Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Amorolfine 5 % w/v medicated nail lacquer

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 55.7 mg of amorolfine hydrochloride equivalent to 50 mg of amorolfine (5% w/v amorolfine).

125 mg / 2.5 ml:
Each bottle with 2.5 ml contains 139.3 mg of amorolfine hydrochloride equivalent to 125 mg of amorolfine.

Excipient with known effect:
Each bottle with 2.5 ml contains 1.2058 g of alcohol (ethanol) which is equivalent to 48.23 % w/w.

150 mg / 3 ml:
Each bottle with 3 ml contains 167.1 mg of amorolfine hydrochloride equivalent to 150 mg of amorolfine.

Excipient with known effect:
Each bottle with 3 ml contains 1.4469 g of alcohol (ethanol) which is equivalent to 48.23 % w/w.

250 mg / 5 ml:
Each bottle with 5 ml contains 278.5 mg of amorolfine hydrochloride equivalent to 250 mg of amorolfine.

Excipient with known effect:
Each bottle with 5 ml contains 2.4115 g of alcohol (ethanol) which is equivalent to 48.23 % w/w.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Medicated nail lacquer

Clear solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of onychomycosis caused by amorolfine-sensitive dermatophytes, yeasts or moulds, without nail matrix involvement in adults.

4.2 Posology and method of administration

Posology
The nail lacquer should be applied to the affected finger or toenails once weekly.

Method of administration
For topical use. To be applied to the affected nails.

1. Prior to each application, the diseased nail areas (particularly nail surfaces) must be filed down as much as possible with a nail file supplied with the pack. Then, the nail surface is cleaned and degreased with a swab - soaked with nail lacquer remover - supplied with the pack. Prior to each subsequent application of Amorolfine medicated nail lacquer, this process of filing down and cleaning must be repeated, so as to remove existing lacquer residues.
Warning! Nail files used for treatment must no longer be used for the care of healthy nails.

2. The nail lacquer is then applied with a spatula over the entire surface of the diseased nail and left to dry.

For each of the nails to be treated, the spatula should be immersed into the nail lacquer.

Warning! The spatula must not be wiped off on the neck of the bottle.

The bottle must be tightly closed immediately after applying the lacquer to the nails. The nail lacquer should be left to dry for approximately 3-5 minutes.

After use, the spatula must be cleaned with the swab soaked in nail lacquer remover.

It is important to clean the hands after applying Amorolfine medicated nail lacquer. If Amorolfine medicated nail lacquer is applied to the fingernails, users should wait until these are dry before washing their hands.

Duration of treatment
Treatment should be continued without interruption until the nail is regenerated and the infected areas are definitively cured.

In general, the duration of treatment is 6 months for fingernails and 9 to 12 months for toenails (it depends essentially on the intensity, localisation and extent of the infection).

After a 3-month use without improvement, a doctor should be consulted.

Paediatric Population
Due to a lack of experience, children and adolescents should not be treated with Amorolfine medicated nail lacquer.

Elderly
There are no specific dosage recommendations for use in elderly patients.

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

During the application of Amorolfine no cosmetic nail lacquer or artificial nails shall be used.

However, with repeated use of Amorolfine medicated nail lacquer, any nail varnish applied should be removed before applying a new coat of Amorolfine medicated nail lacquer.
Impermeable gloves should be worn when handling organic solvents, as the layer of Amorolfine lacquer on the fingernails will otherwise be removed. Due to lack of experience, children should not be treated with Amorolfine medicated nail lacquer.

Amorolfine medicated nail lacquer should not be applied to the skin surrounding the nail.

Avoid contact of the lacquer with eyes, ears and mucous membranes.

The medicinal product should be kept out of the reach of children.

Systemic or local allergic reactions may occur after the application of Amorolfine medicated nail lacquer. If such allergic reactions occur, use with Amorolfine medicated nail lacquer should be stopped immediately and medical advice sought. In such a case, Amorolfine medicated nail lacquer should be carefully removed with a nail polish remover and Amorolfine medicated nail lacquer should no longer be used.

Patient care should be determined by a physician in patients suffering from peripheral vascular diseases, diabetes, immune system disorders, as well as in patients with nail dystrophy or seriously damaged nails (over two thirds of the nail plate is affected). In these cases, a systemic therapy should be envisaged.
Patients with a history of injury, skin conditions such as psoriasis or any other chronic skin condition, oedema, breathing disorders (Yellow nail syndrome), painful, distorted/deformed nails or any other symptoms should seek medical advice prior to commencing treatment.

Amorolfine contains ethanol
This medicinal product contains 482.3 mg of ethanol in each ml of medicated nail lacquer which is equivalent to 48.23 % w/w. It may cause a burning sensation on damaged skin.

As ethanol is a flammable substance, Amorolfine medicated nail lacquer should not be used near an open flame, a burning cigarette or some appliances (e.g. hair dryers).

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy
Reproductive toxicology studies showed no evidence of teratogenicity in laboratory animals but embryotoxicity was observed at high oral doses. Experience with amorolfine during pregnancy and breastfeeding are limited. The systemic absorption of amorolfine during and after topical administration is very low and therefore the risk to the human fetus appears to be negligible. However, because there is no relevant experience, amorolfine should not be used during pregnancy.

Breastfeeding
It is unknown whether amorolfine is excreted in human milk. Because there is no relevant experience, amorolfine should not be used during breast feeding.

Fertility
Animal studies have shown reproductive toxicity at high oral doses (see section 5.3).

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Tabulated list of adverse reactions:

System Organ Class	Incidence	Adverse reactions
Immune system disorders	Not known* (cannot be estimated from the available data)	Hypersensitivity (systemic allergic reaction, including outside the site of application, which may be associated with swelling of the face, lips, tongue or throat, respiratory problems and/or a severe skin rash)
Skin and subcutaneous tissue disorders	Rare (≥1/10,000 to <1/1,000)	Nail changes, onychoclasis (broken nails), nail discolouration and onychorrhexis (brittle nails)
	Very rare (<1/10,000)	Skin burning sensation
	Not known* (cannot be estimated from the available data)	Erythema, pruritus, contact dermatitis, urticaria, blisters

*Data based on post-marketing studies

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:
HPRA Pharmacovigilance; website: www.hpra.ie.

4.9 Overdose

No systemic signs of overdose are expected following topical application of amorolfine 5% nail lacquer.
In case of accidental oral ingestion, appropriate symptomatic measures should be taken if needed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifungals for dermatological use, other antifungals for topical use, ATC code: D 01AE 16

Mechanism of action
Amorolfine is a topical antifungal agent. It belongs to the class of morpholine derivatives. Its fungistatic and fungicidal effect is due to a modification in the fungal cell membrane, with sterol biosynthesis being the main point of attack. The ergosterol level is reduced while, at the same time, unusual sterically nonplanar sterols accumulate.

In vitro, amorolfine has a broad antifungal spectrum.
It is effective against:
Dermatophytes: trichophytes, microspores, epidermophytes;
Yeasts: *Candida, Malassezia* or *Pityrosporum spp., Cryptococcus*;
Moulds: *Alternaria, Hendersonula, Scopulariopsis, Scytalidium, Aspergillus*;
Dematiaceae: *Cladosporium, Fonsecaea, Wangiella*;
Dimorphic fungi: *Coccidiodes, Histoplasma, Sporothrix*.
With the exception of *Actinomyces*, bacteria are not susceptible to amorolfine.

5.2 Pharmacokinetic properties

Absorption
Amorolfine penetrates the nail plate via the nail lacquer and thus eradicates the difficult-to-access fungi within the nail bed.

Distribution
Systemic absorption of the active substance is very low with this route of administration.

Elimination
Even in long-term treatment, there are no signs of accumulation in the human body.

5.3 Preclinical safety data

High systemic exposure in pregnant rabbits has precipitated a slight increase in embryonic resorption (embryotoxicity). However, no teratogenic effect was seen at these doses. Experience with amorolfine during pregnancy and breastfeeding in humans are limited. Amorolfine hydrochloride has been tested up to toxic doses both *in vitro* and *in vivo*. No mutagenic potential was found in any of these tests. There have been no long-term carcinogenic studies.

The extremely low systemic exposure from the use of Amorolfine medicated nail lacquer suggests that any foetal risk to humans is negligible.
Animal experiments with topical use of amorolfine hydrochloride showed mild to moderate skin irritation, especially when used under occlusive conditions. However, as occlusive dressings are not recommended for the treatment of topical fungal infections in humans, the relevance of increased local irritation under these extreme conditions is deemed to be minor. There was no evidence of any phototoxic, allergic or photoallergic potential for amorolfine hydrochloride in any of the respective animal experiments performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol anhydrous
Ammonio Methacrylate Copolymer (type A)
Ethyl acetate
Butyl acetate

Triacetin

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

2.5 ml and 3 ml bottle
After first opening: 6 months

5 ml bottle
After first opening: 9 months

6.4 Special precautions for storage

Keep the container tightly closed.

Keep the medicated nail lacquer away from fire or flames (the alcohol base is inflammable).

6.5 Nature and contents of container

Amber glass type I or type III bottle stopped with HDPE cap with a Teflon liner.

Pack size: 2.5 ml, 3 ml and 5 ml

All packs contain 30 alcohol cleansing swabs (soaked with isopropyl alcohol as nail lacquer remover and sealed in composite foil, 10 spatulas and 30 nail files.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Discard the medicinal product if deteriorated, e.g. hardened.

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

7 MARKETING AUTHORISATION HOLDER

Rowex Ltd
Newtown
Bantry
Co. Cork
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0711/309/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22nd March 2019
Date of last renewal: 6th February 2024

10 DATE OF REVISION OF THE TEXT