1. NAME OF THE MEDICINAL PRODUCT

Tiocomax Cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 20g of Tiocomax Cream contains 1% Tioconazole w/w

For a full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Cutaneous cream

A white cream free from specks.

4. CLINICAL PARTICULARS

4.1 Therapeutic indication

Tioconazole is a broad spectrum imidazole antifungal agent. Tiocomax Cream is indicated for the topical treatment of infections due to:

- Candidiasis
- Dermatophytoses including tinea pedis, tinea corporis, tinea cruris, tinea unguium (onchomycoses) and other candida infections of the skin.
- Pityriasis versicolor (tinea versicolor)

4.2 Posology and method of administration

Posology

There is no separate dosage schedule for the young or elderly.

Method of administration

Tiocomax cream should be thinly applied unto the affected area and rubbed in 1 to 2 times daily with gentle massage. The duration of treatment will depend on infecting organisms and the site of infection. Treatment for majority of infections is usually 2 – 4 weeks. Nail infections may require treatment for up to 6 months but may be exceeded to 12 months. Treatment of fungal infections of the feet should be continued for about 2 weeks after the disappearance of all signs of the disease to prevent relapses.

Continue therapy despite early symptomatic relief.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Tiocomax is contraindicated in individuals who have been shown to be hypersensitive to imidazole antifungal agents.
Use is contraindicated during pregnancy (see section 4.6)

4.4 Special warnings and precautions for use

For external use only on unbroken skin. Avoid contact with the eyes and sensitive areas of the skin. If symptoms persist consult your doctor. Discontinue use if excessive irritation occurs. Wash hands thoroughly after use. Keep all medicines out of the reach of Children.

4.5 Interaction with other medicinal products and other forms of interaction

None known.

4.6 Pregnancy and lactation

Pregnancy

In animal studies tioconazole was not teratogenic. At high doses it increased the incidence of renal abnormalities in rat embryos, but this effect was minor and transient and was not evident in weaned animals. There is insufficient evidence as to the drug's safety in human pregnancy although absorption after topical administration is negligible. Because of the extensive duration of treatment required for nail infections, the use of Tiocomax is contra-indicated throughout pregnancy.

Breast-feeding

It is unknown whether this drug is excreted in human milk. Because many drugs are excreted in human milk, nursing should be temporarily discontinued while Tiocomax is administered.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Tiocomax Cream is well tolerated following local application. Symptoms of localirritation have been reported by some patients, but are usually seen during the first week of treatment and are transient and mild. Systemic allergic reactions are uncommon. However, if a sensitivity reaction develops with the use of Tiocomax Cream, treatment should be discontinued and appropriate therapy instituted.

The undesirable effects listed below were reported with frequencies corresponding to Common (≥1/100, ≤1/10), Uncommon (≥1/1000, <1/100), Rare (≥1/10,000, < 1/1,000), Very Rare (< 1/10,000), not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System Organ Class	Frequency	Undesirable effects
Immune system disorders	Unknown	Allergic reactions
Nervous system disorders	Unknown	Paraesthesia
Skin and subcutaneous tissue disorders	Unknown	Bullous eruption, dermatitis contact, dry skin, edema periorbital, nail disorder (including nail discolouration, periungual inflammation and nail pain), pruritus, skin irritation, skin exfoliation, urticaria
General disorders and administration site conditions	Uncommon	Uncommon Dermatitis, rash
	Common	Oedema peripheral
	Unknown	Pain

Anaphylactoid reactions have been reported in patients treated with other formulations than the dermatological preparation

4.9 Overdose

No cases of overdosage with Tiocomax Cream have been reported. Overdosage by topical application of tioconazole is unlikely because of negligible systemic absorption. In the event of excessive oral ingestion by mistake, gastrointestinal symptoms may occur. Appropriate means of gastric lavage should be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Imidazole and triazole derivatives. ATC Code: D01AC07.

Tioconazole is an imidazole which is active against commonly occurring dermatophyte and yeast-like fungal species. It is fungicidal in murine models vs. Candida spp., T. rubrum and T. mentacrophytes. In vitro it is fungicidal to pathogenic dermatophytes, yeasts and other fungi. All dermatophytes and Candida spp. were inhibited by 6.25 or 12.5 mg/l respectively. It is also inhibitory vs. Staph. spp. and Strep. spp. at 100 mg/l or less.

Oral doses (200 mg/kg) did not affect behaviour in rats but 25 mg/kg i.v. produced dose-related respiratory distress, gasping, tremors and prostration. Slight but dose-related impairment of performance of mice on the rotating rod occurred from 25 mg/kg. Slight anti-cholinergic and anti-histamine (H1) activity was recorded in vitro but no effect on mice pupil size in vivo. Oral tioconazole prolonged alcohol and pentobarbital sleeping time at 150 and 37.5 mg/kg respectively.

In the anaesthetised cat i.v. tioconazole 2.5 - 10 mg/kg produced brief falls in blood pressure and increased heart rate, haematuria, tremors and twitches.

5.2 Pharmacokinetic properties

Absorption
Absorption is rapid and extensive on oral administration to rats, monkeys and man, the major metabolite being a glucuronide conjugate of tioconazole. Tissue uptake in rat and monkey was highest in liver, kidney and intestinal tract with excretion in all species mainly in faeces.

Rat studies using oral, dermal and vaginal administration of C14 labelled tioconazole confirm significantly lower absorption via the topical route.

In man, oral formulations of tioconazole (500mg) gave plasma concentrations of 1300ng/ml. Topical administration of dermal cream 1% (20mg/day) for 28 days, or vaginal cream 2% (100mg/day) for 30 days gave negligible mean peak plasma levels, i.e. 10.1 and 11.5ng/ml respectively.

Distribution
After single dose administration of tioconazole vaginal ointment 6.5% w/w (tioconazole 300mg) the mean peak plasma concentration was 18ng/ml in humans, achieved approximately 8 hours post dose.

5.3 Preclinical safety data
None relevant to the prescriber.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Sorbitan Monostearate
Polysorbate 60
Synthetic Spermaceti
Cetostearyl Alcohol
Isopropyl Myristate
Benzyl Alcohol
Deionised Water

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Store below 30°C.

6.5 Nature and contents of container
The product is packed directly into sealed internally lacquered aluminium tubes; these are enclosed in an outer carton. The product pack size is 20g.

6.6 Special precautions for disposal
No special requirements.

7 APPLICANT/MANUFACTURER
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