Submission for Medicine Reclassification

Purpose

Use this form to request a change to the legal classification of a medicine in New Zealand for consideration by the Medicines Classification Committee (MCC).

Before you start

Please read the guidance *'How to change the legal classification of a medicine in New Zealand'*. This form should be completed in conjunction with the directions in this guidance document.

Submitting

Please prepare concise, well-referenced answers to the questions in this form. Complete the form as per the instructions provided with each question, and complete the mandatory field declaration at the start of this form. Once completed, please email this form and any appendices to the MCC Secretariat (committees@health.govt.nz) by the published submission deadline.

By submitting this form, you are confirming that all information is true and accurate, and understanding that this information and any supporting information that is not considered commercially confidential under the Official Information Act 1982 will be published on the Medsafe website.

Mandatory Field Declaration

☒ I confirm that the mandatory fields (indicated next to each question by *) are completed.

Please note: submissions with incomplete mandatory fields before the submission deadline will not be accepted.

Submission Overview*

Please provide a concise summary of the proposal and background context. Include the current access situation, what change is sought, and why the change is needed.

This proposal is to amend the Pharmacy-only medicine classification for terbinafine to include its additional use in preparations for application to the nails along with the current dermal use.

The change is requested to increase consumer access to an alternative over the counter anti-fungal preparation appropriate for application to the nails, for the treatment of mild to moderate fungal infections of the fingernails and toenails in adults caused by dermatophytes and/or other terbinafine-sensitive fungi. Fungal nail infections are easily recognizable and can be monitored and managed by the consumer with advice available from the pharmacist if needed, as it is sold in pharmacies.

The proposed Pharmacy-only product is a topical antifungal solution, containing 10% terbinafine hydrochloride, for application to all affected nails in the treatment of onychomycosis and is referred to as MOB015B in the clinical program and non-clinical studies in the Appendices. MOB015B is also used this submission.

Part A - Administrative Information & Proposed Classification

1. Name and contact details of the company/organisation/individual requesting a reclassification*

Do you wish to have personal names and contact details removed prior to publication?
☒Yes ☐No
If yes, please clearly mark the fields you wish to be redacted.

On behalf of the applicant, NP Brands (NZ) Ltd
[redacted]

2. International non-proprietary (INN) name of the substance*

Please see the World Health Organization site on International Non-proprietary Names for more information: https://www.who.int/teams/health-product-and-policy-standards/inn

Terbinafine

3. Current classification of the substance*

The current classification of a substance can be found on the Medsafe website: https://www.medsafe.govt.nz/profs/class/classintro.asp

If the substance is not yet classified in New Zealand, please state this.

Terbinafine	**except** in medicines for dermal use	Prescription
Terbinafine	for dermal use **except** in medicines for tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	Pharmacy Only
Terbinafine	for dermal use in medicines for tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	General Sale

4. Proposed classification*

Please provide the proposed classification statement for the substance. If your proposed classification statement refers to healthcare professionals, or imposes conditions on supply to certain healthcare professionals, consultation with relevant professional bodies may be beneficial. If relevant, please outline any consultation undertaken and their outcome.

You may also wish to explain what you want the classification to achieve (e.g. to enable supply of these medicines by a pharmacist).

Terbinafine	**except** in medicines for dermal use	Prescription
Terbinafine	for dermal use and in preparations for application to the nails **except** in medicines for tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	Pharmacy Only
Terbinafine	for dermal use in medicines for tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	General Sale

5. International classification*

Please provide the classification status of the substance in other countries (particularly Australia, UK, USA, and Canada). If seeking alignment with other jurisdiction(s), please provide any justification for harmonisation with these countries. The following resources may be helpful:

-Australia: The Poisons Standard

-United Kingdom: The Prescription Only Medicines (Human Use) Order 1997

-Canada: the Prescription Drug List and the Natural Health Products Ingredients Database

- Australia: *The Poisons Standard*

  Schedule 2 Pharmacy medicines

  TERBINAFINE for dermal use **except** in preparations for the treatment of tinea pedis.

  Schedule 4 Prescription only medicines and prescription animal remedies

  TERBINAFINE **except**:

  (a) when included in Schedule 2; or

  (b) in preparations for dermal use for the treatment of tinea pedis.

  A rescheduling application is with the Secretariat to request the amendment of the current Schedule 2 entry to:

  TERBINAFINE for dermal use and for application to the nails except in preparations for the treatment of tinea pedis

- *United Kingdom: The Prescription Only Medicines (Human Use) Order 1997*

  Schedule 1

Exemptions from the restrictions on the sale and supply of prescription only medicines				
Substance	*Maximum strength*	*Route of administration, use or pharmaceutical form*	*Treatment limitations*	*Maximum quantity*
Terbinafine	[1.0 per cent]	[External use for the treatment of tinea pedis, tinea cruris and tinea corporis. In the form of a gel]		[Container or package containing not more than 30 grams of medicinal product]
[Terbinafine Hydrochloride]	[1.0 per cent]	[Preparations, other than spray solutions, for] [external use for the treatment of tinea pedis and tinea cruris]		[Container or package containing not more than 15 g of medicinal product.]
		[(2) Spray solutions for external use for the treatment of tinea corporis, tinea cruris and tinea pedis]		[(2) Container containing not more than 30ml of medicinal product]

  The United Kingdom electronic medicines compendium Search Results - (emc) (emc) regulates 6 topical products containing 1% terbinafine as cream, spray, gel or cutaneous solution. The products are prescription-only, pharmacy or General Sales List medicines.

- The Health Canada Drug Product Database Search criteria - Drug Product Database online query includes 2 currently marketed topical products that contain 1% terbinafine as a cream and a spray. Both are prescription-only medicines.

The following table provides the regulatory status for the terbinafine 10% (98 mg/mL) nail solution products currently approved in Europe. The product has been launched and marketed in Sweden for 2.5 years and Norway for 18 months. The proposed Pharmacy-only product would contain the same active at the same concentration in the same solution dosage form as these overseas reference products.

Name of the Medicinal Product	**Country**	**Marketing Authorization Number***	**Date(s) of Authorization**	**Non-prescription/ prescription**
Lamisil Nail 98 mg/ml Lösung zur Anwendung auf der Haut	Austria	141820	18-Aug-2023	Non-prescription
Lamisil Nail 98 mg/ml solution pour application cutanée	Belgium	BE662330 BE662329	07-Mar-2024	Non-prescription
Terbinafin Moberg Pharma 98 mg/ml kožní roztok	Czech Republic	0260514 0260517 0280150	31-Aug-2023	Prescription
Onychosil 98 mg/ml, kutanopløsning	Denmark	67637	08-Aug-2023	Prescription
Terclara 98 mg/ml, kutanopløsning	Denmark	67638	08-Aug-2023	Prescription
Onychosil 98 mg/ml liuos iholle	Finland	40845	10-Oct-2023	Prescription
Terclara 98 mg/ml liuos iholle	Finland	40843	10-Oct-2023	Prescription
TERBINAFINE MOBERG PHARMA 98 mg/mL, solution pour application cutanée	France	34009 302 767 9 2 34009 302 767 8 5 34009 302 767 7 8	04-Sep-2023	Prescription
Terbinafin Moberg Pharma 98 mg/ml külsőleges oldat	Hungary	OGYI-T-24270/01 OGYI-T-24270/03 OGYI-T-24270/05 OGYI-T-24270/04	02-Aug-2023	Non-prescription
Terbza 98 mg/ml cutaneous solution	Ireland	PA23368/001/001	28-Jul-2023	Prescription
PevaOnico 98 mg/ml soluzione cutanea	Italy	050747017 050747031 050747056 050747043	02-May-2024	Non-prescription
Terbisil 98 mg/ml oplossing voor cutaan gebruik	Netherlands	RVG 129854	07-Feb-2024	Non-prescription
Terbinafin Moberg Pharma 98 mg/ml liniment, oppløsning	Norway	22-14691	24-Aug-2023	Non-prescription
Terclara 98 mg/ml liniment, oppløsning	Norway	22-14684	24-Aug-2023	Non-prescription
Pevaryl Uñas 98 mg/ml solucion cutanea	Spain	89103	24-Oct-2023	Prescription
Terbinafin Moberg Pharma 98 mg/ml kutan lösning	Sweden	63250	01-Aug-2023	Non-prescription
Terclara 98 mg/ml kutan løsning	Sweden	63251	02-Aug-2023	Non-prescription

6. New Zealand product details

Please provide the following information:

-List the approved medicines that contain the substance. Products can be searched on the Medsafe website: https://www.medsafe.govt.nz/regulatory/dbsearch.asp

-State the dose form(s), strength(s), route(s) of administration, and/or pack size(s) of medicines containing the substance that are approved in New Zealand. Does this submission only apply to certain dose forms, strengths, and/or pack sizes?

This submission only applies to terbinafine topically applied to the nails in a 10% solution in a 5mL and 10mL pack size. There are no topical medicines in the Medsafe database that include terbinafine at 10%.

The following Pharmacy-only medicine classification products contain terbinafine with the sponsor NP Brands (NZ) Ltd:
Lamisil Dermgel, Topical gel 1% w/w (Pharmacy only) – pack sizes 5g, 7.5g, 15g, 30g
Lamisil Spray, Topical spray 10 mg/g (Pharmacy only) – pack sizes 15mL, 30mL
Lamisil, Topical cream 1 % (Pharmacy only) – pack size 15g

Products that have a 'Not available' or 'Approval lapsed' status have not been provided as they are not currently supplied.

7. Related substances in the same class

How are other medicines in the same class of the substance classified? Does the proposed reclassification of the substance align with those of the same class, or does it deviate?

The proposal is to allow access to terbinafine in a solution for application to the nails as a Pharmacy-only medicine, which aligns the classification of terbinafine with similar antifungal substances being supplied in products for use on nails.

Antifungal medicines in nail lacquers or solutions currently approved for supply in New Zealand include:
Ciclopirox - Rejuvenail, Nail lacquer 8% w/w (Pharmacy only)
Miconazole - Daktarin Tincture, Topical solution 2% w/v (Pharmacy only)
Amorolfine - Loceryl, Nail lacquer 5 % (Pharmacy only) and MycoNail, Nail lacquer 5 % (Pharmacy only)

The Pharmacy-only classification for amorolfine is for topical use and for miconazole it is for external use, both of which then allow for application to the nails in the scope of use. Ciclopirox is classified as Pharmacy-only medicine in preparations for application to the nails containing 8% or less.

The current classification Pharmacy-only classification for terbinafine limits it to dermal use. Based on clinical supporting data, this reclassification application has been made

to align the access to terbinafine with the similar antifungal medicines amorolfine, ciclopirox and miconazole.

From the Medicines Classification Database
https://www.medsafe.govt.nz/profs/class/classintro.asp accessed 23/07/2026

Ingredient	Conditions (if any)	Classification
Amorolfine	**except** when specified elsewhere in this schedule; **except** in preparations for the treatment of tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	Prescription
	in preparations for topical use **except** in preparations for the treatment of tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	Pharmacy Only
	in preparations for the treatment of tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	General Sale
Ciclopirox	**except** for external use	Prescription
	for external use in medicines containing more than 2%; in preparations for application to the nails containing more than 8%	Restricted
	for external use in medicines containing 2% or less **except** when for the treatment of tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board; in preparations for application to the nails containing 8% or less	Pharmacy Only
	for external use in medicines containing 2% or less when for the treatment of tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	General Sale
Miconazole	**except** when specified elsewhere in this schedule; **except** in medicines for tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	Prescription
	for the treatment of oral candidiasis; for vaginal use	Restricted
	for external use **except** in medicines for tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	Pharmacy Only
	for external use in medicines for tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	General Sale
Terbinafine	**except** in medicines for dermal use	Prescription
	for dermal use **except** in medicines for tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	Pharmacy Only
	for dermal use in medicines for tinea pedis only or when sold in practice by a podiatrist registered with the Podiatrists Board	General Sale

8. Warning statements

Do you propose any additional warning statements to be included on products to manage any risk associated with the proposed reclassification? Please see the Label Statements Database on

the Medsafe website for examples of warning statements:
https://www.medsafe.govt.nz/regulatory/labelling.asp

The proposed labelling safety information on the 'Pharmacy only' medicine terbinafine 10% solution product includes:

- Do not use in children and adolescents below 18 years of age.
- Ask your doctor before use if you are pregnant, think you are pregnant or breastfeeding.
- Consult your doctor or pharmacist if symptoms persist.
- For external use only.
- Only for use on nails.
- Avoid contact with eyes and mucous membranes.

Part B - Benefit/Risk Assessment

MEDICINE DETAILS

9. Approved indications*

What are the approved indications for medicines containing this substance in New Zealand? Does this submission only apply to certain indications? Do these indications only apply to certain doses/strengths? Please provide details.

Pharmacy only medicines in New Zealand that contain terbinafine have the following indications:
Lamisil Dermgel, Topical gel 1% w/w (Pharmacy only)
- *used to treat fungal infections of the skin such as athlete's foot, ringworm & jock itch.*
Lamisil Spray, Topical spray 10 mg/g (Pharmacy only)
- *used to treat fungal infections of the skin such as athlete's foot, ringworm & jock itch.*
Lamisil, Topical cream 1 % (Pharmacy only)
- *used to treat fungal infections of the skin such as athlete's foot, ringworm & jock itch.*

The indication for the proposed amendment to the terbinafine Pharmacy-only classification is only for the treatment of mild to moderate fungal infections of the fingernails and toenails in adults caused by dermatophytes and/or other terbinafine-sensitive fungi. The terbinafine topical solution for the nails is intended to be supplied in a strength of 10% w/w terbinafine hydrochloride corresponding to 98 mg/mL terbinafine.

10.Contraindications and precautions*

Please address the following, citing key sources where available:
-Contraindications: what are they and how easy are they to identify and prevent?
-Precautions: what are they and how easy are they to understand?
-Class effects: what class effects need to be considered, and what are the risks?
-Interactions: are there any food/drink/drug interactions?
-Therapeutic index: does the medicine have a narrow therapeutic index? What are the risks of the medicine being used in an over-the-counter environment?
- *Special populations: are there any restrictions when taking the medicine, i.e. driving restrictions or operating machinery? Are there any other special populations where exposure to the medicine needs to be restricted?*

Contraindications
Topical terbinafine 10% solution is contraindicated in patients who are hypersensitive to the active ingredient or any of the excipients (Appendix A SmPC 2024).

Special warnings and precautions for use (Appendix A SmPC 2024)
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.

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.

Class effects
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).

Tabulated list of adverse reactions for topical terbinafine (Appendix A SmPC 2024):

System Organ Class	Frequency	Adverse reaction
Skin and subcutaneous tissue disorders	Common	Nail discolouration, Onycholysis, Onychomadesis, Paronychia, Dermatitis contact, Erythema
	Uncommon*	Skin irritation, Dermatitis, Nail disorder, 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.

Systemic bioavailability of terbinafine from topical application of the proposed Pharmacy-only medicine product is considered negligible (Appendix A SmPC 2024). Therefore, the risk for side effects related to the cardiovascular, respiratory, or central nervous system is negligible.

Sedative effects
No sedative effects are anticipated due to the low systemic exposure of terbinafine when applied to the nails. There is no evidence that there is any effect of topical terbinafine on the ability to drive or operate machines (Leaflet Appendix B).

Interactions
No drug interaction studies have been performed due to a very low systemic absorption of 10% terbinafine solution when applied to the nails.

The systemic exposure to terbinafine following application onto the nails is very low, particularly when compared to approved oral terbinafine (Table in [redacted]). Therefore, the risk for drug interactions is negligible.

Topical terbinafine has no known interactions with commonly used substances or food.

Topical terbinafine has not been assessed as having a narrow therapeutic index and has been used in an OTC environment for many years in New Zealand and elsewhere.

Special populations
Children
The common English Summary of Product characteristics (Appendix A SmPC 2024) states that there are no data available for paediatric use and that the safety and efficacy of the product have not yet been established in children and adolescents below 18 years of age. The use of MOB015B in paediatric patients was under investigation in an ongoing phase IIb clinical trial during the reporting period of the PSUR (28-Jul-2023 to 30-Sep-2025). No further information is available at this time. The proposed Pharmacy-only product will be indicated only for adults until data to support use in children are available.

Elderly
A total of 134 subjects aged ≥ 65 years were included in the two pivotal studies and treated with terbinafine 10% solution using the same treatment regime as the other subjects. There were no overall differences in efficacy of treatment in the ≥ 65-year age group compared to the less than 65-year age group.

Renal impairment
The risk for adverse effects is very low due to the low systemic exposure of terbinafine applied to the nails.

Severe liver impairment
The risk for adverse effects is very low due to the low systemic exposure of terbinafine applied to the nails.

Pregnancy and breast-feeding
No adverse effects during pregnancy are anticipated, since systemic exposure to terbinafine following application onto the nails is negligible.

A large amount of data are available relating to the use of terbinafine in pregnant women which indicate no foetal malformation or feto/neonatal toxicity. In a published, 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 (N=891), topical terbinafine-exposed (N=3174), and unexposed pregnancies (40,650) (Andersson et al. 2020). As a precautionary measure, it is preferable to avoid the use of MOB015B during pregnancy, but its use may be considered during pregnancy, if necessary.

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.

The labelling for the proposed Pharmacy-only medicine product will advise users to consult their doctor or pharmacist before use if they are pregnant or breastfeeding in line with the Common English labelling text provided as example (Labelling Appendix C).

11.Undesirable effects*

Please address the following:

- *Undesirable effects: what are the known adverse effects, their frequencies, and risks/consequences? Do they vary for special populations?*
- *Regulatory status: are there any significant safety concerns for the medicine under review? Have there ever been any withdrawals of the medicine (during a specific time period or in a specific jurisdiction)?*
- *Withdrawal: can withdrawal effects occur following cessation of use?*

Side effects can occur with following frequencies (Leaflet Appendix B):
Common (may affect up to 1 in 10 people)

- whitish or yellowish nail discolouration
- detachment of the nail from the nail bed
- separation of part of the nail that may lead to shedding from the free edge of the nail
- inflammation of the nail fold or cuticle with or without bacterial infection
- red itchy rash as a reaction to contact with the medicine
- skin redness

Uncommon (may affect up to 1 in 100 people)

- nail disorders and skin reactions around the treated nails: skin irritation, skin inflammation, itchy skin

Some side effects like for example nail discolouration and nail detachment can also be caused by the fungal infection.

No withdrawal effects are expected to occur following cessation of use.

Periodic Safety Update Report

The first company Periodic Safety Update Report ([redacted]) for 10% terbinafine hydrochloride (known in clinical development as MOB015B) covers the period from first approval 28 July 2023 to 30 September 2025. It includes pertinent safety data received during this reporting interval and summarizes all safety information received from worldwide sources by the marketing authorization holder (MAH) Moberg Pharma AB.

No new information that would impact the benefit-risk profile of MOB015B in the approved indications became available during the current reporting interval. No actions were taken for safety reasons. The overall benefit-risk profile of MOB015B in the approved indications remains unchanged and positive.

Neither Moberg Pharma AB nor the regulatory authorities have taken any actions relating to the safety of MOB015B during or since the reporting interval with regard to marketing authorisation withdrawal or suspension, failure to obtain a marketing authorisation renewal, restrictions on distribution, clinical trial suspension, dosage modification, changes in target population or indications, formulation changes, and urgent safety restriction.

BENEFIT CONSIDERATIONS

12.Safe access*

Describe the current access issues and how the proposed classification change would address them. Include:

- *Use history: how many people in New Zealand (and overseas) use this medicine? To what extent is this medicine used for the proposed indication(s) (i.e. duration of use; frequency of use)?*
- *Inappropriate access: what is the evidence that access is currently inappropriate? Are any groups particularly impacted? How would the reclassification improve safe access to the substance?*
- *Practice impact: how would the reclassification impact access/administration by other healthcare professionals (e.g. midwives, paramedics)?*

The current Pharmacy-only medicine classification limits the access of topical terbinafine to products for dermal use only. As this does not necessarily cover the use on nails, the proposal is to include the application to nails.

The proposed 10% terbinafine nail treatment product has been launched and marketed in Sweden for 2.5 years and Norway for 18 months. During the reporting interval (28 July 2023 to 30 September 2025) of the first company Periodic Safety Update Report ([redacted]), the estimated exposure from post-marketing settings and cumulatively was approximately [redacted]. Cumulatively, 1217 subjects have received MOB015B under the clinical development program since the development international birth date (DIBD) on 17 Oct 2012.

Terbinafine was first launched in 1991 in Europe under the brand name Lamisil (Novartis) and is available worldwide in both topical and oral formulations for different indications. Terbinafine-containing products have been marketed in the EU and US for more than 30 years. Consequently, the safety profiles of oral and topical terbinafine are well established and well characterised.

13.Improved clinical outcomes*

Describe the expected clinical benefits as a result of the proposed reclassification. What is the evidence that the proposed change in access is beneficial for the individual? Is there any benefit of improved consumer involvement in their health? Are there any other benefits, from a consumer viewpoint?

Current therapeutic approaches for onychomycosis include mechanical or chemical nail avulsion, topical therapy, oral therapy or a combination of all of these modalities. However, treatment decision depends on the clinical pattern of onychomycosis, the

thickness and the number of affected nails, as well as patient's age, use of other medications, motivation and preferences.

Terbinafine is a highly lipophilic, synthetic allylamine and is regarded as an effective treatment of dermatophytic infections (Jessup et al 2000, Newland et al 2009).

The proposed Pharmacy-only product is a topical antifungal solution, containing 10% terbinafine hydrochloride, for application to all affected nails in the treatment of onychomycosis. The proposed Pharmacy-only product is referred to as MOB015B in the clinical program and in this submission.

The pharmacology of terbinafine is well-characterized and no additional non-clinical studies were performed to assess the pharmacology of terbinafine.

The systemic exposure to terbinafine following application of MOB015B onto the nails is very low, particularly when compared to oral terbinafine (approximately 2000-fold lower). Therefore, the risk of side effects related to secondary pharmacology or the cardiovascular, respiratory, or central nervous system as well as for pharmacodynamic drug interactions is negligible.

Systemic exposure to orally administered terbinafine has demonstrated rare hepatotoxic and other systemic adverse events which may be avoided through the use of a topical formulation. The major advantage of the proposed Pharmacy-only product is the topical delivery of effective concentrations of terbinafine to the nail plate and nail bed to drive clinical efficacy, while at the same time avoiding the risk of systemic exposure and development of systemically induced serious adverse events or potential for drug-drug interactions reported after oral terbinafine use.

The clinical development program for the proposed Pharmacy-only product (referred to as MOB015B) was designed to assess the safety, efficacy and pharmacokinetics of the product in the treatment of onychomycosis. The following table provides an overview of the seven completed clinical studies and the number of subjects treated.

Clinical Development Program Study Number	Study objective	Dosing and application sites	Duration of treatment	Number of Subjects treated
MOB015B-II	Safety and efficacy Pharmacokinetics	Once daily all affected nails	48 weeks	25 patients with onychomycosis
MOB015B-III	Safety and efficacy	Once daily all affected nails	48 weeks	296 patients with onychomycosis
MOB015B-IV	Safety and efficacy	Once daily all affected nails	48 weeks	246 patients with onychomycosis
MOB015B-V	Cumulative irritation	Continual patch exposure	21 days	45 healthy volunteers
MOB015B-VI	Skin sensitization	Skin patch, 10 repeated 48-hour applications over 6 weeks	6 weeks	250 healthy volunteers
MOB015B-VII	Photoallergy	Skin patch, 7 repeated 24-hour applications over 6 weeks	6 weeks	71 healthy volunteers
MOB015B-VIII	Systemic absorption	Once daily all toenails	28 days	20 patients with onychomycosis

Three of these studies (Study MOB015B-II, MOB015B-III and MOB015B-IV) evaluated the efficacy, safety and tolerability of MOB015B in subjects with onychomycosis. Three studies (MOB015B-V, MOB015B-VI and MOB015B-VII) were dermal safety studies conducted in healthy volunteers. In these studies, MOB015B was administered under occlusive conditions directly to the skin. One study (MOB015B-VIII) was a systemic absorption study under maximal use conditions in subjects with onychomycosis.

The two pivotal Phase III studies (MOB015B-III and MOB015B-IV) conducted in a total of 542 patients were both prospective, multicenter, randomized, two-arm, and comparator-controlled, with similar eligibility criteria and study visit schedules. These studies confirm the positive safety results from the single center, open-label Phase II pilot study (MOB015B-II). They also provided robust data on the efficacy of the proposed Pharmacy-only product (MOB015B) for the topical treatment of onychomycosis.

Refer to [redacted] for further information.

Tavakkol et al 2024, summarising the study results from MOB015B-VIII, has been published. This article confirms that topically used substance MOB015B primarily accumulates in the nail plate, allowing the release into the nail bed. Furthermore, the very low level of systemic exposure is reflected in the favourable safety and tolerability profile observed during the study.

The clinical development program provides support for a good safety profile and efficacy for terbinafine for application to the nails as proposed and its suitability for inclusion in the Pharmacy-only medicine classification for this purpose.

A multicentre, randomised, parallel-group, double-blind, vehicle-controlled and open-label, active-controlled study (Blume-Peytavi et al 2022) was conducted to evaluate the efficacy and safety of terbinafine 10% nail lacquer in the treatment of onychomycosis. This study included a comparison of topical terbinafine 10% to its vehicle and open-label topical amorolfine 5% with a primary endpoint of complete cure rates at week 60. A total of 953 patients were recruited for the study with 799 patients completing the study per protocol. The study concluded that terbinafine 10% nail lacquer was an effective treatment for mild-to-moderate onychomycosis improving both clinical and mycological criteria compared with vehicle. Furthermore, the study results suggested that there may be some benefits compared to the currently available topical agent, amorolfine 5%. Treatment was well-tolerated and safe, with no important adverse reactions arising in the study.

Amorolfine has a Pharmacy-only classification in preparations for topical use except in preparations for the treatment of tinea pedis (and for use by a registered podiatrist). Our submission seeks to align the access provided by the Pharmacy-only entry for terbinafine with that for amorolfine, ciclopirox and miconazole. Blume-Peytavi et al 2022 demonstrates that terbinafine is as safe and effective as amorolfine when used for the same indication. This provides further support for our request to amend the Pharmacy-only entry of terbinafine to include use on nails and align it with the entries for amorolfine, ciclopirox and miconazole.

The risk for systemic toxicity is negligible ((Table in [redacted], Appendix A SmPC 2024) and the non-clinical assessment of MOB015B focused on its dermal toxicity.

14.Public health benefits

If relevant, outline broader public health benefits resulting from the proposed reclassification. Examples could include (but are not limited to):

- *Greater herd immunity due to improved access to a communicable disease vaccine*
- *Reduced health system pressure due to over-the-counter availability*
- *Support for wider public health goals (e.g. reduce smoking rates)*
- *Prevention of antimicrobial resistance by restricting access to certain medicines*
- *Reduced poisoning incidents by removing over-the-counter availability*
- *Reduce crime or illicit manufacture of certain substances*
- *Limiting environmental impact of certain medicines*

- Reduced health system pressure due to over-the-counter availability

Onychomycosis does not usually resolve without prolonged treatment to eradicate the fungus. If left untreated, the fungus will spread and can eventually destroy the nail.

Fungal nail infections are easily recognizable and can be monitored and managed by the consumer, with advice available from the pharmacist if needed.

Easy recognition of the familiar symptoms of fungal infections of the nail allows for appropriate self-medication with topical antifungal and the scope for misdiagnosis is limited. Fungal infections of the nail are typically characterised by discolouration and/or thickening of the nail plate which can be quickly and simply recognised by consumers. In the unlikely event that a consumer does use the product on a severely infected nail, despite the instructions on the carton, there is negligible risk to overall health, either directly through use of the treatment, or indirectly through failure to resolve the infection.

Other unusual conditions that can cause nail dystrophies include psoriasis, eczematous conditions, senile ischaemia, physical trauma, and lichen planus. However, these conditions are associated with other symptoms involving the skin and or nail that can distinguish them from fungal infections.

The risk of masking a serious disease or compromising medical management of a disease is extremely low and the use of the product does not require ongoing or close medical diagnosis or management.

RISK CONSIDERATIONS

15.Medication errors and abuse/misuse potential*

Could the proposed reclassification increase the risk of inappropriate use or medication errors? Please address the following:

- *Reports: what are the reported medication errors post-market? What are the reported cases of abuse/misuse/accidental overdose, in New Zealand and overseas?*
- *Inappropriate use: what is the addiction potential of the medicine? What are the risks of incorrect or inappropriate self-selection, and how are these mitigated? What are the risks associated with self-management? Are there risks of patients using these medicines 'off-label'?*

Periodic Safety Update Report

The first company Periodic Safety Update Report ([redacted]) for 10% terbinafine hydrochloride (known in clinical development as MOB015B) covers the period from first approval 28 July 2023 to 30 September 2025. It includes pertinent safety data received during this reporting interval and summarizes all safety information received from worldwide sources by the marketing authorization holder (MAH) Moberg Pharma AB.

During the reporting interval of the PSUR, the estimated exposure from post-marketing settings and cumulatively was approximately [redacted]. Cumulatively, 1217 subjects have received MOB015B under the clinical development program since the development international birth date (DIBD) on 17 Oct 2012.

As this is the first PSUR for the product the cumulative and interval post-marketing exposure are the same. Only the brand Terclara is currently marketed and therefore used in the context of post-marketing experience.

The current reference safety information (RSI) is the common English EU Summary of Product Characteristics (SmPC) for Terbinafin Moberg Pharma (v 2.0), dated 24 July 2024. The SmPC (Appendix A) was updated during the reporting period but not for safety reasons. The update was to the text in the Nature and contents of container section of the SmPC.

There are no important identified and potential risks and no missing information for MOB015B. During the reporting period, the company did not identify any new safety concern, and the list of relevant important risks and missing information remains unchanged. There were no ongoing or closed signals at the Data Lock Point of this PSUR, and no new signals were validated during the reporting period.

No new information that would impact the benefit-risk profile of MOB015B in the approved indications became available during the current reporting interval. No actions were taken for safety reasons. The overall benefit-risk profile of MOB015B in the approved indications remains unchanged and positive.

Neither Moberg Pharma AB nor the regulatory authorities have taken any actions relating to the safety of MOB015B during or since the reporting interval with regard to marketing authorisation withdrawal or suspension, failure to obtain a marketing authorisation renewal, restrictions on distribution, clinical trial suspension, dosage modification, changes in target population or indications, formulation changes, and urgent safety restriction.

The PSUR concluded that:

- Review of the safety information received during the reporting period indicates that the benefit-risk balance of MOB015B, when used in its approved indications and in accordance with the information included in the RSI, remains positive. No further actions are deemed necessary or are proposed.
- Moberg Pharma AB will, as part of its ongoing pharmacovigilance activities, continue to monitor all relevant safety information reported in relation to their terbinafine 10% solution products.

Inappropriate use
There is no evidence to indicate potential misuse/abuse or dependency with use of topical terbinafine. There is no potential for conversion of terbinafine into illicit, prohibited or Schedule 8 substances.

Topical terbinafine has a low potential for harm from inappropriate use. Easy recognition of the familiar symptoms of fungal infections of the nail allows for appropriate self-medication with topical antifungal with the supply in pharmacies allowing for advice to be readily available from the pharmacist if needed.

The risk of masking a serious disease or compromising medical management of a disease is extremely low and the use of the product does not require ongoing or close medical diagnosis or management.

16.Overdose*

Is there a potential for overdose of the medicine? Are there any reports of overdose, and what are the consequences of an overdose? What risks are there of accidental ingestion, for example by children? Does the proposed reclassification increase the risk of overdose?

There is no potential for overdose of the medicine.

The proposed terbinafine 10% solution will be packed in plastic tubes with a silicone tip applicator and closed with a plastic cap, so the risk of accidental oral ingestion is low. The proposed labelling for the Pharmacy-only terbinafine 10% solution product For application to the nails will include the following warnings:

- For external use only
- Only for use on nails.

The intended pack sizes are small (5mL and 10mL) containing 98 mg/mL terbinafine. Swallowing the whole 10mL pack would result in ingesting 980 mg terbinafine which is equivalent to ingesting less than four 250mg terbinafine tablets.

17.Communal harm

Are there any community-wide harmful consequences that may result from the proposed classification change? Examples could include (but are not limited to):

- *Increased risk of antibiotic resistance due to overuse of antibiotics*
- *Promotion of inappropriate use (e.g. on social media)*
- *Reduced opportunities for clinical assessment for certain conditions*
- *Increased use of unapproved substitutes*
- *Higher healthcare system burden*

There are no anticipated community-wide harmful consequences that may result from the proposed classification change.

18.Risk mitigation strategies*

What risk mitigation strategies (if any) are required? Please address the following:

- *Strategies: is healthcare professional education, integration of care, provision of consumer information, etc needed? Should the medicine be provided with necessary tools to enable correct dosing (e.g. liquids supplied with a measuring device)? Should there be limits on pack size, or maximum daily dose? What is the evidence that these proposed risk mitigation strategies would be effective?*
- *Data: what post-market surveillance activities would be carried out?*
- *Support: is the proposed reclassification supported by professional bodies, interest groups, or other relevant groups?*

The proposed labelling for the Pharmacy-only terbinafine 10% solution product for application to the nails will include safety warnings and directions to allow for appropriate safe use of the product by the consumer.

Moberg Pharma AB, as part of its ongoing pharmacovigilance activities, will continue to monitor all relevant safety information reported in relation to their terbinafine 10% solution products. ([redacted]).

REGULATORY & ECONOMIC IMPACT

19.Regulatory impact

What are potential regulatory impacts (intended or unintended) of reclassification? The following points may be helpful for your discussion:

- *Is it possible that other products will inadvertently be captured by the classification? If so, are there caveats in the classification statement that could manage this?*
- *Are there any other legal restrictions that need to be considered (e.g. Misuse of Drugs Act 1975, Dietary Supplement Regulations 1985)?*
- *Would the proposed reclassification be an incentive for companies to supply (or not supply) certain products in New Zealand?*
- *Please suggest any issues that may need to be considered by Medsafe when drafting a classification statement.*

The reclassification application is specific to the medicinal substance and site of administration; therefore, it is expected there will be a very low possibility of any other products inadvertently being captured by the classification.

There are no other legal restrictions that should need to be considered.

The applicant is intending to supply the proposed terbinafine 10% solution for application to the nails if the reclassification is successful.

There are no further issues that should need to be considered other than the information provided in this application.

20.Economic impact

What are potential economic impacts of the proposed change? Does the change relieve any unnecessary burden on the health system? Or could it place unnecessary pressure on the system? Is there likely to be any impact on costs for the consumer?

The duration of treatment for fingernails can be up to 6 months while for toenails it is 9 to 12 months due to the slow growth of the nail and treatment can therefore carry significant cost. The reclassification of terbinafine will provide access for the consumer to a well-established brand of antifungal for use in a topical product for the nails without the additional cost of a medical appointment and prescription for the oral terbinafine medication for the treatment of onychomycosis and thus the overall burden on the health system.

Summary*

Please provide a summary of the proposal, including:

- *A summary of the need for the substance to be reclassified*
- *An integrated summary of the potential benefits and harms of the proposed reclassification; how do the potential benefits outweigh the potential harm?*

This application seeks to align the schedule entry for terbinafine with the entries for the other similar antifungal nail treatment substances. Easy recognition of the familiar symptoms of fungal infections of the nail allows for appropriate self-medication by the consumer with topical antifungal and the scope for misdiagnosis is limited. The proposed reclassification will allow convenient access for the consumer which will lower the expense to the consumer for a treatment with a long duration. A pharmacist will be available to provide advice to consumers if necessary.

The proposed labelling for the Pharmacy-only terbinafine 10% solution product for application to the nails will advise users to consult their doctor or pharmacist if symptoms persist.

Systemic exposure to orally administered terbinafine has demonstrated rare hepatotoxic and other systemic adverse events which may be avoided through the use

of a topical formulation. The proposed Pharmacy-only product (MOB015B) has the advantage of topical delivery of effective concentrations of terbinafine to the nail plate and nail bed providing clinical efficacy, while at the same time avoiding the risk of systemic exposure and development of systemically induced serious adverse events or potential for drug-drug interactions reported after oral terbinafine use. Systemic exposure to terbinafine following application of MOB015B onto the nails is approximately 2000-fold lower than following oral use of 250 mg terbinafine tablets (Table in [redacted], Appendix A SmPC 2024). Therefore, the risk for systemic side effects is low.

The clinical development program has shown the proposed topical 10% terbinafine product to be substantially safe and appropriate treatment for fungal infections of the nail.

Topical terbinafine has an extremely low abuse potential, a low potential for harm from inappropriate use, no known interactions with commonly used substances, alcohol or food. The risk of masking a serious disease or compromising medical management of a disease is extremely low and the use of the product does not require ongoing or close medical diagnosis or management.

The same amendment has been proposed for the Australian Schedule 2 entry for terbinafine and the rescheduling application is with the Secretariat for consideration. The intention is to harmonise the supply of a terbinafine 10% topical nail application in Australia and New Zealand.

References*

Please provide references for your submission. Submissions should be supported by high-quality, well-referenced evidence from credible and authoritative sources, where available.

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Appendices

Please provide any supporting documentation as labelled appendices.

Appendix A - Common English Summary of Product Characteristics (SmPC 2024) Terbinafine 98 mg/mL cutaneous solution, Moberg Pharma, Date of Revision 24/07/2024

Appendix B - Common English text for leaflet, Terbinafin Moberg Pharma, Date of Revision 27 June 2023

Appendix C - Common English text for carton and tube labelling, Terbinafin Moberg Pharma

[redacted]

Appendix A

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

Appendix A continued

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.

Appendix A continued

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, Onycholysis, Onychomadesis, Paronychia, Dermatitis contact, Erythema
	Uncommon*	Skin irritation, Dermatitis, Nail disorder, 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.

Appendix A continued

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

Appendix A continued

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 07 24

Appendix B

Package leaflet: Information for the patient

Terbinafin Moberg Pharma 98 mg/mL cutaneous solution
terbinafine

[For medicines available only on prescription:]
Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

[For medicines available without a prescription:]
Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
Always use this medicine exactly as described in this leaflet or as your doctor or pharmacist has told you.
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.
- You must talk to a doctor if your symptoms do not improve or get worse after 6 months for fingernails and 9 to 12 months for toenails.

What is in this leaflet

1. What Terbinafin Moberg Pharma is and what it is used for

Terbinafin Moberg Pharma contains the active substance terbinafine, which belongs to a group of medicines known as antifungals. It kills a variety of fungi that can cause nail infections.

[For medicines available only on prescription:]
Terbinafin Moberg Pharma is used to treat mild to moderate **fungal infections** of the **fingernails and toenails** in adults.

[For medicines available without a prescription:]
Terbinafin Moberg Pharma is used to treat mild to moderate **fungal infections** of the **fingernails and toenails** in adults.
[SE OTC addition:] Terbinafin Moberg Pharma can be used when you have previously been diagnosed by a doctor and the infection does not involve the nail growth zone. You may also need to start a new treatment if the infection recovers.

[To be completed nationally]

Appendix B continued

2. What you need to know before you use Terbinafin Moberg Pharma

Do not use Terbinafin Moberg Pharma

- if you are allergic to terbinafine hydrochloride or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or pharmacist before using Terbinafin Moberg Pharma if :
- the part of the nail next to the cuticle is affected
- you have diabetes
- you have a disease affecting the immune system or take any medicines that might affect the immune system
- you have poor circulation, swelling or ulcers, in your legs or feet (peripheral vascular disease)
- you have injured, painful or severely damaged nails
- you have psoriasis that causes red itchy skin and scaly patches or any other chronic skin condition
- you have yellow nails together with oedema and breathing difficulties (yellow nail syndrome)

Terbinafin Moberg Pharma is for use only on nails. Avoid contact with eyes and mucous membranes. Rinse thoroughly with running water, in case of any contact with the eyes or mucous membranes.

Children and adolescents

Terbinafin Moberg Pharma should not be used by children and adolescents under 18 years of age, due to the lack of experience in this age group.

Other medicines and Terbinafin Moberg Pharma

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. It is unlikely that Terbinafin Moberg Pharma will influence or be influenced by other medicines you are using as it acts only locally in the nail.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

The use of Terbinafin Moberg Pharma may be considered during pregnancy and breast-feeding, if the doctor considers it necessary.

Do not allow infants to come into contact with any treated areas. Make sure infants do not suck on your treated nails.

Driving and using machines

Terbinafin Moberg Pharma does not affect your ability to drive and use machines.

Terbinafin Moberg Pharma contains propylene glycol

This medicine contains 0.7 g propylene glycol in each millilitre solution.

Appendix B continued

3. How to use Terbinafin Moberg Pharma

[For medicines available only on prescription:]
Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

[For medicines available without prescription:]
Always use this medicine exactly as described in this leaflet or as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Only for use on fingernails and toenails.

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

Dosage

Adults

- Apply a thin layer **once daily** over the entire surface of the **affected nails and under the free nail edge**, using the tip of the tube.
- Do not apply 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.

Do not apply Terbinafin Moberg Pharma to the nail bed if the affected nail or parts of the affected nail have detached from the underlying nail bed.

Duration of treatment

Treatment should be continued until each treated nail is clear or its appearance has improved significantly, and new, healthy nail has regrown. In general, the duration of treatment for fingernails is about 6 months while for toenails it is 9 to 12 months. You may experience some degree of improvement after 12 weeks, but it takes longer for the nail to be completely cured.

[For medicines available without prescription:]
You must talk to a doctor if your symptoms do not improve or get worse after 6 months of treatment for fingernails and 9 to 12 months for toenails.

If you use more Terbinafin Moberg Pharma than you should

Due to how this medicine is used, an overdose is highly unlikely. If you, or anyone else, accidentally swallows the solution, contact your doctor or hospital straight away for advice..

If you forget to use Terbinafin Moberg Pharma

If you miss an application, apply the solution as soon as possible on the same day. Then continue your treatment as before.
Do not use a double dose to make up for a forgotten use.

If you stop using Terbinafin Moberg Pharma

Do not stop using Terbinafin Moberg Pharma before the infected nails are clear of visible disease, or your doctor or pharmacist recommends.

Appendix B continued

Fungal nail infections may return if you do not use the solution regularly, or you stop treatment too early.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Side effects can occur with following frequencies:
Common (may affect up to 1 in 10 people)
- whitish or yellowish nail
- detachment of the nail from the nail bed
- separation of part of the nail that may lead to shedding from the free edge of the nail
- inflammation of the nail fold or cuticle with or without bacterial infection
- red itchy rash as a reaction to contact with the medicine
- skin redness

Uncommon (may affect up to 1 in 100 people)
- nail disorders and skin reactions around the treated nails: skin irritation, skin inflammation, itchy skin

Some side effects like for example nail discolouration and nail detachment can also be caused by the fungal infection.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Terbinafin Moberg Pharma

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the tube and carton after EXP. The expiry date refers to the last day of that month.

Store below 25 °C. Do not freeze.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Terbinafin Moberg Pharma contains

- The active substance is terbinafine. One millilitre of solution contains terbinafine hydrochloride equivalent to 98 mg terbinafine.

- The other ingredients are propylene glycol (E 1520), urea, lactic acid, disodium edetate (EDTA), sodium hydroxide (for pH-adjustment) and purified water.

Appendix B continued

What Terbinafin Moberg Pharma looks like and contents of the pack

Terbinafin Moberg Pharma is a clear, colourless cutaneous solution packed in plastic tubes with a silicone tip applicator and closed with a plastic cap.

Pack sizes: 5 mL, 10 mL
Not all pack sizes may be marketed.

Marketing Authorisation Holder

[To be completed nationally]

Manufacturer
[To be completed nationally]

This medicine is authorised in the Member States of the European Economic Area under the following names:
[To be completed nationally]

This leaflet was last revised in 2023-06-27

Appendix C

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
CARTON

1. NAME OF THE MEDICINAL PRODUCT

Terbinafin Moberg Pharma 98 mg/mL cutaneous solution
terbinafine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 mL solution contains terbinafine hydrochloride equivalent to 98 mg terbinafine.

3. LIST OF EXCIPIENTS

Excipients: propylene glycol (E 1520), urea, lactic acid, disodium edetate (EDTA), sodium hydroxide (for pH-adjustment), purified water

4. PHARMACEUTICAL FORM AND CONTENTS

Cutaneous solution
5 mL
10 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Cutaneous use. Only for use on nails.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25 °C. Do not freeze.

Appendix C continued

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

[For medicinal products subject to medical prescription:]
Anti-fungal nail treatment

[For medicinal products not subject to medical prescription:]

Front panel:
For treatment of mild to moderate fungal infections of the nails in adults.

Back panel:
For treatment of mild to moderate fungal infections of the fingernails and toenails in adults.
[SE OTC addition:] Terbinafin Moberg Pharma can be used when you have previously been diagnosed by a doctor and and the infection does not involve the nail growth zone. You may also need to start a new treatment if the infection recovers.

Cover each affected nail with a thin layer of solution once daily, preferably at bedtime. The solution should also be applied under the free edge of the nail. Allow to dry for approximately 5 minutes and do not wash or let the nails get wet for at least 8 hours. Do not apply the solution on the surrounding skin.

Treatment should be continued until each treated nail is clear or its appearance has improved significantly, and new, healthy nail has regrown. In general, the duration of treatment for fingernails is about 6 months while for toenails it is 9 to 12 months.

You must talk to a doctor if your symptoms do not improve or get worse after 6 months for fingernails and 9 to 12 months for toenails.

[To be completed nationally]

16. INFORMATION IN BRAILLE

Terbinafin Moberg Pharma 98 mg/mL cutaneous solution

Appendix C continued

17. UNIQUE IDENTIFIER – 2D BARCODE

[For medicinal products subject to medical prescription:]

2D barcode carrying the unique identifier included.

[For medicinal products not subject to medical prescription:]

<Not applicable>

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

[For medicinal products subject to medical prescription:]

PC
SN
NN

[For medicinal products not subject to medical prescription:]

<Not applicable>

Appendix C continued

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
TUBE

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Terbinafin Moberg Pharma 98 mg/mL cutaneous solution
terbinafine
Cutaneous use. Only for use on nails.

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

5 mL
10 mL

6. OTHER

[For medicinal products not subject to medical prescription:]
Treatment of fungal nail infections in adults.

[To be completed nationally]