# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

Terbinafin Moberg Pharma 98 mg/mL cutaneous solution

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Terbinafine hydrochloride equivalent to 98 mg/mL terbinafine.

Excipients with known effect
Each milliliter of solution contains 0.7 g propylene glycol.
For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Cutaneous solution
Clear, colourless 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.Terbinafin Moberg Pharma is indicated in adults.

### 4.2 Posology and method of administration

The product is intended for use on fingernails and toenails only.

Posology
Terbinafin Moberg Pharma should be applied to all affected nails once daily.
In general, the duration of treatment for fingernails is about 6 months while for toenails it is 9 to 12 months.
Alternative therapy including oral therapy should be considered in cases of inadequate response at the end of the treatment period.

*Paediatric population*
The safety and efficacy of Terbinafin Moberg Pharma in children and adolescents below 18 years of age have not yet been established. No data are available.

Method of administration
Cutaneous use only (for application on the nails).

Before application of Terbinafin Moberg Pharma, remove any nail polish or other cosmetic product from the nails and adjacent skin.

Apply Terbinafin Moberg Pharma in a thin layer once daily over the entire surface of the affected nails and under the free nail edge of the nail using the tip of the tube. Do not apply Terbinafin Moberg Pharma on the surrounding skin. Wait about 5 minutes until the solution has completely dried. The treated nails should not be washed or get wet for at least 8 hours. Therefore, application in the evening before going to bed and after showering or bathing is recommended.

Terbinafin Moberg Pharma does not need to be removed by any solvent or abrasives (i.e., nail filing).

Do not apply Terbinafin Moberg Pharma to the nail bed if the affected nail or parts of the affected nail

has detached from the underlaying nail bed.

## 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

For external use only. Contact with eyes and mucous membranes should be avoided. In case of accidental contact with the eyes or mucous membranes, rinse thoroughly with running water.

In cases of predisposing factors, such as diabetes and immune disorders, the addition of a systemic therapy should be considered. 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.

Terbinafin Moberg Pharma contains 0.7 g propylene glycol in each milliliter of solution.

*Paediatric population*
Terbinafin Moberg Pharma should not be used in children and adolescents below 18 years of age due to the lack of clinical experience in this age group.

## 4.5 Interaction with other medicinal products and other forms of interaction

No drug interaction studies have been performed with Terbinafin Moberg Pharma due to a very low systemic absorption.

## 4.6 Fertility, pregnancy and lactation

Pregnancy
No adverse effects during pregnancy are anticipated, since systemic exposure to terbinafine is negligible. The use of Terbinafin Moberg Pharma may be considered during pregnancy, if necessary.

In a propensity score–matched comparison study conducted in Denmark including 4065 terbinafine exposed pregnancies as well as 40,650 unexposed pregnancies, no significant differences in the risk of major malformations or spontaneous abortion were identified between oral terbinafine-exposed, topical terbinafine-exposed, and unexposed pregnancies.

Breast-feeding
Terbinafine is excreted into breast-milk. After topical use only low systemic exposure is expected. Terbinafine should only be used in a nursing mother if the expected benefit justifies the risk to the infant.
In addition, 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

Terbinafin Moberg Pharma has no influence on the ability to drive and use machines.

## 4.8 Undesirable effects

Summary of the safety profile
Treatment-related adverse events reported in more than 1% of subjects in two randomized controlled studies were nail discolouration, onycholysis, onychomadesis, paronychia, dermatitis contact and erythema.

Tabulated list of adverse reactions
Adverse reactions are listed by MedDRA System Organ Class and frequency. Frequencies are defined as follows: 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).

**Table 1: Adverse reactions**

| System Organ Class | Frequency | Adverse reaction |
|---|---|---|
| **Skin and subcutaneous tissue disorders** | Common | Nail discolouration,<br>Onycholysis,<br>Onychomadesis,<br>Paronychia,<br>Dermatitis contact,<br>Erythema |
| | Uncommon* | Skin irritation,<br>Dermatitis,<br>Nail disorder,<br>Pruritis |

*Uncommon adverse reactions, affected either the treated nails or the surrounding skin. These reactions were similar to the common 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 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 listed in Appendix V.

## 4.9 Overdose

Due to the route of administration, overdose is highly unlikely. No systemic signs of overdose are expected following application of Terbinafin Moberg Pharma because of the low systemic absorption of topical terbinafine. In case of accidental oral ingestion, appropriate symptomatic measures should be taken if needed.

# 5. PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other antifungals for topical use; ATC code: D01AE15.

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.

Clinical efficacy and safety

A total of 953 subjects received Terbinafin Moberg Pharma in the clinical development program across seven studies.

Safety and efficacy were investigated in two randomized, controlled, multicentre, international Phase III studies in patients with toenail onychomycosis. Terbinafin Moberg Pharma has shown to be superior to vehicle (study MOB015B-IV).
Study MOB015B-III involved 452 subjects aged between 19 and 76 years (mean 56.3) and compared Terbinafin Moberg Pharma with a commercially available formulation of ciclopirox 8% nail lacquer (N = 296 and 156, respectively). Study MOB015B-IV involved 365 subjects aged between 12 and 74 years (mean 55.0) and compared Terbinafin Moberg Pharma with its vehicle (N = 246 and 119, respectively).
All treatments were applied every day for 48 weeks to all affected nails. The subjects were followed for an additional 4 weeks after the end of treatment at which time final efficacy assessments were performed at Week 52. All the efficacy assessments were carried out on the target great toenail. The results of the key endpoints at 52 weeks are shown in the table below, demonstrating clinical benefit.

**Table 2: Pooled analysis of study MOB015B-III and MOB015B-IV: Results at the end of study (Week 52)**

| | **Study MOB015B-III** | | **Study MOB015B-IV** | | **Pooled data** |
|---|---|---|---|---|---|
| End points | Terbinafin Moberg Pharma n = 296 | Ciclopirox n = 156 | Terbinafin Moberg Pharma n = 246 | Vehicle n = 119 | Terbinafin Moberg Pharma n = 542 |
| Complete cure [1] | 6 (2.0%) | 2 (1.3%) | 11 (4.5%) | 0 (0.0%) | 17 (3.1%) |
| Mycological cure [2] | 238 (80.4%) | 64 (41.0%) | 172 (69.9%) | 33 (27.7%) | 410 (75.6%) |
| Treatment success [3] | 57 (19.3%) | 25 (16.0%) | 38 (15.4%) | 5 (4.2%) | 95 (17.5%) |

[1] Complete cure of target toenail; conversion to negative fungal culture of dermatophytes, negative direct potassium hydroxide (KOH) microscopy and 0% clinical disease involvement of the target toenail
[2] Mycological cure; conversion to negative dermatophyte culture and negative direct KOH microscopy
[3] Treatment success is defined as clinical disease involvement rated as 'completely clear' (0%) or 'almost clear' (less or equal to 10%) and mycological cure
n = Number of subjects

At week 12 mycological cure was shown in 42.8% of subjects in the Terbinafin Moberg Pharma group, increasing to 75.6% at Week 52.

In the two Phase III studies, 542 subjects received Terbinafin Moberg Pharma treatment for 48 weeks and had an additional 4 weeks of follow-up. 100 subjects (18.5%) reported treatment-related adverse events; there were no treatment-related serious adverse events (for adverse events see section 4.8).

Paediatric population
The safety and efficacy of Terbinafin Moberg Pharma has not been established in paediatric patients with onychomycosis.

The European Medicines Agency has deferred the obligation to submit the results of studies with Terbinafin Moberg Pharma in one or more subsets of the paediatric population in treatment of onychomycosis (see section 4.2 for information on paediatric use).

Elderly population
A total of 134 subjects aged ≥ 65 years were included in the two pivotal studies and treated with Terbinafin Moberg Pharma using the same treatment regime. There were no overall differences in efficacy of treatment in the ≥ 65-year age group compared to the less than 65-year age group.

### 5.2 Pharmacokinetic properties

The systemic absorption of topical terbinafine is several orders of magnitude lower than for orally administered terbinafine. The systemic exposure to terbinafine has been assessed in a Phase I systemic absorption study under maximal use conditions in subjects with onychomycosis. In this study all toenails were treated with Terbinafin Moberg Pharma once daily for 28 days. All subjects demonstrated exposure with a mean $C_{max}$ on Day 28 of 718 pg/mL (median 733 pg/mL). The mean plasma terbinafine concentration after 4 weeks of treatment was approximately 2000 times lower than the mean plasma level (1.39 µg/mL) observed after oral administration of 250 mg terbinafine once daily for 28 days. Therefore, systemic bioavailability of terbinafine from topical application of Terbinafin Moberg Pharma is considered negligible.

### 5.3 Preclinical safety data

Terbinafine administered onto the skin of rats and minipigs induced minimal erythema and/or oedema in some of the animals. The same findings were observed in some untreated animals. However, with increasing terbinafine concentration, the incidence increased and the effects became more pronounced. At 10% terbinafine (the same concentration as in the product), moderate edema and moderate to severe erythema were observed at very rare occasions in rats, but not in minipigs.

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.

Topical administration of Terbinafin Moberg Pharma leads to very low systemic exposure. Therefore, the risk for systemic toxicity is minimal.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Propylene glycol (E 1520)
Urea
Lactic acid
Disodium edetate (EDTA)
Sodium hydroxide (for pH-adjustment)
Purified water

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

2 years

### 6.4 Special precautions for storage

Store below 25 °C. Do not freeze.

### 6.5 Nature and contents of container

Plastic tubes (polyethylene or polyethylene laminated with aluminum or low-density / high-density polyethylene) with a silicone tip applicator and closed with a polypropylene cap.
Pack sizes: 5 mL (laminated polyethylene), 5 or 10 mL (polyethylene).
Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal

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

## 7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

## 8. MARKETING AUTHORISATION NUMBER(S)

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

## 10. DATE OF REVISION OF THE TEXT

2024-09-16