PROFESSIONAL INFORMATION

SCHEDULING STATUS S1

1. NAME OF THE MEDICINE

Terbane® Nail (medicated nail lacquer)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of medicated nail lacquer contains terbinafine hydrochloride equivalent to 78,22 mg of terbinafine (10 % *w/w*).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Medicated nail lacquer.

Clear, colourless to yellowish, slightly viscous topical solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Mild to moderate fungal infections of the nails caused by dermatophytes and/or other terbinafine-sensitive fungi.

TERBANE NAIL is indicated in adults.

Consideration should be given to official guidance on the appropriate use of antifungal medicines.

4.2 Posology and method of administration

The medicated nail lacquer is intended for use on fingernails and toenails.

Posology:

After an initial 4-week period of daily treatment, TERBANE NAIL should be applied to the affected nails once weekly.

In general, the treatment duration for fingernails is about 6 months while for toenails it is about 9 to 12 months.

An additional oral therapy should be considered in cases of inadequate response to topical treatment at the end of the treatment period and in cases of severe nail infection, including one or more finger- and/or toenails and/or matrix involvement. In these situations, medical advice should be sought.

Dosing in special populations:

Paediatric population:

The safety and efficacy of TERBANE NAIL in children and adolescents aged below 18 years have not yet been established.

Method of administration

Cutaneous use only (for application on the nails).

Before application of TERBANE NAIL, remove any nail polish or other cosmetic product from the nails and immediately adjacent skin. Clean and dry the affected areas thoroughly.

A thin layer of TERBANE NAIL using the applicator should be applied over the entire surface of the affected nails, 5 mm of surrounding skin and, if possible, under the free nail edge as well as the skin under the nail. The patient should wait about 30 seconds until the lacquer has completely dried.

The treated nails should not be washed or get wet for at least 6 hours. Therefore, application in the evening before going to bed and after showering or bathing is recommended. After that time, normal hygienic practices can be followed.

TERBANE NAIL does not need to be removed by any solvent or abrasives (i.e., nail filing). It is sufficient to carefully wash the nails with water.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

In case of involvement of more than 3 nails or more than half of the nail plate is altered or nail matrix is involved, and in cases of predisposing factors, such as diabetes and immune disorders, the addition of a systemic therapy should be considered.

Duration of disease, extent of involvement of the nail plate and nail thickness may influence results of therapy.

TERBANE NAIL is for external use only.

Patients with a history of diabetes, immune disorders, peripheral vascular disease, injured, painful or seriously damaged nails, skin conditions such as psoriasis or any other chronic skin condition, and yellow nail syndrome (oedema in the lower limbs, breathing disorders and yellow nail discolouration) should seek medical advice prior to commencing treatment.

Contact with any part of the body different from the affected area should be avoided until the lacquer is completely dried. Irritation may occur in case of accidental contact with the eyes or mucous membranes. In case of accidental contact with these areas, rinse thoroughly with running water.

The impact of nail polish or other cosmetic nail products on the efficacy of TERBANE NAIL has not been evaluated.

Paediatric population:

TERBANE NAIL should not be used in children and adolescents below 18 years of age due to a lack of clinical experience in this age group.

TERBANE NAIL contains 616 mg alcohol (ethanol) in each ml of solution. It may cause a burning sensation on damaged skin.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed. However, after application as recommended, the systemic bioavailability of terbinafine is considered negligible (see section 5.2), thus no systemic interactions are foreseen.

Other medicines should not be used on the affected areas.

4.6 Fertility, pregnancy and lactation

Pregnancy:

There are no available data on the use of terbinafine in pregnant women. Animal studies do not indicate any harmful effects with respect to pregnancy or the health of the foetus (see section 5.3).

TERBANE NAIL should not be used during pregnancy unless clearly necessary.

Breastfeeding:

Terbinafine is excreted into breastmilk. After topical use only low systemic exposure is expected. TERBANE NAIL use during breastfeeding is not recommended.

Infants must not be allowed to come into contact with any treated area.

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 NAIL has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile:

Adults:

The safety profile of TERBANE NAIL in adults is based on pooled data from 2 randomised, double-blind, vehicle-controlled studies (PM1331 and PM0731) in patients with mild to moderate onychomycosis. A total of 556 patients were treated with TERBANE NAIL at the recommended dose regimen and 454 patients were treated with the vehicle. The most commonly reported adverse drug reaction was erythema (0,9 % in the TERBANE NAIL arm; no events of erythema were reported in the vehicle arm) at the site of application. All events of erythema were mild and transient.

Table 1: Adverse reactions in onychomycosis patients treated with TERBANE NAIL

System Organ Class	Frequency	Adverse reaction
Skin and subcutaneous tissue disorders	Frequent	Nail discolouration, Onycholysis, Onychomadesis, Paronychia, Contact Dermatitis, Erythema.
	Less frequent*	Skin irritation, Dermatitis, Nail disorder, Pruritus.

* Less frequent adverse reactions affected either the treated nails or the surrounding skin. These reactions were similar to the frequent adverse reactions included in the table or can be described as skin irritation, dermatitis or nail disorders.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of TERBANE NAIL is important. It allows continued monitoring of the benefit/risk balance of TERBANE NAIL. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Suspected adverse reactions can also be reported directly to the HCR via https://pvi1j.solutions.iqvia.com or the e-mail address, adverse.event.sac@sandoz.com.

4.9 Overdose

Due to the route of administration, overdose is very unlikely. No systemic signs of overdose are expected following topical application of TERBANE NAIL. In the event of accidental oral ingestion, appropriate symptomatic measures should be taken.

5. PHARMACOLOGICAL PROPERTIES

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

Pharmacotherapeutic group: Antifungals for dermatological use; Other antifungals for topical use.

ATC code: D01AE15.

5.1 Pharmacodynamic properties

Mechanism of action:

Terbinafine is an allylamine which has a broad spectrum of antifungal activity in fungal infections 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 is fungicidal against dermatophytes and moulds.

The 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 substances.

5.2 Pharmacokinetic properties

Terbinafine medicated nail lacquer has demonstrated good permeation properties through keratin. By achieving fungicidal concentrations at the site of infection, the active substance leads to inhibition of squalene epoxidase, which has a fungistatic and a fungicidal effect (see section 5.1).

Given the limited area treated by the topical route of administration, the amount of terbinafine reaching the systemic circulation after TERBANE NAIL treatment is negligible.
Average terbinafine plasma concentrations at steady-state (± standard deviation [SD]) after once weekly application of TERBANE NAIL (197 ± 134 pg/mL) are more than 3 orders of magnitude lower than those obtained after oral terbinafine administration (1,70 ± 0,77 µg/mL). Following prolonged use of TERBANE NAIL (up to 52 weeks), there is no indication of drug accumulation in the body.

Average terbinafine concentrations in the nail at steady-state (± SD) after once weekly application of TERBANE NAIL (9 245 ± 6 325 µg/g) are more than 3 orders of magnitude higher (up to 11 000-fold) than those obtained after oral terbinafine administration (1,01 µg/g). Nail concentrations at steady-state with topical TERBANE NAIL were also many orders of

magnitude higher than the minimum inhibitory concentration (MIC) for dermatophytes (≥ 500 000 MIC).

5.3 Preclinical safety data

Preclinical data available for oral terbinafine reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and reproductive and developmental toxicity.

Preclinical data available for the TERBANE NAIL shows minimal irritation potential on skin. Sensitisation studies showed that TERBANE NAIL is devoid of allergenic potential. The phototoxic potential of TERBANE NAIL 10 % was investigated with artificial sunlight and no phototoxic effects were observed.

In dermal (semi-occlusive) toxicity studies in animals, no drug-induced systemic effect was seen with TERBANE NAIL 10 % or 15 % while no or slight local signs of irritation (erythema, scabs, scaling) were evident at the application site.

Terbinafine plasma levels following both 4-week and 9-month daily dermal application of TERBANE NAIL (5 %, 10 %, and 15 % terbinafine) showed low systemic exposure to terbinafine, with no detectable dose-dependency.

Environmental risk assessment studies have shown that terbinafine hydrochloride may pose a risk for aquatic compartment(s).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol 96 %

Hydroxypropyl chitosan (HPCH)

Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

Discard 6 months after first opening the bottle.

6.4 Special precautions for storage

Store at or below 25 °C.

Keep the bottle tightly closed to avoid drying up of the content.

Keep the bottle in the outer carton to protect the product from light.

For the shelf life after first opening of the medicine, see section 6.3.

Nature and contents of container

A clear type III glass bottle with a low-density polyethylene (LDPE) applicator. The applicator incorporates a short LDPE spatula, embedded in an outer polypropylene bottle screw cap. The bottle cap is attached to the applicator, however, is not in contact with the solution.

Pack sizes: 3,3 mL, 6,6 mL.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Sandoz SA (Pty) Ltd[1]

Magwa Crescent West

Waterfall City

Jukskei View

Midrand

2090

8. REGISTRATION NUMBER

56/20.2.2/1092

9. DATE OF FIRST AUTHORISATION

22 October 2024

10. DATE OF REVISION OF THE TEXT

Not applicable.

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