
DAKTARIN[®]

Miconazole, Miconazole nitrate

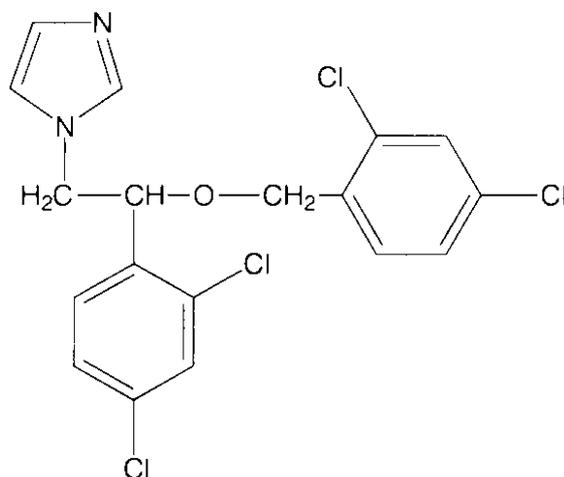
CREAM, POWDER, SPRAY POWDER, LOTION, TINCTURE

PRODUCT INFORMATION

Description

Miconazole is 1-[2,4-dichloro-beta-(2,4-dichlorobenzyloxy)phenethyl]imidazole derivative and is a synthetic 1-phenethylimidazole derivative. It is a white, microcrystalline powder, practically insoluble in water but soluble in ethanol (10%).

Miconazole nitrate is 1-[2,4-dichloro-beta-(2,4-dichlorobenzyloxy)phenethyl]imidazole nitrate, and is a synthetic 1-phenethylimidazole derivative. It is a white, microcrystalline powder, very slightly soluble in water and in ether; soluble in 140 parts of ethanol (96%), and slightly soluble in chloroform.



Miconazole: $C_{18}H_{14}Cl_4 N_2O$ mol wt 416.14

Miconazole nitrate: $C_{18}H_{14}Cl_4 N_2O.HNO_3$ mol wt 479.16

DAKTARIN Cream is a water-miscible white cream with a pH 2.6-3.6, containing miconazole nitrate 2% w/w. The vehicle contains butylated hydroxyanisole, liquid paraffin, ethylene glycol, apricot kernel oil PEG-6 esters, tefose 63 and purified water with benzoic acid as a preservative.

DAKTARIN Powder contains miconazole nitrate 2% in a powder containing silica-colloidal anhydrous, zinc oxide and talc. It is a white homogenous powder.

DAKTARIN Spray Powder delivers miconazole nitrate 2% as a dry powder. It also contains ethanol, propane, butane, sorbitan sesquioleate, stearylalkonium hectorite and talc-purified.

DAKTARIN Lotion contains miconazole nitrate 2% in an aqueous lotion base containing butylated hydroxyanisole, liquid paraffin, tefose 63, apricot kernel oil PEG-6 esters with benzoic acid as a preservative. It is a white, homogenous, odourless lotion with a pH 2.5-3.5.

DAKTARIN Tincture contains miconazole base 2% in an alcoholic solution containing propylene glycol, ethanol, and acrylates copolymer. It is a colourless to faintly yellow solution with a pH 5.5 to 7.

Pharmacology

Category: Antifungal (topical)

Microbiology : Miconazole exhibits antifungal activity against *Candida albicans*, the dermatophytes - *Trichophyton rubrum*, *T.mentagrophytes*, *Epidermophyton floccosum* and *Pityrosporum orbicular* (*Malassezia furfur*). Miconazole penetrates the fungal cell wall, alters cellular membranes, and interferes with intracellular enzymes and biosynthesis of ergosterol.

Pharmacokinetics:

Absorption - Systemic absorption of miconazole is limited, with a bioavailability of less than 1% following application of miconazole. Plasma concentrations of miconazole and/or its metabolites were measurable 24 and 48 hours after application.

Systemic absorption has also been demonstrated after repeated application of miconazole to infants with diaper dermatitis. Plasma levels of miconazole were undetectable or low in all infants.

Distribution - Absorbed miconazole is bound to plasma proteins (88.2%) and red blood cells (10.6%).

Metabolism and Excretion - The small amount of miconazole that is absorbed is eliminated predominantly in feces as both unchanged drug and metabolites over a four-day post-administration period. Smaller amounts of unchanged drug and metabolites also appear in urine.

Indications

Daktarin Cream, Lotion, Powder and Spray Powder are indicated for the topical treatment of the following fungal infections:

- Cutaneous candidiasis (moniliasis), caused by *Candida albicans*;
- Tinea corporis, tinea cruris and tinea pedis caused by *Trichophyton rubrum*, *T.mentagrophytes* and *Epidermophyton floccosum*.
- Tinea versicolour caused by *Pityrosporum orbicular* (*Malassezia furfur*).

Daktarin Tincture is indicated for the topical treatment of tinea unguium caused by *Candida albicans*, *Trichophyton rubrum*, *T.mentagrophytes* and *Epidermophyton floccosum*.

Contraindications

DAKTARIN Cream, Lotion, Powder, Spray Powder and Tincture are contraindicated in the following situations:

- Patients with known hypersensitivity to the active ingredient and/or any of the other excipients in these presentations;
- Patients with known hypersensitivity to similar antifungal agents such as ketoconazole.

Precautions

- Not all strains of a particular organism may be susceptible to miconazole.
- As with other drugs of this class, prolonged use may result in overgrowth of non-susceptible micro-organisms.
- Intractable candidiasis may be the presenting symptom of unrecognised diabetes. Appropriate tests should therefore be performed in patients not responding to treatment.
- Discontinue DAKTARIN if sensitisation or irritation is reported during use.
- Daktarin must not come into contact with the eyes.
- Tincture is an alcoholic solution and should not be applied to open lesions.
- Avoid spraying DAKTARIN Spray Powder in the eyes.
- DAKTARIN powder contains talc. Avoid inhalation of the powder to prevent irritation of airways, In particular, when treating infants and children, careful application should be used to prevent inhalation by the child.

Interactions with Other Drugs – Miconazole administered systemically is known to inhibit CYP3A4/2C9. Due to the limited systemic availability after topical application, clinically relevant interactions occur very rarely. In patients on oral anticoagulants, such as warfarin, caution should be exercised and the anticoagulant effect should be monitored. The effects and side effects of some other drugs (e.g., oral hypoglycemics and phenytoin), when co-administered with miconazole, can be increased and caution should be exercised.

Use in Pregnancy - Pregnancy Category (A)

Although no problems have been documented, despite assumed extensive use of this drug in pregnancy, safety for use during pregnancy has not been established through prospective studies.

Use During Lactation - It is not known whether miconazole is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when DAKTARIN is administered to a mother who is breast-feeding.

Adverse Reactions

Clinical Trial Data

Adverse drug reactions reported among 834 patients who received miconazole 2% cream and/or placebo cream base in 21 double-blind clinical trials are presented in Table 1 below. Included in the table are all adverse events considered to be related to study drug. A dash indicates that the adverse reaction was not reported by patients in the specified treatment group.

Table 1: Adverse drug reactions reported by patients in either treatment group in 21 double-blind clinical trials of miconazole 2% cream versus placebo.		
System Organ Class	Miconazole 2% Cream	Placebo Cream Base
Adverse drug reaction	(n=426), %	(n=408), %
Overall adverse drug reactions	1.9	1.2
Skin and subcutaneous tissue disorders		
Skin burning sensation	0.2	0.7
Skin inflammation	0.2	--
Skin hypopigmentation	0.2	--
General disorders and administration site conditions		
Application site irritation	0.7	0.5
Application site burning	0.2	0.2
Application site pruritus	0.2	--
Application site reaction NOS	0.2	--
Application site warmth	0.2	--

Note: Individual patients may have reported more than a single event.

Postmarketing Data

Adverse drug reactions from spontaneous reports during the worldwide post-marketing experience with DAKTARIN that meet threshold criteria are included in Table 2. The adverse drug reactions are ranked by frequency, using the following convention:

Very common	≥1/10
Common	≥1/100 and <1/10
Uncommon	≥1/1,000 and <1/100
Rare	≥1/10,000, <1/1,000
Very rare	<1/10,000, including isolated reports

The frequencies provided below reflect reporting rates for adverse drug reactions from spontaneous reports, and do not represent more precise estimates of incidence that might be obtained in clinical or epidemiological studies.

Table 2: Postmarketing reports of adverse drug reactions

Immune system disorders

Very rare anaphylactic reaction, hypersensitivity, angioneurotic edema

Skin and subcutaneous tissue disorders

Very rare urticaria, contact dermatitis, rash, erythema, pruritus, skin burning sensation

General disorders and administration site conditions

Very rare application site reactions, including application site irritation

Dosage and Administration

A thin layer of DAKTARIN Cream or Lotion, sufficient to cover the affected area should be applied and rubbed well into the skin. In patients with tinea pedis, tinea cruris, tinea corporis and cutaneous candidiasis, the cream or lotion should be applied twice daily, and in patients with tinea versicolour, once daily.

DAKTARIN Powder should be applied directly to the lesions and also dusted inside articles of clothing in contact with the affected areas. This should be carried out twice daily.

The DAKTARIN Spray Powder can must be well shaken before use. It should be held about 15cm from the area to be treated and a thin layer is applied twice daily.

Treatment must be continued, without interruption until the lesions have completely healed. Candida infections should be treated for 2 weeks and dermatophyte infections for one month.

Nail Infections: before treatment commences, the nail should be cut as short as possible. A thin layer of DAKTARIN Tincture should be applied to the affected nail, the area around it and if possible under it twice daily. After the infected nail has come off, the treatment should be continued without interruption until a new nail has grown and the lesions are completely cured (usually for at least 2 months). If the nail falls off during the course of treatment, this is due to the infection not to DAKTARIN Tincture. Before reapplying the product, clean the nail of any product buildup with acetone based nail polish remover.

NOTE - To improve the therapeutic results of treatment, certain hygienic measures must be taken such as washing the infected regions every day, disinfecting and frequently changing stockings and shoes.

Overdosage

Treatment of overdose is symptomatic and supportive. In the event of overdose, or if accidentally swallowed, contact the Poisons Information Centre on 13 11 26 in Australia or 0800 764 766 in New Zealand.

Presentation

DAKTARIN Cream tubes of 15g, 30g & 70g with 'Instructions for Use' leaflet.

DAKTARIN Lotion in a 30g bottle.

DAKTARIN Powder in a 30g "puffer" pack.

DAKTARIN Tincture in a 30mL bottle with brush.

DAKTARIN Spray Powder in a 100g pressurised can.

STORE BELOW 25°C

Sponsor

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Australia

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