SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Betadine 5% w/w Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Povidone-iodine 5% w/w

Excipients with known effect :

Cetostearyl alcohol

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream

Reddish-brown viscous cream

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Betadine Cream is indicated for treatment and prevention of infections in minor wounds (cuts and abrasions) and burns.

4.2 Posology and method of administration

For topical use only

Posology:

Betadine Cream is only intended to be applied to the skin. Clean and dry the wound area before application. The amount applied depends upon the size of the wound. Apply a small pea sized amount to the affected area (once or twice daily) up to a maximum of 7 consecutive days. If required, a dressing or bandage can be applied.

Method of administration:

Do not use if the tamper evident seal is broken.

The dose recommended should not be exceeded. The maximum daily application should not exceed over 1% of the total body surface area.

Age	**Maximum Recommended Dose**
Infants and children less than 2 years of age	Consult a doctor
Children 2-6 years	1-2 small pea sized amount each day
Children 7-8 years	2 small pea sized amount twice a day
Children 9-12 years	3 small pea sized amount twice a day
Children 13-18 years	5 small pea sized amount twice a day
Adults	8-9 small pea sized amount twice a day

4.3 Contraindications

Betadine Cream should not be used in:

- Hypersensitivity to iodine or povidone or to any of the excipients listed in section 6.1.
- Thyroid dysfunction.
- During radioiodine scintigraphy or radioiodine treatment. An interval of at least 4 weeks is required prior to or after radioiodine investigations/treatments (see section 4.5).
- Products containing mercury, should not be used concomitantly due to formation of a substance which can damage the skin.
- Children below the age of 1.

4.4 Special warnings and precautions for use

Betadine cream may cause local skin reactions (e.g.contact dermatitis), see section 4.8.

In instance of skin irritation, contact dermatitis or hypersensitivity discontinue use. Povidone-iodine use could lead to transient skin discolouration at the application site caused by the drug products own colour.

Do not smoke or go near naked flames – risk of severe burns. Fabric (clothing, bedding, dressings, etc.) that has been in contact with this product burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product buildup but not totally remove it.

Do not use in Children less than 2 years old, or if you are pregnant or breastfeeding, unless advised to do so by your doctor.

In such cases benefit/risk assessment should be performed and povidone-iodine should only be administered if clearly necessary (see section 4.6).
For external use only.

4.5 Interaction 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 components leads to a weakening effect of both substances.

Products containing mercury, 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 discolorations at the application sites.

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

Absorption of iodine from povidone iodine cream may lower the radioiodine uptake of the thyroid. This can lead to interference with various investigations (thyroid scintigraphy, determination of protein-bound iodine (PBI), radioiodine diagnostics) and can interfere with treatment of the thyroid with iodine (radioiodine therapy). 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

Pregnancy

There is insufficient data on the use of povidone iodine during pregnancy. Animal studies are limited with respect to reproductive toxicity (see section 5.3). Absorbed iodine has been shown to cross the placental barrier, and during pregnancy, Betadine Cream, should only be used if the clinical condition of the woman requires treatment with povidone iodine.

Breastfeeding

Absorbed iodine is excreted in breast milk to such an extent that effects on breastfed newborns are likely. Iodine can be concentrated in breast milk, compared to serum and may induce transient hypothyroidism with elevation of TSH (thyroid stimulating hormone) in the newborn. In these cases, a check of the child’s thyroid function may be necessary. Betadine Cream should not be used during breastfeeding.

Fertility

There are no data on the effects of povidone iodine on fertility.

4.7 Effects on ability to drive and use machines

Betadine Cream has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The following frequencies are the basis for assessing undesirable effects:

- Very common (≥ 1/10)
- Common (≥ 1/100 to < 1/10)
- Uncommon (≥ 1/1,000 to <1/100)
- Rare (≥ 1/10,000 to < 1/1,000)
- Very rare (<1/10,000)
- Not known (cannot be estimated from the available data)

Immune system disorders

Rare	Hypersensitivity
Very rare	Anaphylatic reaction

Endocrine disorders

Very rare	Hyperthyroidism (sometimes with symptoms such as tachycardia or restlessness) *
Unknown	Hypothyroidism ***

Metabolism and nutrition disorders

Unknown	Electrolyte imbalance **
	Metabolic acidosis **

Skin and subcutaneous disorders

Rare	Contact dermatitis (with symptoms such as erythema, small blisters and pruritus)
Very rare	Angioedema
Not known	Skin discolouration

Renal and urinary disorders

Unknown	Acute renal failure**, Blood osmolarity abnormal**

* In patients with a history of thyroid disease (see under Special Warnings and Special Precautions for Use) following a notable uptake of iodine

** May occur following uptake of large amounts of povidone iodine (e.g. in the treatment of burns)

*** Hypothyroidism following prolonged or extensive use of povidone iodine

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. Doctor or healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

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

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.

Treatment is symptomatic and supportive.

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 utilised (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 venous haemodiafiltration is less effective than haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiseptics, ATC code: D08AG02

Mechanism of action

Povidone-iodine is a complex of elemental iodine (I2, the active moiety) and the synthetic polymer povidone, (PVP), which acts as a sustained release reservoir of iodine (PVP does not have any intrinsic antibacterial activity) and also enables easier contact of iodine to cell membranes. As povidone-iodine comes in contact with the skin and mucous membranes, iodine dissociates from the povidone-iodine polymer complex; it is the free iodine that rapidly causes microbicidal activity, whereas iodine bound to the polymer serves as an iodine reservoir. This gradual release of iodine reduces the drawbacks associated with the presence of elemental iodine and maintains its highly effective microbiocidal activity. The free iodine rapidly penetrates microorganisms and attacks the key groups of proteins, amino acids, nucleotides and unsaturated fatty acids. It reacts with thiol, sulfhydryl and hydroxyl groups of the amino acids in the enzymes and structural proteins of the microorganisms thereby oxidising them.

Pharmacodynamic effects

Povidone-iodine has demonstrated a rapid anti-bacterial (gram positive and gram negative), anti-fungal and viricidal activity (enveloped and non-enveloped viruses). No development of resistance has been observed for povidone-iodine, during >60 years of extensive use in hospitals, dental and medical practices. Povidone-iodine remains effective against antibiotic resistance micro-organisms and there is no change in its sensitivity.

5.2 Pharmacokinetic properties

This product is only intended for topical application.

Absorption

The pharmacokinetics of povidone-iodine are influenced by the dissociation of povidone, a large hydrophilic molecule and iodine, a small lipophilic molecule and its subsequent reduction to iodide in the body.

Distribution

Absorbed iodine/iodide is distributed throughout the body via the circulatory system. A portion (approximately 30%) is removed by the thyroid for hormonal synthesis. Iodine is also distributed (albeit to a minor extent) to different organs including liver, blood and thyroid gland after 24 hours.

Povidone is negligibly absorbed following topical application.

Metabolism

Iodine is reduced to iodide and is concentrated from the blood stream into the thyroid follicular cell through the action of the sodium/iodide symporter (NIS). The thyroid -stimulating hormone (TSH) stimulates iodide transport from the blood into thyroid cells, oxidation of iodide to iodine and iodine binding to tyrosine. The metabolism of povidone is minimal (< 0.3%).

Excretion

Iodine, unless utilised in the thyroid, is excreted mainly *via* urine. Little inorganic iodide is lost in faeces. Small amount is excreted *via* bile. Iodine crosses the placenta and is also excreted in breast milk.

The excretion of povidone is mainly *via* urine and in a small amount also *via* bile. Povidone does not cross the placenta and is not excreted in breast milk.

5.3 Preclinical safety data

Acute and chronic toxicity

Acute, subchronic and chronic toxicity studies with povidone-iodine show toxicity, following systemic administration, at relatively high doses and as such the toxicity is not considered relevant to clinical use.

Genotoxicity

Several *in vitro* genetic toxicology studies suggest that povidone-iodine may be mutagenic, while other studies have shown negative findings, including separate *in vivo* studies. Taking into account the toxicity of povidone-iodine to the *in vitro* test systems, the weight of evidence suggests that povidone-iodine is not genotoxic. No long-term studies in animals have been conducted to evaluate the carcinogenic potential povidone-iodine.

Reproductive and developmental toxicity

Developmental oral toxicity (teratology) studies in the rabbit indicate that a low molecular weight povidone-iodine complex (16-75 mg/kg/day) caused a dose dependent decrease in body weight gain in the mother. The dams showed a dose dependent loss of weight increase and the average embryo and placenta weights were lower than those of the control animals. This study did not reveal any teratogenic effects.

In a study in the rat, following administration of iodine, the NOAEL was < 28 mg/kg/day for F0 and F1 due to diminished milk secretion and decreased survival of pups. No other effects were reported. Following administration of iodine via drinking water for 100 days in the rat, T3 significantly decreased and T4/T3 significantly increased at 10 mg/kg/day.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cetostearyl Alcohol
White Soft Paraffin
Sodium Hydroxide
Liquid Paraffin
Glycerol (E422)
Sorbitan Stearate
Macrogol Stearate
Polysorbate 60
Potassium Iodate
Purified Water

6.2 Incompatibilities

Povidone-iodine should not be used together with alkali, hydrogen peroxide, taurolidine, tannic acid, and silver and mercury salts.

6.3 Shelf life

3 years
After first opening: 3 months

6.4 Special precautions for storage

Store below 25°C

6.5 Nature and contents of container

Supplied in lacquered aluminium tubes, containing 40 g of the product.

The tubes are enclosed in printed cartons.

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

Taw Pharma (Ireland) Limited
104 Lower Baggot Street
Dublin 2
D02 Y940
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

PL 58442/0003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12/04/2024

10 DATE OF REVISION OF THE TEXT

31/10/2024