SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

PRODUCT NAME

GENERIC: Miconazole Oromucosal Gel BP

BRAND NAME: FUNGARIN

DESCRIPTION:

White homogenous translucent oral gel, sweet in taste and free from gritty particle.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Miconazole BP..... 20 mg

Ethanol (96%) BP.....7.59 mg

In an aqueous gel base ..... q.s.

or the full list of excipients, see 6.1.

Contains Sodium saccharin 0.1% w/w

3. PHARMACEUTICAL FORM:

Semisolid dosage form: Gel

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication:

Oral treatment of candidosis of the oropharynx.
Miconazole gel is for use in adults, children and infants 4 months and older.
Consideration should be given to official guidance on the appropriate use of antifungal agents.

4.2 Posology and method of administration:

For oral administration.
1 measuring spoon(provided) is equivalent to 124 mg miconazole per 5 mL gel.
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 Warning and precautions for use

If the concomitant use of Miconazole Oromucosal Gel with an oral anticoagulant such as warfarin is planned, caution should be excercised and the anticoagulant effect must be carefully monitored and titrated .
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 Miconazole Oromucosal Gel and with other miconazole formulations. 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 .
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.
This medicinal product contains small amounts of ethanol (alcohol)

Serious skin reactions (e.g. Toxic epidermal necrolysis and Stevens-Johnson syndrome) have been reported in patients receiving Miconazole Oromucosal Gel.It is recommended that patients be informed about the signs of serious skin reactions, and that use of Miconazole Oromucosal Gel be discontinued at the first appearance of skin rash..

4.5 Drug 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 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 Pregnancy & 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, FUNGARIN 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 FUNGARIN Oral Gel to nursing mothers.

4.7 Effects on ability to drive and use machines:

FUNGARIN should not affect alertness or driving ability.

4.8 Adverse Effects

Adult Patients

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

Paediatric Patients 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.

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 A07AC01

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polysorbate 20, Pregelatinized Potato starch (PREGEL-PA5), glycerine, Sodium Saccharin, Ethanol, Flavour pineapple, purified water.

6.2 Incompatibilities

Not Applicable

6.3 Shelf Life

24 Months.

6.4 Special precautions for storage:

Keep well closed. Do not store above 30°C. Do not freeze

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

15g, 30g, 40g, 80g Aluminium Collapsible tubes with epoxy phenol lacquered with latex lining.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements

7. APPLICANT

Manufactured by:

S Kant
HEALTHCARE Ltd.

1802-1805, G.I.D.C., Phase III,

Vapi - 396 195. Gujarat, INDIA.

8. WHO PREQUALIFICATION REFERENCE NUMBER

Not applicable

9. DATE OF PREQUALIFICATION / RENEWAL OF PREQUALIFICATION

Not applicable

10. DATE OF REVISION OF THE TEXT

Not applicable