli, Proteus spp., Salmonella typhimurium, Staphylococcus aureus, Staphylococcus albus, Shigella sonnei, Streptococcus haemolythicus (A, B, C, D), Clostridium spp, Bacillus subtillis etc, as well as bacterial spores (Bacillus spp. and Clostridium spp.). PVP Iodine acts against Aspergilus flavus, Aspergilus niger, Candida albicans and Penicillium spp., as well as their spores. PVP-Iodine is effective against protozoa (Trichomonas vaginalis) and viruses (Herpes simplex, Rubeolla, Vaccinia, Poliovirus, Trachoma, Rabbies and Mixoma viruses).
Povidone Iodine is superior to chlorhexidine gluconate, alkyldiamino-ethylglycine hydrochloride, and benzalkonium chloride for killing organisms responsible for nosocomial infections (methicillin resistant Staphylococcus aureus, Serratia marcescens, Pseudomonas aeruginosa, and Burkholderia cepacia). Povidone Iodine is also effective against strains known to be resistant to antiseptics. Most organisms do not develop resistance to elemental Iodine.
An iodophor, Povidone Iodine is a combination of a complex of Iodine with a solubilizing agent or carrier that liberates free Iodine in solution. Povidone Iodine is a complex of Iodine with polyvinylpyrrolidone. Iodophors are widely used at the present time for the purpose of sanitization.
Free Iodine with its oxidative property reacts with -SH or -OH amino acid radicals in microorganism's enzymes and structure proteins, which is its mechanism of action. This non-specific mechanism of action explains the efficacy of PVP Iodine against broad spectar of microorganisms (bacteria, funges, virus, protozoa).
Different organic substances (blood, pus, etc) decrease the efficacy of iodine.

5.2. Pharmacokinetic properties

PVP is a flexible molecule with rigid trodimensional configuration. It hydrophilic and lipophobic properties and the transmembranic pass is possible via pores or pinocytose.
Resorption of PVP depends of molecular weight. After oral or intraduodenal application of PVP having molecular weight of 40.000, negligible quantities are detected in the blood, urine and bile. The marked PVP-I^{131} having a molecular weight of 40.000 is being slightly absorbed from vaginal mucous.
Absorption of Iodine from Povidone Iodine solution is possible after a long term treatment, application on large areas, open wounds and frequent application. The absorption of Iodine results with an elevated blood Iodine concentration, thyroid dysfunction, nephrotoxicity, metabolic acidosis and elevated Iodine excretion in urine.
PVP has complex elimination kinetics. It is mainly eliminated via kidneys and the renal passage limit of PVP is a molecular weight higher than 35-40.000. The T/2 of elimination in

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healthy volunteers for PVP-I^{131} is 11-15 hours.

5.3. Preclinical safety data

Subchronic and chronic toxicity studies in rats had shown reversible and dose dependent elevations of PBI (protein binding Iodine) in serum and nonspecific hystopathological changes in thyroid gland. Preclinical safety data concerning mutagenicity, teratogenicity and embriotoxicity exclude Povidone Iodine toxicity. Cancerogenic potential could not be excluded, because long-term carcinogenic studies are not carried out. Iodine is susceptible to modify fetal thyroid function, because of possible placental distribution.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Macrogol 100

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

Four (4) years.

6.4. Special precautions for storage

To be stored at a temperature below 25^0C.

6.5. Nature and contents of container

PVC/PE strip (alveolus shape), each contains 7 pessaries.
The carton box containing 14 pessaries (2-two strips) and a patient information leaflet inside.

6.6 Special precautions for disposal and other handling

No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER

ALKALOID AD – Skopje
Blvd. Aleksandar Makedonski 12
1000 Skopje, Republic of Macedonia
under the licence:
MUNDIPHARMA AG, Basel, Switzerland

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8. MARKETING AUTHORIZATION NUMBER

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

10. DATE OF (PARTIAL) REVISION OF THE TEXT

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15.04.2016