Summary of Product Characteristics

Azonit® 10 mg/1 gm) Cream
Isoconazole nitrate

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1. Name of the medicinal product

Azonit® 10mg/1 gm Cream.
Isoconazole nitrate Cream.

2. Qualitative and quantitative composition

Azonit® 10mg/1 gm Cream: Each 1 gm cream contains 10 mg Isoconazole nitrate.

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Azonit® 10mg/1 gm Cream: Each 1 gm cream contains 10 mg Isoconazole nitrate.

Azonit® cream is homogenous white cream, packed in collapsible aluminum tubes, intended for topical use.
Pack size: 20 gm

Azonit® Vaginal Cream is homogenous white cream, packed in collapsible aluminum tubes, intended for topical use.
Pack size: 40 gm

4. Clinical particulars

4.1 Therapeutic indications

Superficial fungal skin infections such as tinea pedis, tinea manuum, tinea cruris (fungal infections of the inguinal and genital regions) and erythrasma. A medical prescription is required for infections involving the genital region.

4.2 Posology and method of administration

Azonit® Cream is applied once daily to the infected areas of skin.
For fungal infections, topical treatment over a period of 2-3 weeks is generally required, or even 4 weeks in the case of stubborn infections (especially when the interdigital spaces are involved). Depending on the clinical presentation, longer periods of treatment are also possible.
In order to prevent recurrences, treatment should be continued for at least another 2 weeks after the clinical symptoms have resolved.
For fungal infections of the vagina, **Azonit®** vaginal cream must be applied once daily using the applicator for seven consecutive days. The applicator must be inserted deep into the vagina. Treatment should not be carried out during menstruation.
To avoid reinfection, concurrent treatment of the partner with **Azonit®** cream is recommended, all personal towels, underwear should be changed daily and boiled.
Fungal infections are very stubborn and have a protracted course. For treatment to be successful, you must apply **Azonit®** Cream regularly and follow the recommended cleaning routine:
It is important to dry the infected areas of skin thoroughly after washing, particularly the spaces between the toes, and to change your socks every day. Shoes should be aired well after being worn.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

If used on the face, **Azonit®** Cream should not be allowed to come into contact with the eyes.
To prevent reinfection, the patient's personal linen (flannel, towel and - preferably cotton - underwear) should be changed and boil-washed daily.
It is often advisable to place a strip of gauze smeared with **Azonit®** Cream between the toes or fingers if these areas are affected.
A regular and careful cleaning routine is vital to the success of treatment. In the case of tinea pedis, the spaces between the toes must be dried thoroughly after washing and socks and stockings must be changed every day.
Cetostearyl alcohol can cause local skin reactions (e.g. contact dermatitis).
For **Azonit®** Vaginal cream, some of its ingredients may cause damage to latex products such as condoms or diaphragms. Therefore, these may no lo longer be effective as contraception or as protection against sexually transmitted diseases such as HIV.

4.5 Interaction with other medicinal products and other forms of interaction

No interactions have been documented to date.

4.6 Pregnancy and lactation

Data on the use of isoconazole-containing products during pregnancy indicate no teratogenic risk in humans.
Effective quantities of isoconazole are unlikely to be secreted in breast milk.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Local symptoms such as itching, burning, erythema or vesicle formation can occur in isolated cases under treatment with Isoconazole.
Allergic skin reactions can occur.

4.9 Overdose

Results from acute toxicity studies show that no risk of acute intoxication exists following a single application of a topical overdose (application to a large area under favourable absorption conditions) or following accidental oral ingestion.

5. Pharmacological properties

Pharmacotherapeutic group: Antifungals for topical use
ATC Code: D01AC
Isoconazole nitrate is intended for the treatment of superficial fungal skin infections. It exhibits a very broad spectrum of antimicrobial activity. It is active against

dermatophytes and yeasts, yeast-like fungi (including the organisms which cause pityriasis versicolor), moulds and the organisms which cause erythrasma.

5.2 Pharmacokinetic properties

Isoconazole penetrates the skin rapidly. The peak active ingredient concentrations in the skin were reached after just 1 hour and persisted for at least 7 hours (stratum corneum: approx. 3,500 µg/ml ± 7 mmol/l, living epidermis: approx. 20 µg/ml ± 40 µmol/l, dermis: approx. 3 µg/ml ± 6 µmol/l). Removal of the stratum corneum before application resulted in an approximately twofold increase in the concentrations of isoconazole in the living skin. The active ingredient concentrations in the stratum corneum and the epidermis exceeded the minimum inhibitory concentration and the biocidal antimycotic concentration for the main disease pathogens (dermatophytes, moulds and yeasts) several times over and achieved these levels in the dermis.

Isoconazole is not metabolically inactivated in the skin. Systemic exposure following absorption through the skin is low. Even following removal of the stratum corneum, less than 1% of the applied dose was absorbed over an exposure time of 4 hours.

The fraction absorbed through the skin was too small to enable the metabolism of isoconazole nitrate in the human body to be studied.

Study of metabolism following intravenous administration

0.5 mg ^{3}H-labelled isoconazole nitrate was administered by intravenous injection. Isoconazole was broken down completely and eliminated rapidly.

2,4-dichloromandelic acid and 2-(2,6-dichlorobenzyloxy)-2-(2,4-dichlorophenyl)acetic acid were described as the quantitatively most important metabolites. One third of the labelled substances were eliminated with the urine and two thirds were excreted with the bile. Seventy-five percent of the total dose was eliminated within just 24 hours.

5.3 Preclinical safety data

The results of repeated dose toxicity studies yielded no evidence of specific health risks which might be associated with the therapeutic use of Isoconazole.

In vitro and *in vivo* studies to detect gene and chromosome mutations yielded no evidence of mutagenic potential associated with isoconazole. No *in vivo* carcinogenicity studies have been conducted. On the basis of current knowledge, no evidence of isoconazole-related tumorigenic potential can be derived from the results of mutagenicity testing, repeated dose toxicity studies or from the chemical structure and biochemical mechanism of action of the substance.

In a series of special reproduction toxicity studies, isoconazole exhibited no adverse effects on the individual phases of the reproductive cycle. Above all, there was no evidence of teratogenic potential.

According to the results of local tolerability studies on the skin and mucous membranes, no significant local irritation is to be expected under therapeutic conditions. Based on the results of studies in the rabbit eye, conjunctival irritation is to be expected following accidental contamination of the eye.

6. Pharmaceutical particulars

6.1 List of excipients
Mineral oil, white petrolatum, cetostearyl alcohol, polysorbate 60, edetate disodium, methyl paraben, butylated hydroxyanisole, propylene glycol, distilled water.

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
Azonit® cream: 2 years
Azonit® Vaginal Cream: 3 years

6.4 Special precautions for storage
Store below 30°C.

6.5 Nature and contents of container
Azonit® cream is homogenous white cream, packed in collapsible aluminum tubes, intended for topical use.
Pack size: 20 gm

Azonit® Vaginal Cream is homogenous white cream, packed in collapsible aluminum tubes, intended for topical use.
Pack size: 40 gm

6.6 Special precautions for disposal and other handling
No special requirements.

7. Marketing authorisation holder
Pharma International Company
Amman - Jordan
Tel: 00962-6-5158890 / 5157893
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email: marketing@pic-jo.com

8. Marketing authorisation number(s)
Azonit cream:
Registration Number: 284/2002
Re-Registration Number: 2009/ت ع /223

Azonit vaginal cream:
Registration Number: 151/2003
Re-Registration Number: 2016/BG/ت ع 37

9. Date of first authorisation/renewal of the authorization
Azonit cream:
Registration Date: 16/10/2002
Re-Registration Number: 20/07/2009

Azonit vaginal cream:
Registration Number: 12/06/2003
Re-Registration Number: 07/04/2016

10. Date of revision of the text
07/2017