SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TEKFIN 1% Cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g cream contains:
Active substance:
Terbinafine hydrochloride 10 mg
Excipients with known effect:
Cetyl alcohol 40 mg
Stearyl alcohol 40 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream for topical application.
White, odorless cream with soft consistency and homogeneous appearance, miscible with water.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Tinea pedis
- Tinea corporis/cruris
- Cutaneous candidiasis
- Pityriasis (Tinea) versicolor

4.2 Posology and method of administration

Posology
For adults and adolescents (over 16 years of age), unless otherwise recommended by the doctor;
Depending on the indication, TEKFIN can be applied once or twice daily. Cleanse and dry the affected areas thoroughly before application of TEKFIN. 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.

The likely duration of each treatment is as follows:
Tinea pedis : Once daily for 1 week
Tinea corporis, cruris : Once daily for 1 week
Cutaneous candidiasis: Once or twice daily for 1 week
Pityriasis versicolor : Once or twice daily for 2 weeks

Frequency and duration of administration
Relief of clinical symptoms occurs within a few days. Irregular use or premature discontinuation of treatment carries the risk of recurrence. If no improvement is obtained after 2 weeks, the diagnosis should be re-evaluated.

Method of administration
For topical application.

Additional information on special populations

Renal/Hepatic impairment

No data are available for dose adjustment in patients with renal and hepatic impairment.

Pediatric population

The safety of using this drug in children has not been conclusively proven.
Since there is limited experience with the use of TEKFIN in children under 16 years of age, its use in this age group is not recommended.

Geriatric population

There is no evidence to suggest that elderly patients (65 years and older) require a different dosage or experience different side effects from younger patients.

4.3 Contraindications

Hypersensitivity to terbinafine or any of the excipients contained in TEKFIN.

4.4 Special warnings and precautions for use

TEKFIN is for external use only. Contact with the eyes should be avoided. In case of accidental contact, the eyes should be rinsed thoroughly with plenty of water. If any symptoms develop, the physician should be consulted.

The drug can cause toxic epidermal necrosis. In addition, irritation and tenderness of the skin may be observed.

TEKFIN 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

No drug interactions related to TEKFIN have been reported to date.

Additional information on special populations

No clinical interaction studies have been conducted in special populations.

Pediatric population

Clinical interaction studies in the pediatric population have not been conducted.

4.6 Fertility, pregnancy and lactation

General Recommendation

The pregnancy category is B.

Women of childbearing potential/Contraception

No data are available to support specific recommendations for women of childbearing potential.

Pregnancy

No clinical data on exposure during pregnancy are available for TEKFIN.
Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy / embryonal / fetal development / parturition or postnatal development (see section 5.3).
Since clinical experience in pregnant women is not sufficient, TEKFIN should not be used during pregnancy unless the expected benefits outweigh the possible risks.

Breastfeeding
Terbinafine is excreted in breast milk to a degree that may cause effects on the breastfed child when therapeutic doses of TEKFIN are administered to breastfeeding women.
In addition, infants should not be allowed to touch any treated skin area, including the breasts.
TEKFIN should not be used during breastfeeding.

Reproduction ability/Fertility
Terbinafine did not appear to affect fertility in animal studies, and there are no data to suggest that human fertility may be affected.

4.7 Effects on ability to drive and use machines
TEKFIN 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, skin burning sensation, erythema, scab, etc. may occur at the site of application. These minor 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, terbinafine may be irritating to the eyes. In rare cases, the underlying fungal infection may be aggravated.

Undesirable effects from clinical trials are listed by MedDRA system organ class. In each system organ class, undesirable effects are ranked according to frequency, with the most frequent reactions first. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. In addition, the frequency category corresponding to each undesirable effect is based on the following rule (CIOMS III).

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).

In addition, some undesirable effects have been obtained based on post-marketing experience with TEKFIN, including spontaneous case reports and cases in the literature. Because these reactions are reported voluntarily by a population of uncertain numbers, it is not possible to estimate their frequency reliably, so they are classified as "not known". These undesirable effects are listed in the same way as those obtained from clinical trials.

Immune system disorders:
Not known: Hypersensitivity*

Eye disorders:
Rare: Eye irritation

Skin and subcutaneous tissue disorders:
Common: Skin exfoliation, pruritus
Uncommon: Skin lesion, scab, skin disorder, pigmentation disorder, erythema, skin burning sensation
Rare: Dry skin, dermatitis contact, eczema
Not known: Rash*

General disorders and administration site conditions:
Uncommon: Pain, application site pain, application site irritation
Rare: Condition aggravated
*Based on post-marketing experience.

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

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

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

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: Antifungals for topical use
ATC code: D01AE15

Terbinafine is an allylamine that has a broad spectrum of antimycotic activity on fungal infections of the skin caused by dermatophytes such as *Tinea pedis, Tinea corporis, Tinea cruris, Cutaneous candidiasis, Pityriasis (Tinea) versicolor.* At low concentrations, terbinafine has a fungicidal effect against dermatophytes, molds and some dimorphic fungi. Its activity against yeasts is fungicidal (e.g. *Candida albicans, Pityrosporum orbiculare* or *Malassezia furfur*) or fungistatic, depending on the species.

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

5.2 Pharmacokinetic properties
General properties
Terbinafine is a white to off-white powder. It is soluble in methanol and ethanol; however, it is sparingly or slightly soluble in water. It is also slightly soluble in acetone. It should be protected from light.

Absorption:
Less than 5% of the dose is absorbed following topical application in humans; systemic exposure is thus very low.

Distribution:
Following administration of terbinafine for one week, terbinafine concentrations are high enough for fungicidal action in the affected stratum corneum for at least 7 days after treatment is discontinued.

After topical application, terbinafine levels in the blood are very low. Therefore, the metabolism of terbinafine cannot be studied after topical application.

Oral terbinafine binds strongly to plasma proteins (99%). It rapidly diffuses through the dermis and concentrates in the lipophilic stratum corneum. Oral terbinafine is also secreted in sebum, thus achieving high concentrations in hair follicles, hair and sebum-rich skin. In addition, oral terbinafine is distributed into the nail plate within the first few weeks after commencing therapy.

Biotransformation:
After topical application, terbinafine levels in the blood are very low. Therefore, the biotransformation of terbinafine cannot be studied after topical application.

Orally administered terbinafine is metabolized rapidly and extensively by at least seven CYP isoenzymes, with major contributions from CYP2C9, CYP1A2, CYP3A4, CYP2C8 and CYP2C19.

Biotransformation results in metabolites with no antifungal activity, which are excreted predominantly in the urine. The elimination half-life is 17 hours. No accumulation is possible.

Elimination:
No age-dependent pharmacokinetic changes in steady-state plasma concentrations of orally administered terbinafine have been observed; but the elimination may be slower in patients with renal or hepatic impairment, resulting in higher blood levels of terbinafine.

Linearity/Non-linearity:
Since the drug is applied topically, this information is not available.

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 tumors was observed in males. These changes have not been observed in mice or monkeys and are species-specific.

During the studies of high dose 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
Benzyl alcohol
Sodium hydroxide
Sorbitan monostearate
Cetyl palmitate
Cetyl alcohol
Stearyl alcohol
Polysorbate 60
Isopropyl myristate
Deionized water

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
48 months.

6.4 Special precautions for storage
Store at room temperature below 25°C.

6.5 Nature and contents of container
15 g cream:
White, HDPE, aluminum tubes of 15 g that are screw-capped, printed on the outside and lacquered on the inside.

30 g cream:
White, HDPE, aluminum tubes of 30 g that are screw-capped, printed on the outside and lacquered on the inside.

There is 1 tube in each cardboard box.

6.6 Special precautions for disposal and other handling
Any unused material should be disposed according to local disposal regulations.

7. MARKETING AUTHORIZATION HOLDER
DEVA Holding A.Ş.
Halkalı Merkez Mah. Basın Ekspres Cad. No:1
34303 Küçükçekmece - İSTANBUL/TÜRKİYE

8. MARKETING AUTHORIZATION NUMBER
206/84

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization : 07/12/2005
Date of last renewal :

10. DATE OF REVISION OF THE TEXT