PACKAGE INSERT

SCHEDULING STATUS

Schedule 2.

PROPRIETARY NAME AND DOSAGE FORM

DAKTARIN® Oral Gel.

COMPOSITION

Miconazole 20 mg/g in a homogeneous starch base.

Ethyl alcohol content: 0,73% m/m

Sodium saccharine 1 mg/gram

Excipients:

The other inactive ingredients of the oral gel are glycerol, purified water, pregelatinised potato starch, polysorbate, cocoa flavour and orange flavour.

PHARMACOLOGICAL CLASSIFICATION

A 20.2.2 Antimicrobial (Chemotherapeutic) agents. Fungicides.

PHARMACOLOGICAL ACTION

Pharmacodynamics

Miconazole possesses *in vitro* antifungal activity against the common dermatophytes and yeasts as well as an antibacterial activity against certain gram-positive bacilli and cocci. Its activity is based on the inhibition of the ergosterol biosynthesis in fungi and the change in the composition of the lipid components in the membrane, resulting in fungal cell necrosis.

Pharmacokinetics

Absorption

Miconazole is systemically absorbed after administration as the oral gel. Administration of a 60 mg dose of miconazole as the oral gel results in peak plasma concentrations of 31 to 49 ng/ml, occurring approximately two hours post dose.

Distribution

Absorbed miconazole is bound to plasma proteins (88,2 %), primarily to serum albumin and red blood cells (10,6 %).

Metabolism and elimination

The absorbed portion of miconazole is largely metabolised, less than 1 % of an administered dose is excreted unchanged in the urine. The terminal half-life of plasma miconazole is 20 – 25 hours in most patients. The elimination half-life of miconazole is similar in renally impaired patients. Plasma concentrations of miconazole are moderately reduced (approximately 50 %) during hemodialysis.

INDICATIONS

DAKTARIN oral gel is indicated for the treatment of fungal infections of the mouth (e.g. thrush in babies and oral candidiasis in other age groups) and for fungal stomatitis occurring in association with dentures.

CONTRA-INDICATIONS

DAKTARIN oral gel is contra-indicated in the following situations:

- In patients with a known hypersensitivity to miconazole or to any of the excipients of DAKTARIN oral gel
- In infants less than 6 months of age or in those with swallowing reflex not yet fully developed
- In patients with impaired liver function
- Co-administration of the following medicine that are subject to metabolism by CYP3A4 (See INTERACTIONS):
    - Substrates known to prolong QT-interval e.g. astemizole, bepridil, cisapride, dofetilide, halofantrine, mizolastine, pimozide, quinidine, sertindole and terfenadine
    - Ergot alkaloids
    - HMG-CoA reductase inhibitors such as simvastatin and lovastatin
    - Triazolam and midazolam

WARNINGS

Avoid contact with the eyes.

Particularly in infants and young children, caution is required, to ensure that the gel does not obstruct the throat. Hence, the gel should not be applied to the back of the throat and each dose should be divided into smaller portions. Observe the patient for possible choking.

INTERACTIONS

When using any concomitant medication the corresponding label should be consulted for information on the route of metabolism. Miconazole can inhibit the metabolism of medicines metabolised by the CYP3A4 and CYP2C9 enzyme systems. This can result in an increase and/or prolongation of their effects, including adverse effects.

DAKTARIN oral gel is contra-indicated with the co administration of the following medicines that are subject to metabolism by CYP3A4 (See CONTRA-INDICATIONS):

- Substrates known to prolong the QT-interval, e.g. astemizole, bepridil, cisapride, dofetilide, halofantrine, mizolastine, pimozide, quinidine and sertindole
- Ergot alkaloids
- HMG-CoA reductase inhibitors such as simvastatin and lovastatin
- Triazolam and midazolam

When co-administered with DAKTARIN oral gel the following medicines should be used with caution because of a possible increase or prolongation of the therapeutic outcome and/or

adverse effects. If necessary, their dosage should be reduced and, where appropriate, plasma levels monitored:

- Medicines subject to metabolism by CYP2C9 (see Special Precautions)
    - Oral anti-coagulants such as warfarin
    - Oral hypoglycemics such as sulfonylureas
    - Phenytoin

- Other medicines subject to metabolism by CYP3A4:
    - HIV Protease Inhibitors such as saquinavir
    - Certain antineoplastic agents such as vinca alkaloids, busulfan and docetaxel
    - Certain Calcium Channel Blockers such as dihydropyridines and verapamil
    - Certain Immunosuppressive Agents: cyclosporin, tacrolimus, sirolimus (= rapamycin)
    - Others: alfentanil, alprazolam, brotizolam, buspirone, carbamazepine cilostasol, disopyramide, ebastine, methylprednisolone, midazolam, reboxetine , rifabutin and sildenafil

PREGNANCY AND LACTATION

DAKTARIN oral gel should not be used during pregnancy as safety has not been demonstrated.

There are no data available on the excretion of miconazole in human milk; therefore, DAKTARIN oral gel should not be used in patients who are breastfeeding.

DOSAGE AND DIRECTIONS FOR USE

DAKTARIN oral gel should be spread evenly over the affected areas of the oropharyngeal mucosa and tongue taking care to properly cover oral ulcerations and other lesions.

The application of DAKTARIN oral gel must be repeated three to four times daily depending upon the severity of the infection. Apply the gel regularly until all signs of the infection have disappeared. Continue using for another two days after the infection has cleared.

Application of the gel is preferably done after meals.

For best results in treatment of oral lesions, DAKTARIN oral gel must be kept in contact with the affected areas as long as possible. This can be achieved by retaining the gel in the mouth for the maximum time possible.

In fungal stomatitis, associated with dentures, apply the gel to the lesions in the evening and leave on overnight.

For oral candidosis, dental prostheses should be removed at night and brushed with the gel.

Instructions for use and handling:

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

SIDE-EFFECTS AND SPECIAL PRECAUTIONS

Side-effects

Clinical trial data

System Organ Class

Preferred term

Nervous system disorders

Frequent: Dysgeusia

Gastrointestinal disorders

Frequent: Dry mouth, nausea, oral discomfort and vomiting

General disorders and administration site conditions

Frequent: Product taste abnormal

Infants

System Organ Class

Preferred term

Gastrointestinal disorders

Frequent: Nausea, regurgitation and vomiting

Post - marketing experience

Adverse drug reactions first identified during post-marketing experience with DAKTARIN oral gel are listed below.

Post marketing reports of adverse drug reactions

System Organ Class	Adverse drug reaction
Immune System Disorders	Anaphylatic reaction, angioedema, hypersensitivity
Respiratory, Thoracic and Mediastinal Disorders	Choking (see CONTRA-INDICATIONS)
Gastrointestinal Disorders	Diarrhoea, stomatitis, tongue discolouration
Hepatobiliary Disorders	Hepatitis
Skin and Subcutaneous Tissue Disorders	Toxic epidermal necrolysis, Stevens - Johnson syndrome, urticaria, rash

Special Precautions:

If the concomitant use of DAKTARIN oral gel and oral anticoagulants such as warfarin is envisaged, the INR should be carefully monitored and treatment should be titrated.

It is advisable to monitor with DAKTARIN oral gel phenytoin levels, if used concomitantly.

In patients using certain oral hypoglycemics such as sulfonylureas, an enhanced therapeutic effect leading to hypoglycaemia may occur during concomitant treatment with DAKTARIN oral gel and appropriate measures should be considered. (See INTERACTIONS).

Effects on ability to drive and use machines

DAKTARIN oral gel does not affect alertness or driving ability.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Symptoms

In general miconazole is not highly toxic. In the event of accidental overdose, vomiting and diarrhoea may occur.

Treatment

Treatment is symptomatic and supportive. A specific antidote is not available.

In the event of accidental ingestion of large quantities of DAKTARIN oral gel an appropriate method of gastric emptying may be used, if considered necessary (See INTERACTIONS).

IDENTIFICATION

White, homogeneous gel with orange flavour.

PRESENTATION

DAKTARIN oral gel is supplied in aluminium tubes with white polyethylene caps containing 30 g or 40 g.

STORAGE DIRECTIONS

Keep well closed.

Store at or below 25 ºC.

Do not freeze.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

L/20.2.2/183

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

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