SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TEKFIN 1% dermal spray, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml solution contains;

Active substance:
Terbinafine hydrochloride 10 mg

Excipient(s):
Propylene glycol 50 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Spray for external use.

Colorless - almost colorless, clear solution with a characteristic odor.

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:
Unless recommended otherwise by the doctor, for the adults (>16 years);
TEKFIN may be applied once or twice a day depending on the indication. Clean and dry the relevant area before applying TEKFIN. Apply a sufficient amount of spray until the infected skin area is wet and the spray covers the lesioned skin area and the surrounding area. In intertriginous infections (submammary, interdigital, intergluteal, inguinal), the applied area can be covered with gauze, especially at night.

To use the spray pump, the spray bottle can be held vertically or upside down.
Before using TEKFIN for the first time, the patient should press the activator several times (usually up to 3 times) for an effective spraying.

Approximate treatment duration:
Tinea corporis, cruris :1 week, once daily
Tinea pedis :1 week, once daily
Cutaneous candidiasis :1 week, once or twice daily
Pityriasis versicolor :1 week, twice daily

Frequency and duration of administration:
Regression of clinical symptoms occurs within a few days. Irregular use or premature cessation of treatment increases the risk of disease recurrence. If there are no signs of improvement after two weeks, the diagnosis should be reconsidered.

Method of administration:
For topical use.

Additional information for special populations:
Renal/hepatic impairment:
No data related to dose adjustment in patients with renal and hepatic impairment is available.

Pediatric population:
The safety of its use in children has not been definitively proven.
Since experience with the use of TEKFIN in patients under 16 years of age is limited, its use is not recommended in this group of patients.

Geriatric population:
There is no evidence that elderly people (65 years of age and older) require different dosages or that they experience side effects other than those seen in younger people.

4.3 Contraindications

Hypersensitivity to terbinafine or any of the excipients in TEKFIN.

4.4 Special warnings and precautions for use

May cause toxic epidermal necrosis. Additionally, skin irritation and sensitivity may be observed.

TEKFIN should be used with caution in patients with lesions as the alcohol in its content may cause irritation.

TEKFIN is for external use only. It may irritate eyes. In case of accidental eye contact, the eyes should be rinsed with plenty of water. A physician should be consulted if any symptoms occur.

TEKFIN should not be used on the face.

In case of accidental inhalation, a physician should be consulted if any symptoms occur.

Propylene glycol in TEKFIN may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interactions have been reported with TEKFIN to date.

Additional information for special populations:

No clinical interaction studies have been conducted in special populations.

Pediatric population:
No clinical interaction studies have been conducted in pediatric population. It should not be used in patients under 16 years of age due to insufficient clinical experience.

4.6 Pregnancy and lactation

General recommendation
Pregnancy category: B

Women of childbearing potential/Birth control (Contraception)
There are no data to support specific recommendations for women of childbearing potential.

Pregnancy
There is no available clinical data about the exposure to TEKFIN in pregnancy.

Animal studies have not shown any direct or indirect harmful effects on pregnancy/embryonal/fetal development/delivery or postnatal development (See Section 5.3).

Since clinical experience on pregnant women are not sufficient, TEKFIN should not be used during pregnancy unless the expected benefits outweigh the possible risks.

Lactation
Terbinafine passes to breast milk at levels that may cause effects on the baby when TEKFIN is used in therapeutic doses by breastfeeding women.

Additionally, infants should not be allowed to come into contact with any treated skin area, including the breast.

TEKFIN should not be used during breastfeeding.

Reproduction ability/Fertility
Terbinafine has not been shown to affect fertility in animal studies, and there is no data to suggest that fertility in humans may be affected.

4.7 Effects on ability to drive and use machines
TEKFIN has no effect on driving and using 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 rash, which are reported in sporadic cases and require discontinuation. In case of accidental eye contact, terbinafine may cause eye irritation. Rarely, the underlying fungal infection may be aggravated.

Adverse reactions from clinical studies are listed by MedDRA system organ class. In each system organ class, undesirable effects are listed according to frequency and the most common reactions are listed first. Within each frequency grouping, undesirable effects 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 of TEKFIN were obtained in the form of spontaneous case reports based on the post-marketing experience and the cases reported in the literature. Since these reactions are voluntarily reported by a population of uncertain size, their frequency cannot be reliably calculated; therefore they are classified as "not known". These undesirable effects are listed in the same way as the undesirable effects from clinical studies.

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 discomfort, pigmentation disorder, erythema, burning sensation of the skin
Rare: Dry skin, contact dermatitis, eczema
Not known: Rash*

General disorders and administration site conditions
Uncommon: Pain, application site pain, application site irritation
Rare: Worsening of skin condition
*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 and treatment
The probability of overdose due to low systemic absorption of topically applied terbinafine spray is extremely low. However, accidental ingestion of 30 milliliters of TEKFIN spray containing 300 mg terbinafine hydrochloride can be considered similar to using a TEKFIN 250 mg tablet (adult oral dose unit).

If a higher amount of TEKFIN is taken orally, side effects are expected to occur similar with the TEKFIN tablet overdose. These side effects include headache, nausea, epigastric pain and dizziness.

In case of accidental oral ingestion, TEKFIN's 25.8% w/w alcohol content should be taken into consideration.

The recommended treatment of overdosage includes the elimination of the medicinal product. Activated charcoal may mainly be given and if necessary, symptomatic supportive therapy applied.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifungal for topical use
ATC code: D01A E15

Terbinafine is an allylamine, which has a broad spectrum of antifungal activity in fungal skin infections caused by dermatophytes such as Trichophyton *(T. rubrum, T. mentagrophytes, T. verrucosum, T.violaceum), Microsporum canis* and *Epidermophyton floccosum*. Terbinafine has a fungicidal effect against dermatophytes and moulds when administered at low concentrations. Its effect 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.

5.2 Pharmacokinetic properties

General properties

Terbinafine is a white to off-white powder. It is soluble in methanol and ethanol, but very slightly or slightly soluble in water. It is slightly soluble in acetone. Keep away from light.

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

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

Orally administered terbinafine binds strongly to plasma proteins (99%). It rapidly penetrates into the skin and concentrates in the lipophilic stratum corneum. Orally administered terbinafine is also released from the sebaceous glands, creating high concentrations in hair follicles, areas of skin rich in hair and oil. In addition, orally administered terbinafine has the ability to spread into the nail bed from the first few weeks of treatment.

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

Orally administered terbinafine is rapidly and extensively metabolized by at least 7 CYP isoenzymes, primarily CYP2C9, CYP1A2, CYP3A4, CYP2C8 and CYP2C19.

As a result of biotransformation, metabolites with no antifungal effect are formed, which are mainly excreted through the urinary tract. Elimination half-life is 17 hours. There is no accumulation.

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

Linearity / Non-linearity:
This information is not available since it is applied topically.

5.3 Preclinical safety data
In long-term studies (up to 1 year) in rats and dogs, no significant toxic effects were observed when oral doses of up to 100 mg/kg/day were given. At high oral doses, the liver and possibly also the kidneys have also been identified as potential target organs.

In a two-year oral carcinogenicity study on mice, no neoplastic or other abnormal findings were detected in the treatment with the doses of 130 mg/kg/day (male) and 156 mg/kg/day (female). In a two-year oral carcinogenicity study on rats at the highest dose of 69 mg/kg/day, an increase in the formation of liver tumors was observed in males. Since these changes that may be associated with the peroxisome proliferation were not observed in carcinogenicity studies with mice or other studies on mice, dogs, and monkeys, it has been shown that they are species-specific changes.

In the studies on monkeys with high-dose terbinafine, refractile irregularities were observed in the retina at high doses (non-toxic effect level was 50 mg/kg). These irregularities were due to the presence of a terbinafine metabolite in ocular tissues and disappeared after discontinuation of the medicine. 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 of 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
Ethanol (96%)
Propylene glycol
Cetomacrogol 1000
Deionized water

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 Months

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

6.5 Nature and contents of container
Amber colored glass bottles sealed with a pressure-operated, snap-on type HDPE spray cap.

Each carton box contains 1 bottle.

6.6 Special precautions for disposal and other handling
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER

DEVA Holding A.Ş.
Halkalı Merkez Mah. Basın Ekspres Cad. 34303 No:1
Küçükçekmece/ISTANBUL / TÜRKİYE
Phone: +90 212 692 92 92
Fax: 0212 697 00 24

8. MARKETING AUTHORISATION NUMBER(S)

205/66

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION

Date of first authorization: 21.04.2005

Date of renewal of authorization:

10. DATE OF REVISION OF THE TEXT