1 DECOZOL

Miconazole 2% w/w Oral Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Miconazole 2% w/w

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral gel

DECOZOL is an off-white, homogenous, orange-flavoured oral gel.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

DECOZOL oral gel is indicated for the treatment of clinically significant oral and gastrointestinal candidiasis.

4.2 Dose and method of administration

Infants:

For infants 6-24 months, one quarter (1/4) of a measuring spoon* of gel four times daily after food, or 20 mg/kg/day is recommended.

Children (2years of age and older) and Adults:

Half (1/2) a measuring spoon* of gel four times daily after food.

* A measuring spoon (5 mL) is provided with the gel. One spoonful contains approximately 124 mg of miconazole. All spoonful dose volumes should be administered with this spoon.

DECOZOL oral gel should be placed on the tongue and kept in mouth for as long as possible before swallowing. When treating infants and younger children it is recommended that the measured dose of gel be given in several portions in the front of the mouth. Avoid dosing to the back of the throat to prevent obstruction. With oral thrush in elderly patients where a contributing cause is the dental prosthesis it is recommended that DECOZOL oral gel be applied directly to the dentures in the evening and left on overnight. The treatment should be continued for at least one week after the symptoms have disappeared and generally until all clinical and mycological laboratory tests no longer indicate that active fungal infection is present.

4.3 Contraindications

DECOZOL Oral Gel is contraindicated in the following situations:

1. In patients with a known hypersensitivity to miconazole or to any of the other ingredients of the gel.

2. In infants less than 6 months of age or in those whose swallowing reflex is not yet sufficiently developed.
3. In patients with liver dysfunction.
4. Co-administrating of the following drugs that are subject to metabolism by CYP3A4 (see Interactions):

- Substrates known to prolong the QT-interval eg. Astemizole, bepridil, cisapride, dofetilide, halofantrine, 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

If the concomitant use of DECOZOL oral gel and anticoagulants such as warfarin is envisaged, the anticoagulant effect should be carefully monitored and titrated (see Interactions).

It is advisable to monitor miconazole and phenytoin levels, if they are used concomitantly.

In patients using certain oral hypoglycaemic such as sulfonylureas, an enhanced therapeutic effect leading to hypoglycaemia may occur during concomitant treatment with miconazole and appropriate measures should be considered (see Interactions).

4.5 Interaction with other medicines and other forms of interaction

• Miconazole can inhibit the metabolism of drugs metabolised by the cytochrome 3A4 and 2C9 enzyme systems. This can result in an increase and/or prolongation of the effects, including adverse effects of these drugs.

• Miconazole may increase the anticoagulant effect of coumarin derivatives (e.g. warfarin). Patients taking coumarin anticoagulants who are given DECOZOL oral gel should be monitored for anticoagulant effect and the dosage of the coumarin derivative adjusted, if necessary.

• Similarly miconazole can potentiate the effect of oral hypoglycaemics such as sulfonylureas, so that a reduction of their dosage may be needed. Miconazole slows the metabolism of phenytoin and cyclosporine, tacrolimus and sirolimus. The dosage of these medicines may need to be reduced in patients using DECOZOL oral gel.

• The metabolism of terfenadine, astemizole, triazolam, oral midazolam, quinidine, pimozide, bepridil, halofantrine, sertindole and CYP3A4 metabolised HMG-CoA reductase inhibitors such as simvastatin and lovastatin and cisapride may be inhibited by miconazole. These medicines should, therefore, not be used by patients receiving DECOZOL Oral Gel (see section 4.3).

• Antagonism between miconazole and amphotericin B has been reported in vitro and in vivo. In studies miconazole and amphotericin combination were also shown to be antagonistic in antifungal activity against Candida albicans.

• HIV protease inhibitors (such as saquinavir): In vitro inhibition of the metabolism of saquinavir has been demonstrated. Therefore, the dosage may need to be reduced in patients receiving DECOZOL oral gel. However, clinically relevant interactions between oral miconazole and, indinavir and ritonavir, are not expected.

• Antineoplastic agents: Miconazole, when adminstered orally, may inhibit the metabolism of vinca alkaloids, busulfan and docetaxel resulting in elevation of plasma concentration. Dosage adjustment may be required in these instances.

• CYP3A4-metabolised calcium channel blockers (such as dihydropyridines and verapamil): There is the potential for increased plasma concentrations of these drugs when administered concomitantly with oral miconazole. Dosage adjustments may be required in these instances.

• Carbamazepine, cilostasol, disopyramide, buspirone, alfentanil, sildenafil, alprazolam, intravenous midazolam, rifabutin, methylprednisolone and trimetrexate: Miconazole, when administered orally, may alter the metabolism of these drugs resulting in elevation of plasma concentration. Dosage adjustment may be required in these instances.

• Ergot alkaloids.

4.6 Fertility, pregnancy and lactation

Although there is no evidence that miconazole is embryotoxic or teratogenic in animals, potential hazards of prescribing these medicines during pregnancy should always be weighed against the expected therapeutic benefits.

There are no data available on the excretion of miconazole in human milk; therefore caution should be exercised when breastfeeding women are using DECOZOL.

4.7 Effects on ability to drive and use machines

DECOZOL does not affect alertness or driving ability.

4.8 Undesirable effects

Adverse drug reactions from spontaneous reports during the worldwide post marketing experience miconazole oral gel are presented below. The adverse drug reactions are presented by system/organ class, and are ranked by frequency, using the following convention:

Very common ≥10%;

Common ≥1% to <10%;

Uncommon ≥0.1% to <1%;

Rare ≥0.01% to <0.1%;

Very Rare <0.01%.

The frequency 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.

<u>Immune system disorders</u>

Very rare Allergic conditions, including angioneurotic oedema and anaphylactic reactions.

<u>Respiratory, thoracic and mediastinal disorders</u>

Vary rare choking (see section 4.3).

Gastrointestinal system disorders

Very rare	Nausea, vomiting and diarrhoea, anorexia.

Hepatobiliary disorders

Very rare	Hepatitis.

Skin and subcutaneous disorders

Very rare	Lyell syndrome (Toxic Epidermal Necrolysis), Stevens Johnson syndrome, urticaria, rash.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

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

In the event of accidental ingestion of large quantities of DECOZOL Oral Gel, an appropriate method of gastric emptying may be used, if considered necessary (see Interactions).

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

The oral bioavailability is low (25-30%) because there is little absorption of miconazole from the intestinal tract.

Miconazole is systemically absorbed after administration as the oral gel. Administration of 60 mg dose of miconazole oral gel results in peak plasma concentrations of 31-49 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 oral gel is largely metabolized; less than 1% of the administered dose is excreted unchanged in the urine. The terminal plasma halflife is 20-25 hours in most patients. The elimination half-life of miconazole is similar in any renally impaired patient. Plasma concentrations of miconazole are moderately reduced (approximately 50%) during hemodialysis.

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 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl hydroxybenzoate
Orange oil
Polysorbate 20
Potato starch
Propyl hydroxybenzoate
Propylene glycol
Purified water
Saccharin sodium
Xanthan gum

6.2 Incompatibilities

None known.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 30°C.

6.5 Nature and contents of container

DECOZOL Oral Gel is supplied in 15 g and 40 g tubes with a measuring spoon.

6.6 Special precautions for disposal

Not applicable

7 MEDICINE SCHEDULE

Restricted medicine

8 SPONSOR

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9 DATE OF FIRST APPROVAL

19/04/2012

10 DATE OF REVISION OF THE TEXT

21/06/2019

SUMMARY TABLE OF CHANGES

Date	Section(s) Changed	Change (s)
February 2019	All	Reformat consistent with new Medsafe Data Sheet Template.
June 2019	2	Qualitative and Quantitative Composition changed to Miconazole 2% w/w