

## FUNGITRIN

Oral Gel

### Composition

Each gram contains Miconazole base 2%.

### Action

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.

### Pharmacokinetics

#### *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 Fungitrin 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 half-life 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.

### Indications

- Oral mycosis (thrush) and fungal infections of the upper gastrointestinal tract.
- Fungitrin oral gel can be used for the prevention of oral thrush in patients receiving long-term treatment with antibiotics, steroids, cytotoxic and radiation therapy.

### Contraindications

- In patients with a known hypersensitivity to miconazole or to any of the other ingredients of the gel.
- In infants less than 6 months of age or in those whose swallowing reflex is not yet sufficiently developed.
- In patients with liver dysfunction.
- Co-administrating of the following drugs that are subject to metabolism by CYP3A4 :
- 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.

## Warnings

If a reaction suggesting sensitivity or irritation occurs, discontinue use.

## Pregnancy

### Category C

Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

## Adverse Reactions

There have been isolated reports of irritation, burning and maceration. Nausea may occur. After long-term treatment, diarrhea may appear.

## Drug Interactions

- 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 Miconazole 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 hypoglycemics 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 Miconazole 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. Patients receiving Miconazole Oral Gel should therefore, not use these medicines.
- 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 Miconazole oral gel. However, clinically relevant interactions between oral miconazole and, indinavir and ritonavir, are not expected.
- Antineoplastic agents: Miconazole, when administered 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, cilostazol, 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.

### **Dosage and Administration**

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

Children (2 years of age and older) and Adults: Half (1/2) a measuring spoon\* of gel four times daily.

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

Fungitrin 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 Fungitrin 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.

### **Over Dosage**

Diarrhea, convulsions and possibly cardiac rhythm disorders may occur. Gastric lavage should be applied, followed by a purgative and supportive treatment as appropriate.

### **Presentation**

Tube of 30 grams