PROFESSIONAL INFORMATION

SCHEDULING STATUS

Schedule 2

1. NAME OF THE MEDICINE

DAKTARIN® Oral Gel.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Miconazole 20 mg/g in a homogeneous starch base.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

White, homogeneous gel with orange flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Full term infants: 4 – 24 months: 1.25 mℓ (1/4 measuring spoon) of gel, applied four times a day after meals. Each dose is to be divided into smaller portions and the gel applied to the affected area(s) with a clean finger. The gel is not to be swallowed immediately, but kept in the mouth as long as possible.

Adults and children 2 years of age and older: 2.5 mℓ (1/2 measuring spoon) of gel, applied four times a day after meals. The gel is not to be swallowed immediately, but kept in the mouth as long as possible.

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.

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.

4.3 Contraindications

DAKTARIN oral gel is contraindicated in the following situations:

- In patients with hypersensitivity to miconazole, another ingredient of the formulation, or other imidazole derivatives of DAKTARIN oral gel
- In infants less than 4 months of age or in those with swallowing reflex not yet fully developed and prematurely born infants less than six months of age.
- In patients with impaired liver function
- Use in combination with the following medicine that are subject to metabolism by CYP3A4**:**

  -Substrates known to prolong QT-interval for example astemizole, bepridil, cisapride, dofetilide, halofantrine, mizolastine, pimozide, quinidine and sertindole

  - Ergot alkaloids
  - HMG-CoA reductase inhibitors such as simvastatin and lovastatin
  - Triazolam and midazolam

Use of DAKTARIN oral gel in combination with

- Warfarin (metabolized by CYP2C9)

4.4 Special warnings and precautions for use

Avoid contact with the eyes.

It is important to take into consideration the variability of the maturation of the swallowing function in infants, especially when giving miconazole gel to infants between the ages of 4-6 months. The lower age limit should be increased to 6 months of age for infants who are pre-term, or infants exhibiting slow neuromuscular development.

Particularly in infants and young children (aged 4 months – 2 years), caution is required, to ensure that the gel does not obstruct the throat. Hence, the gel is not to be applied to the back of the throat. Each dose is to be divided into smaller portions and applied into the mouth with a clean finger. Observe the patient for possible choking. Also, due to the risk of choking, the gel must not be applied to the nipple of a breastfeeding woman for administration to an infant.

Miconazole is systemically absorbed and is known to inhibit CYP2C9 and CYP3A4 (see section 5.2) which can lead to prolonged effects of warfarin. Bleeding events, some with fatal outcomes, have been reported with concurrent use of miconazole oral gel and warfarin (see section 4.3).
It is advisable to monitor with DAKTARIN oral gel and 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 must be considered. (See section 4.5).

Severe hypersensitivity reactions including anaphylaxis and angioedema have been reported during treatment with DAKTARIN ORAL GEL. (see If a reaction suggesting hypersensitivity should occur, the treatment should be discontinued.

Serious skin reactions (e.g., Toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS)) have been reported in patients receiving DAKTARIN ORAL GEL (see section 4.8). It is recommended that patients be informed about the signs of serious skin reactions, and that the use of DAKTARIN ORAL GEL be discontinued at the first appearance of skin rash.

4.5 Interaction with other medicines and other forms of interaction

When using any concomitant medication, consult the corresponding product information 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

Refer to the CONTRAINDICATIONS section for coadministration of certain medicines that are subject to metabolism by CYP3A4.

When co-administered with DAKTARIN oral gel, the following medicines must be used with caution because of a possible increase or prolongation of the therapeutic outcome and/or adverse effects. If necessary, reduce their dosage and, where appropriate, monitor plasma levels:

- Medicines subject to metabolism by CYP2C9 Oral anticoagulants such as Warfarin (See section 4.3)
- Oral hypoglycemics such as sulfonylureas
- Phenytoin

- Other medicines subject to metabolism by CYP3A4:
  - HIV Protease Inhibitors such as ritonavir and saquinavir
  - Certain antineoplastic medicines such as vinca alkaloids, busulfan and docetaxel
  - Certain Calcium Channel Blockers such as dihydropyridines and verapamil
  - Certain immunosuppressive medicines: cyclosporin, tacrolimus, sirolimus (= rapamycin)

    Others: alfentanil, alprazolam, brotizolam, buspirone, carbamazepine cilostasol, disopyramide, ebastine, methylprednisolone, midazolam IV, reboxetine, rifabutin and sildenafil

4.6 Fertility, 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 their infants.

4.7 Effects on ability to drive and use machines

DAKTARIN oral gel does not affect alertness or driving ability.

4.8 Undesirable effects

Clinical trial data

Nervous system disorders

Frequent: Dysgeusia

Gastrointestinal disorders

Frequent: Dry mouth, nausea, oral discomfort and vomiting

General disorders and administration site conditions

Frequent: Abnormal taste

Infants

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 section 4.3)
Gastrointestinal Disorders	Diarrhoea, stomatitis, tongue discolouration
Hepatobiliary Disorders	Hepatitis
Skin and Subcutaneous Tissue Disorders	Toxic epidermal necrolysis, Stevens - Johnson syndrome, urticaria, rash, acute generalized exanthemous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS syndrome)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine product is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions via “6.04 Adverse Drug Reaction Reporting Form” found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/index/8

Alternatively, suspected adverse reactions may be reported directly to Janssen Pharmaceutica (see section 7 for contact details or visit www.janssen.com).

4.9 Overdose

Symptoms

In the event of accidental overdose, vomiting and diarrhoea may occur.

Treatment

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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.

5.2 Pharmacokinetic properties

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethyl alcohol content (0,73% m/m), cocoa flavour, glycerol, orange flavor, polysorbate, pregelatinised potato starch, purified water, sodium saccharine (1 mg/g).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Keep well closed.

Store below 30 °C.

Do not freeze.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

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

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

JANSSEN PHARMACEUTICA (Pty.) Ltd.

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8. REGISTRATION NUMBERS

L/20.2.2/183

Botswana Reg. No.: BOT2203808
S3

Malawi Reg. No. PMPB/PL22/3
P

Namibia Reg. No.: 90/20.2.2/00611
NS 1

Tanzania Reg. No.: *TAN 23 HM 0043*
POM

Uganda reg. No.: NDA/MAL/HDP/4778
Class B, Group II

Zambia Reg. No.: 009/010
POM

Zimbabwe Reg. No.: 80/20.3.6/1327
PIM

9 DATE OF FIRST AUTHORISATION

- 18 October 1979 (Date of registration)

10 DATE OF REVISION OF THE TEXT

Date of the most recently revised Professional Information as approved by SAHPRA:

07 February 2023