

Appendix No. 5

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

TERBINAFINE HYDROCHLORIDE CREAM 1%

2. Qualitative and quantitative composition

ACTIVE INGREDIENTS				
APPROVED NAME	SPECIFICATION OR REFERENCE TEXT	QTY/ 15 GM		% OVERAGES
		QTY/ 15 GM	%W/W/ 15 GM	
Terbinafine hydrochloride*	BP	0.153 gm	1.02 %	2.00 %
INACTIVE INGREDIENTS				
APPROVED NAME	SPECIFICATION OR REFERENCE TEXT	QTY/15 GM		REASON FOR INCLUSION
		QTY/ 15 GM	%W/W/ 15 GM	
White soft paraffin	BP	1.200 ml	8.00 %	Emulsifier
Cetomacrogol 1000	BP	0.600 gm	4.00 %	Emulsifier
Sodium propyl paraben	BP	0.015 gm	0.10 %	Preservative
Sodium benzoate	BP	0.030 gm	0.20 %	Diluent
Cetostearyl alcohol	BP	0.750 gm	5.00 %	Emulsifier
Propylene glycol	BP	0.450 ml	3.00 %	Solvent
Light liquid paraffin	BP	1.050 ml	7.00 %	Emulsifier
Stearic acid	BP	0.300 gm	2.00 %	Thickener
Benzyl alcohol	BP	0.150 ml	1.00 %	Preservative
Demineral water	INHOUSE	10.302 ml	68.68 %	Vehicle

*2.00 % Overages are added on label claim

3. Pharmaceutical form

Topical cream

4. Clinical particulars**4.1 Therapeutic indications**

- Fungal infections of the skin caused by Trichophyton (eg. T. Rubrum, T. Mentagrophytes, T. Verrucosum, T. Violaceum), Microsporum canis and Epidermophyton floccosum.
- Yeast infections of the skin, principally those caused by the genus Candida (eg. C. albicans).
- Pityriasis (tinea) versicolor due to Pityrosporum orbiculare (also known as Malassezia furfur).

4.2 Posology and method of administration

Terbinafine Hydrochloride Cream 1% can be applied once or twice daily.

Duration and frequency of treatment

The likely duration of each treatment is as follows:

Tinea Corporis, Cruris:	1 to 2 weeks
Tinea Pedis:	1 week
Cutaneous Candidiasis:	2 weeks
Pityriasis Versicolor:	2 weeks

Relief of clinical symptoms usually occurs within a few days. Irregular use or premature discontinuation of treatment carries the risk of recurrence. If there are no signs of improvement after two weeks, the diagnosis should be verified.

Dosing in special populations:

Paediatric Population

The experience with topical Terbinafine Hydrochloride Cream 1% in children is still limited and its use cannot therefore be recommended.

Elderly Patients

There is no evidence to suggest that elderly patients require different dosages or experience side-effects different to those of younger patients.

Method of administration

For cutaneous use.

Cleanse and dry the affected areas thoroughly before application of Terbinafine Hydrochloride Cream 1%. Apply the cream to the affected skin and surrounding area in a thin layer and rub in lightly. In the case of intertriginous infections (submammary, interdigital, intergluteal, inguinal) the application may be covered with a Gauze Strip, especially at night.

4.3 Contraindications

Hypersensitivity to Terbinafine or any of the excipients contained in the cream.

4.4 Special warnings and precautions for use

Terbinafine Hydrochloride Cream 1% is for external use only. Contact with the eyes should be avoided. May be irritating to the eyes. In case of accidental contact with the eyes, rinse the eyes thoroughly with running water.

Terbinafine Hydrochloride Cream 1% contains cetyl alcohol and stearyl alcohol, which may cause local skin reactions (e.g. contact Dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction

There are no known drug interactions with Terbinafine Hydrochloride Cream 1%.

4.6 Pregnancy and lactation

Pregnancy

There is no clinical experience with Terbinafine Hydrochloride Cream 1% in pregnant women, therefore, unless the potential benefits outweigh any potential risks, Terbinafine Hydrochloride Cream 1% should not be administered during pregnancy.

Foetal toxicity studies in animals suggest no adverse effects.

Breastfeeding

Terbinafine is excreted in breast milk. Therefore mothers should not receive Terbinafine Hydrochloride Cream 1% while breast-feeding. Infants must not be allowed to come into contact with any treated skin, including the breast.

4.7 Effects on ability to drive and use machines

Terbinafine Hydrochloride Cream 1% has no influence 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, Skin Burning sensation, Erythema and Scab may occur at the site of application.

These minor symptoms must be distinguished from hypersensitivity reactions such as widespread pruritis, rash, Bullous Eruptions and hives which are reported in sporadic cases but require discontinuation.

In case of accidental contact with the eyes Terbinafine hydrochloride may be irritating to the eyes.

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

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$), or not known (can not to be estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Immune system disorders

Hypersensitivity

Eye disorders

Eye irritation

Skin and subcutaneous tissue disorders

Skin exfoliation, pruritus, Skin lesion, scab, skin disorder, pigmentation disorder, erythema, skin Rash

General disorders and administration site conditions

Pain, application site pain, irritation, condition aggravated

4.9 Overdose

The low systemic absorption of topical terbinafine cream renders overdosage extremely unlikely. Accidental ingestion of the contents of one 30g tube of Terbinafine Hydrochloride Cream 1%, which contains 300mg terbinafine hydrochloride, is comparable to one Terbinafine 250mg tablet (adult oral unit dose).

Should a larger amount of Terbinafine Hydrochloride Cream 1% be inadvertently ingested, adverse effects similar to those observed with an Overdosage of Terbinafine tablets are to be expected. These include Headache, Nausea, Epigastric Pain and Dizziness.

If accidentally ingested, the recommended treatment of overdosage consists of eliminating the drug, primarily by the administration of activated charcoal, and giving symptomatic supportive therapy, if needed.

5. Pharmacological properties**5.1 Pharmacodynamic properties****Pharmacotherapeutic Group:**

Antifungal for topical use

Terbinafine is an allylamine which has a broad spectrum of antifungal activity. At low concentrations Terbinafine is fungicidal against dermatophytes, moulds and certain dimorphic fungi. The activity versus yeasts is fungicidal or fungistatic depending of the species.

Terbinafine interferes specifically with fungal sterol biosynthesis at an early step. This leads to a deficiency in ergosterol and to an intracellular accumulation of squalene, resulting in fungal cell death. Terbinafine acts by inhibition of squalene epoxidase in the fungal cell membrane. The enzyme squalene epoxidase is not linked to the cytochrome P450 system.

5.2 Pharmacokinetic properties

Less than 5% of the dose is absorbed after topical application to humans; systemic exposure is therefore very slight.

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 100 mg/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 at the highest dose level, 69 mg/kg a day, an increased incidence of liver tumours was observed in males. 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 or in other studies in Mice, Dogs or Monkeys.

During the studies of high dose oral terbinafine in monkeys, Refractile Irregularities were observed in the retina at the higher doses (non-toxic effect level was 50 mg/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 a mutagenic or Clastogenic potential for the drug.

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

- White soft paraffin
- Cetomacrogol 1000
- Sodium propyl paraben
- Sodium benzoate
- Cetostearyl alcohol
- Propylene glycol
- Light liquid paraffin
- Stearic acid
- Benzyl alcohol
- Demineral water

6.2 Incompatibilities

None known

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store in a dry place at a temperature below 30°C.

6.5 Nature and contents of container

15 gm printed lami tube packed in printed and laminated carton.

6.6 Special precautions for disposal and other handling

Not applicable.

7. Marketing Authorization holder

West Coast Pharmaceutical Works Ltd, Ahmedabad

8. Marketing Authorization number(s)

Not applicable.

9. Date of first Authorization/renewal of the Authorization

Not applicable.

10. Date of revision of the text

November, 2016

