

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Travogen - cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g cream contains 10 mg isoconazole nitrate.

(Equivalent to 1% (w/w) isoconazole nitrate.)

1 cm Travogen cream contains 2 mg isoconazole nitrate

Excipient with known effect: 50 mg/g cetostearyl alcohol

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream

White to slightly yellowish transparent cream

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Superficial fungal infections of the skin, such as tinea pedum et manuum, tinea inguinalis, of the genital region and erythrasma. A medical prescription is required when the product is used in the genital region.

4.2 Posology and method of administration

Method of administration

Cutaneous use.

Posology

Travogen cream should be applied once daily on the affected portions of the skin.

A general rule that applies to all fungal infections is that topical treatment must be performed over a period of 2-3 weeks, and in cases of persistent infection (especially when the interdigital spaces are affected), even for 4 weeks. Depending on the symptoms, topical treatment may be used for longer periods of time.

To avoid renewed infection, the treatment should be continued for at least 2 weeks after clinical healing.

Paediatric population

Data on a limited number of infants, toddlers, children and adolescents indicate no negative effects with the use of Travogen cream. Currently available data are described in section 5.1; however, no dosage recommendation can be given.

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

When using Travogen cream on the face, it should be ensured that the cream does not come into contact with the eyes.

The physician should provide the patient with information on hygienic measures during use.

If Travogen cream is used in the genital region, the components liquid paraffin and soft paraffin may, if latex products such as barrier methods, e.g. condoms and diaphragms, are used at the same time, damage these and hence compromise their effectiveness.

Cetostearyl alcohol may cause local skin reactions (e.g. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy

Experience concerning the use of isoconazole-containing preparations during pregnancy has indicated no teratogenic risk in humans. Isoconazole should be used only after careful benefit/risk assessment during pregnancy, especially during the first trimester.

Breast-feeding

It is unknown whether isoconazole is excreted in human milk.

A risk for the breast-fed infant cannot be excluded. Isoconazole should therefore be used only after careful benefit/risk assessment during breastfeeding.

In breast-feeding mothers, Travogen cream must not be used in the breast region, so as to prevent absorption of Travogen by the breast-fed infant.

Fertility

Preclinical data have revealed no risk to fertility.

4.7 Effects on ability to drive and use machines

No influence on the ability to drive and use machines has been observed in patients receiving treatment with Travogen.

4.8 Undesirable effects

In clinical studies, the most commonly occurring adverse reactions with Travogen were burning and irritation at the application site.

The frequency of adverse reactions occurring in clinical studies and described in the following table is defined as follows, according to the MedDRA convention:

Common	≥1/100 to <1/10
Uncommon	≥1/1,000 to <1/100
Rare	≥1/10,000 to <1/1,000
Not known	frequency cannot be estimated from the available data

For adverse reactions derived solely from post-marketing data, frequency cannot be estimated and hence they are listed under “not known”.

System organ classes	Common	Uncommon	Rare	Not known
General disorders and administration site conditions	In the application site area: burning, irritation	In the application site area: dryness pruritus	In the application site area: swelling fissure	In the application site area: erythema blisters
Skin and subcutaneous tissue disorders		Weeping eczema dyshidrosis contact dermatitis		Allergic skin reaction

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 the ADR Reporting Website:

www.medicinesauthority.gov.mt/adrportal

4.9 Overdose

Results of acute toxicity studies show that there is no acute risk of intoxication after single dermal application of an overdose (application over a large surface under favourable absorption conditions) or accidental ingestion.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antifungals for topical use.

Imidazoles and triazole derivatives

ATC code: D01AC05

Isoconazole and its salt, isoconazole nitrate, are indicated for the treatment of superficial fungal infection of the skin. It has a very wide antimicrobial spectrum of action. It acts on dermatophytes and yeasts, yeast-like fungi (including the pathogen of pityriasis versicolor) and mould fungi, as well as Gram-positive bacteria *in vitro* and pathogens of erythrasma.

Paediatric population

17 studies (13 of which randomised, double-blind) provide data on the use of Travogen cream in 143 infants and toddlers (aged 1 month and older), children and adolescents. The duration of use ranged from 2 to 6 weeks. The safety and efficacy profile seems to be comparable to that of adults.

Age distribution and efficacy outcomes are presented in the following table:

Infants and toddlers	Children	Adolescents	Total	Age (years)*	
(1-23 months) n (%)	(2≤ - <12 years) n (%)	(12≤ - <18 years) n (%)	n(%)	Mean	Median
15 (10.5)	54 (37.8)	74 (51.7)	143 (100) (65 women/78 men)	10.2	12

Efficacy				
11 (73.3)	37 (68.5)	57 (77.0)	105 (73.4)	very good (resolved)
3 (20.0)	9 (16.7)	13 (17.6)	25 (17.5)	good
1 (6.7)	3 (5.6)	2 (2.7)	6 (4.2)	moderate
0	5 (9.2)	2 (2.7)	7 (4.9)	low

*Age definition according to ICH E11

5.2 Pharmacokinetic properties

Isoconazole in Travogen cream rapidly penetrates the human skin, reaching peak active substance concentrations in the stratum corneum, as well as in living skin, as early as 1 hour after application. High concentrations were maintained for at least 7 hours: stratum corneum -about 3500 µg/mL (equivalent to 7 mmol/L), living epidermis - about 20 µg/mL (40 µmol/L) and dermis - about 3 µg/mL (6 µmol/L). Removal of the stratum corneum before application increased isoconazole concentrations in living skin by a factor of about 2. Drug concentrations in the stratum corneum and epidermis were more than several-fold higher than the inhibitory and biocidal antifungal concentrations (MIC) for the most important pathogens (dermatophytes, mould fungi and yeasts) and achieved MIC values in the dermis.

In another study, isoconazole nitrate could still be detected above the MIC in the stratum corneum and hair follicles after one week following completion of a 2-week period of use. In some subjects, isoconazole nitrate could still be detected 14 days after the last application.

Isoconazole is not metabolically inactivated in the skin. The systemic burden of percutaneous absorption is low. Even after removal of the stratum corneum, less than 1% of the applied dose was absorbed after an exposure time of 4 hours.

The percutaneously absorbed portion was too low to investigate biotransformation of isoconazole within the human organism.

Investigation of biotransformation after intravenous administration

0.5 mg ³H-labelled isoconazole nitrate was injected intravenously. Isoconazole is fully metabolised and is excreted rapidly.

2.4 2-chloromandelic acid and 2-(2,6-dichloro-benzyloxy)-2(2,4-dichlorophenyl)acetic acid) have been reported to be the most important metabolites in quantitative terms. One third of the labelled substances were eliminated with the urine and two thirds through bile; as much as 75% of the total dose was excreted within 24 hours.

5.3 Preclinical safety data

No *in vivo* carcinogenicity studies have been conducted. According to the present state of knowledge, there is no evidence of a tumorigenic potential of isoconazole to be derived from the results of mutagenicity tests, repeated-dose toxicity studies, the chemical structure or its biochemical mechanism of action.

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction.

According to the results of local compatibility tests on the skin and mucous membranes, no significant local irritation may be anticipated under therapeutic conditions. In view of the results obtained from investigations on the rabbit eye, conjunctival irritation may be expected after accidental contamination of the eye.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

White soft paraffin
Liquid paraffin
Cetyl stearyl alcohol
Polysorbate 60
Sorbitan monostearate
Purified water

6.2 Incompatibilities

None

6.3 Shelf life

5 years
After opening, use within 3 months.

6.4 Special precautions for storage

Do not store above 25°C.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Tubes made of pure aluminium, inner layer made of epoxy resin, outer layer on a polyester base, heat-sealable lacquer on a polyamide base in the tube fold, screw cap made of high-density polyethylene.

Pack sizes: Tubes of 15g & 30 g.

6.6 Special precautions for disposal

No special requirements.

7. Parallel Import License Holder

Neofarma Pharmaceuticals Ltd, 42-46, Mill Street Qormi QRM 3105, Malta

8. PARALLEL IMPORT LICENCE NUMBER

PI908/03801A

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27th February 2012 / 27th February 2022

10. DATE OF REVISION OF THE TEXT

27-02-2022