

<b>Summary of Product Characteristics</b>
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**1-NAME OF THE MEDICINAL PRODUCT (FPP)**

TERBINOL

*Terbinafine hydrochloride***1.1 Strength**

Terbinafine hydrochloride 10 mg/g

**1.2 Pharmaceutical form**

Semi-solid white cream for cutaneous application.

**2- QUALITATIVE AND QUANTITATIVE COMPOSITION****2.1 Qualitative declaration**

Terbinafine hydrochloride 10 mg/g

**2.2 Quantitative declaration**

1 gram of cream Terbinol contains 10 mg terbinafine hydrochloride, equivalent to 8.89 mg of terbinafine.

Excipients with known effect: 40 mg of stearyl alcohol and 40 mg of cetyl alcohol per gram of cream.

For the full list of excipients, see section 6.1

**3- PHARMACEUTICAL FORM**

Semi-solid white cream for cutaneous application.

**4- CLINICAL PARTICULARS****4.1 Therapeutic indications**

- Fungal infections of the skin due to dermatophytes such as *Trichophyton* (eg, *T. rubrum*, *T. mentagrophytes*, *T. verrucosum*, *T. violaceum*), *Microsporum canis* and *Epidermophyton floccosum*).
- Treatment of intertrigo of the toes (athlete's foot) and genital and crural intertrigo.
- Skin infections due to *Candida* (eg *Candida albicans*).
- Pityriasis (tinea) versicolor due to *Pityrosporum orbiculare* (*Malassezia furfur*).

**4.2 Posology and mode of administration**

#### 4.2.1 Posology

Adults and children older than 12 years

Indication	Duration and Frequency of the treatment
Intertrigo of the toes :	1 week, 1 to 2 times a day
Genital and crural intertrigo	1 to 2 weeks, 1 to 2 times a day
Cutaneous Candida	2 weeks, 1 to 2 times a day
Pityriasis versicolor :	2 weeks, 1 to 2 times a day

- Irregular use or inadequate duration of treatment increases the risk of recurrence of symptoms.
- The improvement of clinical symptoms usually appears within a few days. If there is no sign of improvement after 2 weeks, the diagnosis should be re-evaluated.

#### 4.2.2 Special populations

There are no data indicating that **older patients** require a different dosage or have a different adverse event profile from those of younger patients.

#### 4.2.2 Paediatric population

The experience with terbinafine cream in children is limited. It is therefore not recommended to use this medicine in children under 12 years of age.

#### 4.2.3 Method of administration

For cutaneous use.

- The skin must be cleaned and dried. The cream should be applied in a thin layer on and around the affected skin by gently penetrating it.
- In case of eczematous and red infections (under the breast, between the fingers, between the buttocks or in the groin), the skin can be covered with a sterile compress after the application of the cream, especially at night.

#### 4.3 Contraindications

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

#### 4.4 Special warning and precautions for use

##### 4.4.1 General information

- Terbinol cream is limited to external use.

- Terbinol cream can irritate the eyes. Eye contact should be avoided. In case of accidental contact with eyes, rinse thoroughly with water.
- Terbinol cream should be kept out of the reach of children.
- The appearance of erythema, pruritus or paresthesia does not require discontinuation of treatment. However, treatment should be stopped in case of more severe rashes or in case of allergic reactions such as rash or urticaria.

#### **4.4.2 Paediatric population**

The experience with terbinafine cream in children is limited. It is therefore not recommended to use this medicine in children under 12 years of age.

### **4.5 Interactions with other medicinal products and other forms of interactions**

#### **4.5.1 General information**

There are no known interactions between topical forms of terbinafine and other drugs.

#### **4.5.2 Additional information on special populations**

Not applicable

#### **4.5.3 Paediatric population**

The experience with terbinafine cream in children is limited. It is therefore not recommended to use this medicine in children under 12 years of age.

### **4.6 Fertility, pregnancy and lactation**

#### **4.6.1 Pregnancy**

Foetal toxicity and fertility studies in animals suggest no adverse effects. Since clinical experience in pregnant women is very limited, Terbinol cream should not be used during pregnancy.

#### **4.6.2 Lactation**

After oral administration, terbinafine is excreted in human milk. The effect of terbinafine on newborn infants is unknown. After local use only low systemic absorption is expected. However, Terbinol cream should not be used during breast feeding.

#### **4.6.3 Fertility**

In experimental animal studies, no effect of terbinafine on fertility was observed.

### **4.7 Effects on the ability to drive and use machines**

Terbinol cream 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, burning skin sensation, erythema, mange, etc. may occur at the application site.

These mild symptoms should be distinguished from hypersensitivity reactions such as rash that are reported in sporadic cases and require discontinuation of treatment.

In case of accidental contact with the eyes, terbinafine may cause eye irritation.

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

The frequencies of adverse reactions reported with terbinafine 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 ( $< 1/10,000$ )
- not known (cannot be estimated from the available data)

<b>Immune system disorders</b>	
Hypersensitivity *	not known
<b>Ocular affections</b>	
Irritation of the eyes	rare
<b>Affections of the skin</b>	
exfoliation, pruritus	common
cutaneous lesion, scabs, skin abnormalities, pigmentary abnormalities, erythema, burning sensation *	uncommon
dry skin, contact dermatitis, eczema	rare
skin rash *	not known
<b>General disorders and administration site conditions</b>	
pain, application site pain, application site irritation	uncommon

worsening of the condition	rare
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\* Based on experience since the marketing

#### 4.9 Overdose

Due to the weak systemic absorption of topical terbinafine, overdose is extremely unlikely.

##### Symptoms

Accidental ingestion of a 15 g tube of Terbinol cream, which contains 150 mg of terbinafine hydrochloride, is comparable to ingestion of a 250 mg half tablet of terbinafine (an adult oral dose unit) . In the case of accidental ingestion of a larger quantity of terbinafine cream, similar adverse effects as observed during overdose with terbinafine tablets may be expected. These side effects include headache, nausea, epigastric pain and dizziness.

##### Treatment

In case of accidental ingestion, the recommended treatment for overdose is to attempt the elimination of the active ingredient, starting with activated charcoal and applying symptomatic treatment if necessary.

## 5- PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

**Pharmacotherapeutic group and ATC code:** Topic antifungal agent ATC code D01AE15

Terbinafine, an allylamine, is an antifungal agent with a broad spectrum of activity against fungal infections in skin infections caused by dermatophytes, such as *Trichophyton* spp (eg, *T. rubrum*, *T. mentagrophytes*, *T. verrucosum*, *T. violaceum*), *Microsporum* spp and *Epidermophyton floccosum*. At low concentrations, terbinafine is a fungicide against dermatophytes and moulds (*Aspergillus* spp., *Scopulariopsis brevicaulis*). Its activity against yeasts is fungicidal (eg *Pityrosporum orbiculare* or *Malassezia furfur*) or fungistatic, depending on the species. Terbinafine specifically interferes with fungal sterol biosynthesis at an early stage. This effect causes ergosterol deficiency and intracellular squalene accumulation, 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 P-450 system. Terbinafine does not affect the metabolism of hormones and other drugs.

### 5.2 Pharmacokinetic properties

After topical application in humans, less than 5% of the dose is absorbed. The systemic effect is therefore very weak.

### 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 100mg/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, an increased incidence of liver tumours was observed in males at the highest dosage level of 69mg/kg a day. 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, dogs or monkeys. During high-dose studies in monkeys, refractile irregularities were observed in the retina at the higher doses (non-toxic effect level 50mg/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 mutagenic or clastogenic potential.

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

- Sodium hydroxide,
- Benzyl alcohol,
- Sorbitan stearate,
- Cetyl palmitate,
- Cetyl alcohol,
- Stearyl alcohol,
- Polysorbate 60,
- Isopropyl myristate,
- Purified water.

### 6.2 Incompatibilities

None known

### 6.3 Shelf life

- Proposed shelf-life: 24 Months
- Shelf-life after first opening of container: until expiration date

### 6.4 Special precautions for storage

Store below 30°C, in the original package.

**6.5 Nature and contents of container**

15 g Aluminium tube closed with a plastic screw cap in cardboard box.

**6.6 Special precautions for disposal and other handlings**

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

**7- MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESS****7.1 Marketing Authorisation Holder**

Dafra Pharma GmbH, Mühlenberg 7, 4052 Basel, Switzerland.

**7.2 Manufacturer**

Nobel İlaç, San. Ve. Tic. A.S., Sancaklar 81100 Düzce, Turkey.

**8- MARKETING AUHORISATION NUMBER**

See list of MAs per country

**9- DATE OF FIRST REGISTRATION**

See list of MAs per country

**10- DATE OF REVISION OF TEXT**

February 2019