IIT004-00 - Page 1 + 2 - 148 x 210 mm – DRA_90040

Travogen® cream 1%

Broad-spectrum antimycotic

063330-XX

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Manufactured by
LEO Pharma Manufacturing Italy S.r.l.
Important information, please read carefully

Qualitative and Quantitative Composition
1 g Travogen Cream contains 10 mg Isoconazole nitrate (equivalent to 1% (w/w) isoconazole nitrate).

Pharmaceutical Form
White to slightly yellowish opaque cream.

Indications
Superficial fungal infections of the skin, e.g. in the region of the hands, the interdigital spaces of the feet, and in the inguinal and genital regions.

Dosage and Administration
Cutaneous use. Travogen should be applied once daily to the affected areas of skin.
A general rule for fungal infections is that topical therapy be continued for a period of two to three weeks, and for four weeks in refractory infections (particularly infections of the interdigital spaces). Longer period of treatment are also possible.
To avoid recurrence, treatment should be continued for at least another two weeks after clinical healing.

Contraindications
None so far known.

Interaction with other medicament
No interaction studies have been performed.

Special warnings and special precautions for use
Travogen should not be allowed to come into contact with the eyes when being applied to the face.
The physican should advise the patients on hygienic measures and skin care, if applicable, during the treatment.
If Travogen cream is applied to the genital region, the excipients liquid paraffin and soft paraffin may cause damage of latex products for barrier methods such as condoms and diaphragms used concomitantly, thus impairing their effectiveness.

Fertility, pregnancy and lactation
It has been shown in animal studies that there were no adverse effects on birth and lactation, and on the fertility and reproductive functions. Hence based on these studies, no teratogenic risk is to be expected in humans after topical use of isoconazole nitrate -containing preparations during pregnancy.
It is unknown whether isoconazole/isoconazole nitrate is excreted in human milk. A risk of exposure to the suckling child cannot be excluded.
Nursing mothers should avoid application to the nipples, to prevent ingestion of Travogen by the suckling child.
Preclinical data did not indicate any risk on fertility.

Effects on ability to drive or use machines
Isoconazole nitrate has/have no influence on the ability to drive or use machines.

Undesirable Effects
Summary of the safety profile
In clinical studies, most frequently observed adverse reactions included application site burning and application site irritation with Travogen.

Tabulated list of adverse reactions
Frequencies of adverse reactions observed in clinical studies and given in the table below are defined according to the MedDRA frequency convention: common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); frequency not known (cannot be estimated from the available data). The ADRs identified only during post-marketing surveillance, and for which a frequency could not be estimated, are listed under “not known”.

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System Organ Class	Common	Uncommon	Rare	Frequency not known
General disorders and administration site conditions	Application site: - irritation, - burning	Application site: - dryness, - pruritus	Application site: - swelling - fissure	Application site: - erythema, - vesicles
Skin and subcutaneous tissue disorders		Eczema weeping Dyshidrosis Dermatitis contact		Allergic skin reaction

Mock-up Approval Stamp (MAS)

4. PROOF FROM HSI	Graphic Design	Editorial Proof	Second Approver
Date 09/07/19			
New proof requested ☐	**According to:** SOP_000647, SOP_000962, SOP_003993 and SOP_008676 ☐	**According to:** SOP_000647, SOP_000962 and SOP_008676 ☐	Product name ☐
Sign.:			Dosage form ☐
			Strength/Stripes ☐
Date:	1st Sign.: Date:	Sign.: Date:	Pack size ☐
			Prompts ☐
	2nd Sign.: Date:		Material No./Reg. No. ☐
			Barcode ☐
			Sign.: Date:

Pharmacodynamic properties
Pharmacotherapeutic group: Imidazole and triazole derivatives
ATC Code: D01AC05
Isoconazole and its salt isconazole nitrate is for use in the treatment of superficial fungal diseases of the skin. It displays a very broad spectrum of antimicrobial action. It is effective against dermatophytes and yeasts, yeast-like fungi (including the causative organism of pityriasis versicolor) and molds, as well as against the gram-positive bacteria *in-vitro* and against the causative organism of erythrasma .

Pharmacokinetic properties
Isoconazole penetrates rapidly into human skin from Travogen cream and reaches maximum drug concentrations in the horny layer and in the living skin 1 hour after application. High concentrations were maintained for at least 7 hours (horny layer: approx. 3500 µg/ml corresponding to 7 mmol/l, living epidermis approx. 20 µg/ml (40 µmol/l), dermis approx. 3 µg/ml (6 µmol/l). Removal of the horny layer prior to the application increased isoconazole concentrations in the living skin approximately by a factor of 2. Drug concentrations in the horny layer and the epidermis exceeded minimum inhibitory and biocidal antimycotic concentrations (MIC) of most important pathogens (dermatophytes, molds and yeasts) several fold and reached (MIC) values in the dermis.
In a further study, isoconazole nitrate could still be detected above the MIC in the stratum corneum and the hair follicles at one week after termination of a two-week application period. In some subjects, isoconazole nitrate could even be detected 14 days after the last application.
Isoconazole is not metabolically inactivated in the skin. Systemic load due to percutaneous absorption is low. Even after removal of the horny layer less than 1% of the applied dose has reached the systemic circulation within 4 hours exposure time.
The percutaneously absorbed portion was too low to permit investigating the fate of isoconazole within the human organism.

Investigation of metabolism after intravenous administration
After intravenous administration of ^{3}H-ICN to rats and dogs radiolabeled substances (parent drug and all metabolites) were mainly excreted by the biliary pathway. Within 24 hours after administration approximately 85% respectively 80% of the dose were already excreted within 24 hours. In the rat / dog approximately 5 / 7.5% of the recovery were excreted with the urine and 95 / 92.5% with the bile. The bile was also the main excretion pathway for radiolabeled substances after dermal application ^{3}H-ICN to guinea pigs and dogs. This was also confirmed in two humans: after intravenous administration of 0.5 mg^{3}H-ICN one third of radiolabeled substances were excreted with the urine and two thirds were excreted with the feces within 7 days.
The spectrum of metabolites in the animals was very similar to that observed in the two human subjects. The major metabolites found were 2,4-dichloromandelic acid; 2[(2,6- dichlorobenzyl) -oxyl-2-(2,4-dichlorophenyl)- acetic acid and 1-(2,4-dichlorophenyl)-2- imidazole-1-yl-ethanol.

List of excipients
Polysorbate 60
Sorbitan stearate
Cetostearyl alcohol
Paraffin, heavy liquid
Paraffin, white soft
Water, purified

Incompatibilities
Not applicable

Shelf-Life
Please refer to labels

Storage Conditions
Store below 30°C.
Store all drugs properly and keep them out of reach of children.

Instructions for use/handling
No special requirements.

Dosage form and packaging available
Tubes of 20 g

Name and address of manufacturer
LEO Pharma Manufacturing Italy S.r.l.
Via E. Schering, 21, 20090 Segrate (MI) Italy.

Date of Revision of Package Insert
14 April 2016

Singapore **85456725**

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