

## **PACKAGE INSERT**

### **SCHEDULING STATUS**

Schedule 1

### **PROPRIETARY NAME AND DOSAGE FORM**

DAKTARIN® cream

### **COMPOSITION**

Miconazole nitrate 20 mg/g.

Preservative: Benzoic acid 0,2 % m/m

### **PHARMACOLOGICAL CLASSIFICATION**

A. 13.9.2 Dermatological preparations. Fungicides.

### **PHARMACOLOGICAL ACTION**

#### **Pharmacodynamics**

Miconazole nitrate is a synthetic 1-phenethylimidazole derivative. *In vitro*, low concentrations of miconazole nitrate are fungistatic against all Phycomycetes, Ascomycetes and Adelomycetes tested (e.g. Saprolegnia, Candida, Cryptococcus, Aspergillus, Dermatophytes, Phialophora, Sporotrichum) and fungicidal against *Trichophyton mentagrophytes*, *Trichophyton rubrum*, *Epidermophyton floccosum*, *Trichophyton interdigitale* and *Microsporum canis*.

Thus the miconazole nitrate is a broad-spectrum anti-fungal agent. As yet there is no evidence of drug resistance developing to miconazole nitrate.

Miconazole nitrate also possesses some antibacterial activity against gram-positive organisms.

In addition, miconazole nitrate has a very rapid alleviating effect on the pruritis, which frequently accompanies infection.

#### **Pharmacokinetics**

##### Absorption:

Systemic absorption of miconazole is limited, with a bioavailability of less than 1% following topical application of miconazole.

##### 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**

Dermatomycoses, e.g.:

- Tinea pedis (athlete's foot)
- Tinea corporis (Tinea circinata)
- Tinea manuum

Tinea cruris due to:

- Trichophyton mentagrophytes
- Trichophyton rubrum
- Microsporum audouinii
- Epidermophyton floccosum

Candidial infections:

Infections of the skin (.e.g. intertrigo)

Perianal infections

Stomatitis angularis (cheilitis, perleche)

Balanoposthitis

### **CONTRA-INDICATIONS**

DAKTARIN cream is contra-indicated in individuals with a known hypersensitivity to miconazole or another ingredient of the formulation.

### **INTERACTIONS**

Miconazole administered systemically is known to inhibit CYP3A4/2C9. Due to the limited systemic availability after topical application (see Pharmacokinetic properties), clinically relevant interactions occur very rarely. However, 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 DAKTARIN cream, can be increased and caution should be exercised.

### **PREGNANCY AND LACTATION**

#### Pregnancy

Although there is no evidence that miconazole is embryotoxic or teratogenic in animals, safety in human pregnancy has not been demonstrated.

#### Lactation

It is not known whether miconazole is excreted in human breast milk. Therefore, safety has not been demonstrated in breastfeeding women.

### **DOSAGE AND DIRECTIONS FOR USE**

For external use only.

DAKTARIN cream should be applied to the lesion twice daily and thoroughly rubbed into the skin with a finger.

When all lesions have disappeared (usually after 2 to 5 weeks), treatment should be continued for a further 10 to 14 days to prevent relapse.

#### *Instructions for use and handling*

To open the tube, unscrew the cap. Then pierce the seal of the tube with the pin on the top of the cap.

## **SIDE-EFFECTS AND SPECIAL PRECAUTIONS**

### **Side-effects**

#### 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 medicine. 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.

<b>System Organ Class Adverse drug reaction</b>	<b>Miconazole 2% cream (n= 426), %</b>	<b>Placebo cream base (n=408), %</b>
<b><i>Overall adverse drug reactions</i></b>	<b><i>1.9</i></b>	<b><i>1.2</i></b>
<u>Skin and subcutaneous tissue disorders</u>		
Skin burning sensation	0.2	0.7
Skin inflammation	0.2	--
Skin hypopigmentation	0.2	--
<u>General disorders and administration site conditions</u>		
Application site irritation	0.7	0.5
Application site burning	0.2	0.2
Application site pruritus	0.2	--
Application site reaction (Not otherwise specified)	0.2	--
Application site warmth	0.2	--

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

#### Post marketing data

Adverse drug reactions from spontaneous reports during the worldwide post-marketing experience with DAKTARIN.

Table 2:

<b>SYSTEM ORGAN CLASS</b>	<b>Adverse Event</b>
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Immune system disorders	Hypersensitivity, angioneurotic oedema and anaphylactic reactions
<i>Skin and subcutaneous system disorders</i>	Urticaria, contact dermatitis, rash, erythema, pruritus, skin burning sensation
<i>General disorders and administration site conditions</i>	Application site reactions, including application site irritation

**Special precautions**

If a reaction suggesting sensitivity or irritation should occur, the treatment should be discontinued. DAKTARIN cream must not come into contact with the eyes.

**Effects on ability to drive and use machines**

Not applicable

**KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT**

Symptoms

Topical use: Excessive use can result in skin irritation, which usually disappears after discontinuation of therapy.

Treatment

**Accidental ingestion:** DAKTARIN cream is intended for topical use, not for oral use. Should accidental oral ingestion of large quantities of this product occur, an appropriate method of gastric emptying may be used if considered necessary.

**IDENTIFICATION**

A smooth white cream, miscible with water.

**PRESENTATION**

DAKTARIN cream is supplied in a tube containing 30 g of cream.

**STORAGE DIRECTIONS**

Store below 25°C.

KEEP OUT OF REACH OF CHILDREN.

**REGISTRATION NUMBER**

G/13.9.2/106

**NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION**



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