SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

DAKTARIN™ Oral Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g of gel contains 20 mg of miconazole.

Excipients with known effect:
Ethanol: maximum 7.485 mg/g
Polysorbate 20: 2.150 mg/g
Benzyl alcohol – 2.30 pg/g
Benzyl benzoate – 1.38 pg/g

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral gel

White gel with orange taste

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Oral treatment of candidosis of the oropharynx.

Miconazole gel is for use in adults, children and infants 4 months and older.

4.2 Posology and method of administration

For oral administration.

The provided measuring device is equivalent to 122 mg for 5 ml.

Oropharyngeal candidosis

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

The treatment should be continued for at least a week after the symptoms have disappeared.

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

4.3 Contraindications

Known hypersensitivity to miconazole, other imidazole derivatives or to any of the excipients listed in section 6.1.

In infants less than 4 months of age or in those whose swallowing reflex is not yet sufficiently developed (see section 4.4)

In patients with liver dysfunction.

Coadministration of the following drugs that are subject to metabolism by CYP3A4: (See Section 4.5 Interactions with Other Medicinal Products and Other Forms of Interaction)

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

4.4. Special warnings and precautions for use

Miconazole is systemically absorbed and is known to inhibit CYP2C9 and CYP3A4 (see Section 5.2 Pharmacokinetic Properties) 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 4.5 Interaction with Other Medicinal Products and Other Forms of Interaction and section 4.8 Undesirable effects).If the concomitant use of

Daktarin Oral Gel with an oral anticoagulant such as warfarin is planned, caution should be exercised and the anticoagulant effect must be carefully monitored and titrated (see section 4.5).

Patients should be advised that if they experience unexpected bleeding or bruising, nosebleeds, coughing up blood, blood in the urine, black tarry stools or coffee ground vomit, to stop treatment with miconazole and seek medical advice.

Severe hypersensitivity reactions, including anaphylaxis and angioedema, have been reported during treatment with Daktarin and with other miconazole formulations (see section 4.8). If a reaction suggesting hypersensitivity or irritation should occur, the treatment should be discontinued.

It is advisable to monitor miconazole and phenytoin levels, if these two drugs are used concomitantly.

In patients using certain oral hypoglycaemics such as sulphonylureas, an enhanced therapeutic effect leading to hypoglycaemia may occur during concomitant treatment with miconazole and appropriate measures should be considered (See Section 4.5 Interactions with Other Medicinal Products and Other Forms of Interaction).

Choking in infants and young children
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 should not be applied to the back of the throat. Each dose should 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 breast-feeding woman for administration to an infant.

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 5-6 months of age for infants who are pre-term, or infants exhibiting slow neuromuscular development.

Serious skin reactions (e.g. Toxic epidermal necrolysis and Stevens-Johnson syndrome) 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 use of Daktarin Oral Gel be discontinued at the first appearance of skin rash.

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

This medicine contains 23 mg of alcohol (ethanol) in each 2.5 ml dose corresponding to 7.5 mg/g. The amount in each 2.5 ml dose is equivalent to

less than 1 ml of beer or 1 ml of wine. The small amount of alcohol in this medicine will not have any noticeable effects.

This medicine contains benzyl benzoate which may cause allergic reactions.

This medicine contains 2.3 picograms of benzyl alcohol per gram. Benzyl alcohol may cause allergic reactions and mild local irritation. Benzyl alcohol has been linked with the risk of severe side effects including breathing problems (called “gasping syndrome”) in young children. Do not give to your newborn baby (up to 4 weeks old), unless recommended by your doctor. Do not use for more than a week in young children (less than 3 years old), unless advised by your doctor or pharmacist. Ask your doctor or pharmacist for advice if you are pregnant or breast□feeding. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called “metabolic acidosis”). Ask your doctor or pharmacist for advice if you have a liver or kidney disease. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called “metabolic acidosis”).

This medicine contains polysorbate which can cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

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

Oral miconazole is contraindicated with the coadministration of the following drugs that are subject to metabolism by CYP3A4 (See Section 4.3 Contraindications);

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

When coadministered with oral miconazole the following drugs should be used with caution because of a possible increase or prolongation of the therapeutic outcome and/or adverse events. If necessary, their dosage should be reduced and, where appropriate, plasma levels monitored:

Drugs subject to metabolism by CYP2C9 (see Section 4.4 Special warnings and precautions for use);

- Oral anticoagulants such as warfarin,
- Oral hypoglycaemics such as sulphonylureas
- Phenytoin

Other drugs 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: carbamazepine, cilostazol, disopyramide, buspirone, alfentanil, sildenafil, alprazolam, brotizolam, midazolam IV, rifabutin, methylprednisolone, trimetrexate, ebastine and reboxetine.

4.6 Fertility, Pregnancy and lactation

In animals, miconazole has shown no teratogenic effects but is foetotoxic at high oral doses. The significance of this to man is unknown. However, as with other imidazoles, Daktarin Oral Gel should be avoided in pregnant women if possible. The potential hazards should be balanced against the possible benefits.

It is not known whether miconazole is excreted in human milk. Caution should be exercised when prescribing Daktarin Oral Gel to nursing mothers.

4.7 Effects on ability to drive and use machines

Daktarin should not affect alertness or driving ability.

4.8 Undesirable effects

The safety of Daktarin Oral Gel was evaluated in 111 patients with oral candidiasis or oral mycoses who participated in 5 clinical trials. Of these 111 patients, 88 were adults with oral candidiasis or oral mycoses who participated in 1 randomised, active-controlled, double-blind clinical trial and 3 open-label clinical trials. The other 23 patients were paediatric patients with oral candidiasis who participated in 1 randomised, active-controlled, open-label clinical trial in paediatric patients (aged ≤1 month to 10.7 years). These patients took at least one dose of Daktarin Oral Gel and provided safety data.

Based on the pooled safety data from these 5 clinical trials (adult and paediatric), the most commonly reported (≥1% incidence) adverse reactions were nausea (6.3%), product taste abnormal (3.6%), vomiting (3.6%), oral discomfort (2.7%), regurgitation (1.8%), and dry mouth (1.8%). Dysgeusia was reported in 0.9% of patients.

Adult Patients

Based on the pooled safety data from the 4 clinical trials in adults, common adverse reactions reported included nausea (4.5%), product taste abnormal (4.5%), oral discomfort (3.4%), dry mouth (2.3%), dysgeusia (1.1%), and vomiting (1.1%).

Paediatric Patients

In the 1 paediatric clinical trial, the frequency of nausea (13.0%) and vomiting (13.0%) was very common, and regurgitation (8.7%) was common. As identified through post-marketing experience, choking may occur in infants and young children (See Section 4.3 Contraindications and Section 4.4 Special Warnings and Special Precautions). The frequency, type, and severity of other adverse reactions in children are expected to be similar to that in adults.

Description of selected adverse reactions

Increases in INR and bleeding events such as epistaxis, contusion, haematuria, melaena, haematemesis, haematoma and haemorrhages have been reported in patients treated with oral anticoagulants such as warfarin in association with miconazole oral gel (see sections 4.4 and 4.5). Some events had fatal outcomes.

Table A includes all identified adverse reactions, including those that that have been reported from post-marketing experience.

The frequency categories use the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); and not known (cannot be estimated from the available clinical trial data).

Table A: Adverse Drug Reactions in Patients Treated with DAKTARIN Oral Gel

System Organ Class	Adverse Drug Reactions		
	Frequency Category		
	Common (≥1/100 to <1/10)	**Uncommon** (≥1/1,000 to <1/100)	**Not Known**
Immune System Disorders			Anaphylactic reaction, Hypersensitivity
Nervous System Disorders		Dysgeusia	
Respiratory, Thoracic and Mediastinal Disorders			Choking
Gastrointestinal Disorders	Dry mouth, Nausea, Oral discomfort, Vomiting, Regurgitation		Diarrhoea, Stomatitis, Tongue discolouration
Hepatobiliary Disorders			Hepatitis
Skin and Subcutaneous Tissue Disorders			Angioedema, Toxic epidermal necrolysis, Stevens-Johnson syndrome, Urticaria, Rash, Acute generalised exanthematous pustulosis, Drug reaction with eosinophilia and systemic symptoms, Fixed drug eruption
General Disorders and Administration Site Conditions	Product taste abnormal		

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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

ATC Code: A01A B09 and A07A C01

Miconazole possesses an 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 metabolized; less than 1% of an administered dose is excreted unchanged in the urine. The terminal half-life of plasma miconazole is 20 to 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. About 50% of an oral dose may be excreted in the faeces partly metabolized and partly unchanged.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of local irritation, single and repeated dose toxicity, genotoxicity, and toxicity to reproduction.

6.1. List of excipients

Glycerol
Ethanol
Carbomers
Polysorbate 20 (E432)
Saccharin sodium (E954)
Sodium hydroxide
Cocoa flavour (contains benzyl alcohol, benzyl benzoate and ethanol)
Orange flavour
Purified water

6.2 Incompatibilities

None known

6.3 Shelf life

Before opening: 3 years.

After first opening: Discard once the treatment for one episode of fungal infection is completed

6.4 Special precautions for storage

Do not store above 30ºC

6.5 Nature and contents of container

This medicine is a white, homogenous gel. It is packed in 15 g, 40 g or 80 g aluminium tubes and closed with a polypropylene screw cap.

Not all pack sizes may be marketed.

A 5 ml polypropylene spoon, marked with ¼ and ½ graduations (1.25 & 2.5

ml) is provided.

6.6 Special precautions for disposal

Not applicable

7 MARKETING AUTHORISATION HOLDER

McNeil Products Limited
50-100 Holmers Farm Way
High Wycombe
Buckinghamshire
HP12 4EG
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 15513/0413

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19/07/1977 / 18/09/2003

10 DATE OF REVISION OF THE TEXT

01/10/2025