1.3Product Information
1.3.1 SPC, Labeling and Package Leaflet
SPC-Summary of Product Characteristics

1. Name of the Medicinal Product
Tabisafe Cream (Terbinafine Hydrochloride Cream 1%)

2. Qualitative and Quantitative Composition
Each 1 gm Cream contains:

Terbinafine Hydrochloride BP 10mg
Cream Base q.s.

3. Pharmaceutical Form
Cream
Route of Administration: Topical

4. Clinical particulars
4.1 Therapeutic indications

- Fungal infections of the skin due to dermatophytes such as Trichophyton (eg, T. rubrum, T. mentagrophytes, T. verrucosum, T. violaceum), Microsporum canis and Epidermophyton floccosum).
- Treatment of intertrigo of the toes (athlete's foot) and genital and crural intertrigo.
- Skin infections due to Candida (eg Candida albicans).
- Pityriasis (tinea) versicolor due to Pityrosporum orbiculare (Malassezia furfur).

4.2 Posology and method of administration
4.2.1 Posology

Adults and children older than 12 years

Indication	Duration and Frequency of the treatment
Intertrigo of the toes :	1 week, 1 to 2 times a day
Genital and crural intertrigo	1 to 2 weeks, 1 to 2 times a day
Cutaneous Candida	2 weeks, 1 to 2 times a day
Pityriasis versicolor :	2 weeks, 1 to 2 times a day

- Irregular use or inadequate duration of treatment increases the risk of recurrence of symptoms.
- The improvement of clinical symptoms usually appears within a few days. If there is no sign of improvement after 2 weeks, the diagnosis should be re-evaluated.

4.2.2 Special populations

There are no data indicating that **older patients** require a different dosage or have a different adverse event profile from those of younger patients.

4.2.2 Paediatric population

The experience with terbinafine cream in children is limited. It is therefore not recommended to use this medicine in children under 12 years of age.

4.2.3 Method of administration

For cutaneous use.

- The skin must be cleaned and dried. The cream should be applied in a thin layer on and around the affected skin by gently penetrating it.
- In case of eczematous and red infections (under the breast, between the fingers, between the buttocks or in the groin), the skin can be covered with a sterile compress after the application of the cream, especially at night.

4.3 Contraindications

Hypersensitivity to the active substance, terbinafine,

4.4 Special warnings and precautions for use

4.4.1 General information

- Tabisafe cream is limited to external use.
- Tabisafe cream can irritate the eyes. Eye contact should be avoided. In case of accidental contact with eyes, rinse thoroughly with water.
- Tabisafe cream should be kept out of the reach of children.
- The appearance of erythema, pruritus or paresthesia does not require discontinuation of treatment. However, treatment should be stopped in case of more severe rashes or in case of allergic reactions such as rash or urticaria.

4.4.2 Paediatric population

The experience with terbinafine cream in children is limited. It is therefore not recommended to use this medicine in children under 12 years of age.

4.5 Interaction with other medicinal products and other forms of interaction

4.5.1 General information

There are non-know interactions between topical forms of terbinafine and other drugs.

4.5.2 Additional information on special populations

Not applicable

4.5.3 Paediatric population

The experience with terbinafine cream in children is limited. It is therefore not recommended to use this medicine in children under 12 years of age

4.6 Pregnancy and lactation
4.6.1 Pregnancy

Foetal toxicity and fertility studies in animals suggest no adverse effects. Since clinical experience in pregnant women is very limited, Tabisafe cream should not be used during pregnancy.

4.6.2 Lactation
After oral administration, terbinafine is excreted in human milk. The effect of terbinafine on newborn infants is unknown. After local use only low systemic absorption is expected. However, Tabisafe cream should not be used during breast feeding.

4.6.3 Fertility

In experimental animal studies, no effect of terbinafine on fertility was observed.

4.7 Effects on ability to drive and use machines

Tabisafe cream has no effect on the ability to drive and use machines.

4.8 Undesirable effects
Local symptoms such as pruritus, skin exfoliation, application site pain, application site irritation, pigmentation disorder, burning skin sensation, erythema, mange, etc. may occur at the application site

These mild symptoms should be distinguished from hypersensitivity reactions such as rash that are reported in sporadic cases and require discontinuation of treatment.

In case of accidental contact with the eyes, terbinafine may cause eye irritation.

In rare cases, the underlying fungal infection can be aggravated.

The frequencies of adverse reactions reported with terbinafine are defined as:

- 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)
- not known (cannot be estimated from the available data)

Immune system disorders	
Hypersensitivity *	not known
Ocular affections	
Irritation of the eyes	rare
Affections of the skin	
exfoliation, pruritus	common
cutaneous lesion, scabs, skin abnormalities, pigmentary abnormalities, erythema,	uncommon:

burning sensation	
dry skin, contact dermatitis, eczema	rare
skin rash *	not known:
General disorders and administration site conditions	
pain, application site pain, application site irritation	uncommon:
worsening of the condition	rare

* Based on experience since the marketing

4.9 Overdose

Due to the weak systemic absorption of topical terbinafine, overdose is extremely unlikely.

symptoms

Accidental ingestion of a 30 g tube of Tabisafe cream, which contains 150 mg of terbinafine hydrochloride, is comparable to ingestion of a 250 mg half tablet of terbinafine (an adult oral dose unit) . In the case of accidental ingestion of a larger quantity of terbinafine cream, similar adverse effects as observed during overdose with terbinafine tablets may be expected. These side effects include headache, nausea, epigastric pain and dizziness.

Treatment

In case of accidental ingestion, the recommended treatment for overdose is to attempt the elimination of the active ingredient, starting with activated charcoal and applying symptomatic treatment if necessary.

5- PHARMACOLOGICAL PROPERTIES

Antifungals for topical use
ATC code: D01A E15

5.1 Pharmacodynamics properties

Terbinafine is an antimycotic with a broad-spectrum of anti-fungal activity belonging to the allylamine group. At low concentrations terbinafine is fungicidal against dermatophytes, moulds and certain dimorphic fungi. The activity against yeasts, e.g. Candida species is fungicidal or fungistatic depending on the species.

Terbinafine interferes with fungal sterol biosynthesis by the inhibition of squalene epoxidase in the fungal cell membrane, which leads to an intracellular accumulation of squalene, resulting in fungal cell death.

5.2 Pharmacokinetic properties

After topical application in humans, less than 5% of the dose is absorbed. The systemic effect is therefore very weak.

Less than 5% of the dose is absorbed after topical application; systemic exposure is therefore very slight. Terbinafine does not influence the cytochrome P-450 enzyme system and the metabolism of hormones and other drugs depending on cytochrome P-450 system

5.3 Preclinical safety data

In long-term studies (up to 1 year) in rats and dogs no marked toxic effects were seen in either species up to oral doses of about 100mg/kg a day. At high oral doses, the liver and possibly also the kidneys were identified as potential target organs. In a two-year oral carcinogenicity study in mice, no neoplastic or other abnormal findings attributable to treatment were made up to doses of 130 (males) and 156 (females) mg/kg a day. In a two-year oral carcinogenicity study in rats, an increased incidence of liver tumours was observed in males at the highest dosage level of 69mg/kg a day. The changes which may be associated with peroxisome proliferation have been shown to be species-specific since they were not seen in the carcinogenicity study in mice, dogs or monkeys. During high-dose studies in monkeys, refractile irregularities were observed in the retina at the higher doses (non-toxic effect level 50mg/kg). These irregularities were associated with the presence of a terbinafine metabolite in ocular tissue and disappeared after drug discontinuation. They were not associated with histological changes. A standard battery of in vitro and in vivo genotoxicity tests revealed no evidence of mutagenic or clastogenic potential.

No adverse effects on fertility or other reproduction parameters were observed in studies in rats or rabbits.

6. Pharmaceutical Particulars

6.1 List of Excipients

Cetosteraryl Alcohol BP
Cetomacrogol 1000 BP
Light liquid paraffin BP
White petroleum jelly BP
Sodium propyl jelly BP
Sodium Methyl Paraben BP
Propylene Glycol BP
Di-Sodium EDTA BP
Tween 80 BP
Citric Acid BP
Purified water BP

6.2 Incompatibilities

None known

6.3 Shelf Life

3 years

6.4 Special precautions for Storage

Do not store above 30°C. Store in the original package.

6.5 Nature and contents of Container

30 g Lemi tube closed with a polyethylene screw cap in cardboard box along with insert

6.6 Special precautions for disposal and other handlings

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

7. REGISTRANT

7.1 Marketing Authorisation Holder

Merit Organics Ltd

Plot No 2104/2/A, G.I.D.C , Sarigam , Bhilad,

Dist- Valsad-396155, Gujarat , INDIA

7.2 Manufacturer

Merit Organics Ltd

Plot No 2104/2/A, G.I.D.C , Sarigam , Bhilad,

Dist- Valsad-396155, Gujarat , INDIA

Applicant: ANNYGOD PHARMACEUTICAL COMPANY LTD, 28 UKWULU STREET, AWADA OBOSI, ANAMBRA STATE

8. MARKETING AUHORISATION NUMBER

9. DATE OF REVISION OF THE TEXT

Applicable once the registration is obtained.

10. DATE OF REVISION OF TEXT