SCHEDULING STATUS S1

1. NAME OF THE MEDICINE

TERBANE 10 mg (cream)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 g Terbane cream contains 10 mg terbinafine hydrochloride.

For the full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

A white or almost white cream of homogenous appearance.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Adults and children over the age of 12 years:

Fungal infections of the skin caused by dermatophytes such as *Trichophyton* (eg. *T. rubrum*, *T. mentagrophytes*, *T. verrucosum*, *T. violaceum*) and *Epidermophyton floccosum*.

Yeast infections of the skin, principally those caused by *Candida albicans*.

Pityriasis (tinea) versicolor due to *Pityrosporum orbiculare* (also known as *Malassezia furfur*).

4.2 Posology and method of administration

Duration and frequency of treatment:

Tinea corporis and *Tinea cruris* (ringworm of the body, jock itch): once daily application for one week.

Tinea pedis (athlete's foot): once daily application for one week.

Cutaneous candidiasis (skin thrush): one week.

Pityriasis versicolor: two weeks.

Relief of 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.

Do not use for longer than one month.

Use of TERBANE in the elderly:

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

Method of administration:

For cutaneous use.

TERBANE can be applied once or twice daily.

Cleanse and dry the affected areas thoroughly before treating with TERBANE. Apply the cream to the affected skin and surrounding area in a thin layer and rub in lightly. In the case of intertriginous infections (sub-mammary, interdigital, intergluteal, inguinal) the application may be covered with gauze, especially at night.

4.3 Contraindications

Hypersensitivity to terbinafine or to any of the excipients listed in section 6.1.

Safety in infants and children under 12 years has not been established.

Safety in pregnancy and lactation has not been established.

Terbinafine is excreted in breast milk.

4.4 Special warnings and precautions for use

TERBANE cream is for external use only.

TERBANE may be irritating to the eyes. Contact with eyes should be avoided. In case of accidental contact with the eyes, rinse eyes thoroughly with running water.

TERBANE should be kept out of the reach of children.

In the event of allergic reaction, the cream should be removed and the treatment interrupted.

Instruct patients not to smoke or go near naked flames - risk of severe burns. Fabric (clothing, bedding, dressings, etc.) that has been in contact with this product burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up, but not totally remove it.

Candidiasis: It is not recommended to use acid pH soap. This provides favourable growth conditions for *Candida* spp.
TERBANE contains 10 mg benzyl alcohol in each gram of cream. Benzyl alcohol may cause allergic reactions and mild local irritation. TERBANE also contains cetostearyl alcohol which may cause local skin reactions (e.g. contact dermatitis).

4.5 Interaction with other medicines and other forms of interaction

No medicine interactions are known with the topical forms of terbinafine.

4.6 Fertility, pregnancy and lactation

Pregnancy:

There is no clinical experience with TERBANE in pregnant women. Foetal toxicity studies conducted in animals suggest no adverse effects (see section 5.3). TERBANE should not be used during pregnancy.

Breastfeeding:

Terbinafine is excreted in breast milk. After topical use, only a low systemic exposure is expected (see section 5.2). TERBANE should not be used during breastfeeding. In addition, infants must not be allowed to come into contact with any treated skin, including the breast.

Fertility:

No effects of terbinafine on fertility have been seen in animal studies (see section 5.3).

4.7 Effects on ability to drive and use machines

TERBANE 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, scab, etc. may occur at the site of application.

These harmless symptoms must be distinguished from hypersensitivity reactions including rash, which are reported in sporadic cases and require discontinuation of therapy.

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

In rare cases the underlying fungal infection may be aggravated.

Immune system disorders:

Not known: Hypersensitivity

Eye disorders:

Less frequent: Eye irritation

Skin and subcutaneous tissue disorders:

Frequent: Skin exfoliation, pruritus

Less frequent: Skin lesion, scab, skin disorder, pigmentation disorder, erythema, skin burning sensation, dry skin, dermatitis contact, eczema

Not known: Rash

General disorders and administration site conditions:

Less frequent: Pain, application site pain, application site irritation, condition aggravated

These symptoms must be distinguished from allergic reactions, which are rare but require discontinuation.

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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://sahpra.org.za/wp-content/uploads/2020/01/%206.04_ARF1_v5.1_27Jan2020.pdf.

Suspected side effects can also be reported directly to the HCR via Patientsafety.sacg@novartis.com.

4.9 Overdose

The low systemic absorption of topical terbinafine renders overdose extremely unlikely.

Symptoms:

Accidental ingestion of one 30 g tube of terbinafine cream, which contains 300 mg terbinafine hydrochloride, is comparable to ingestion of one terbinafine 250 mg tablet (adult oral unit dose).

Should a larger amount of terbinafine cream be inadvertently ingested, adverse effects similar to those observed with an over dose of terbinafine tablets are to be expected. These include headache, nausea, epigastric pain and dizziness.

Treatment:

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

5. PHARMACOLOGICAL PROPERTIES

Pharmacological classification: A 20.2.2 Antimicrobial (chemotherapeutic) agents. Fungicides

5.1 Pharmacodynamic properties

Terbinafine is an allylamine that has a broad spectrum of antimycotic activity. It has an antimycotic effect on fungal infections of the skin caused by dermatophytes such as *Trichophyton* (e.g. *T. rubrum, T. mentagrophytes, T. verrucosum, T. violaceum*)*, Microsporum canis* and *Epidermophyton floccosum.* At low concentrations, terbinafine has a fungicidal effect against dermatophytes and moulds. Its activity against yeasts is fungicidal (e.g. *Pityrosporum orbiculare* or *Malassezia furfur*) or fungistatic depending on 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. Terbinafine does not influence the metabolism of hormones or other medicines.

5.2 Pharmacokinetic properties

Less than 5 % of the dose is absorbed after topical application to humans.

Systemic exposure is thus very low.

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 medicine 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 medicine.

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

Benzyl alcohol, cetostearyl alcohol, cetyl palmitate 15, isopropyl myristate, polysorbate 60, purified water, sodium hydroxide, sorbitan stearate.

Contains preservative: benzyl alcohol 1,0 % *m/m*.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store in a cool place, at or below 25 °C.

6.5 Nature and contents of container

Collapsible inside lacquered aluminium tubes of 7,5 and 15 g with plastic screw caps.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Sandoz SA (Pty) Ltd[1]

Waterfall 5-lr

Magwa Crescent West

Waterfall City

Jukskei View

2090

8. REGISTRATION NUMBER

A39/20.2.2/0009

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15 August 2008

10. DATE OF REVISION OF THE TEXT

12 October 2020

Additional country registration details:

Country	*Product name*	*Scheduling status (or Category of distribution)*	*Registration number*
Namibia	Terbane 10mg	NS1	10/20.2.2/0039
Zambia	Terbane 10mg	POM	039/029

ATC Code: D01AE15 - Other antifungals for topical use

Name and address of manufacturer:

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Adelgade 27
DK-8660 Skanderborg,
Denmark

or

Salutas Pharma GmbH
Betriebsstätte Osterweddingen
Lange Gohren 3
D-39171 Osterweddingen,
Germany

[1]Company Reg. No.: 1990/001979/07