

New Zealand Datasheet

Name of Medicine

LOCERYL

Amorolfine Nail Lacquer 5%

Presentation

LOCERYL nail lacquer is a clear colourless liquid.

Uses

Actions

Class: Amorolfine is a topical antimycotic. Amorolfine belongs to a new chemical class. Its fungistatic or fungicidal effect is based on an alteration of the fungal cell membrane targeted primarily on sterol biosynthesis. The ergosterol content is reduced, and at the same time unusual, sterically nonplanar sterols accumulate.

Site and Mode of Action: Amorolfine has a broad spectrum of action. It is effective against:

Yeasts: *Candida*, *Cryptococcus*

Dermatophytes: *Trichophyton*, *Microsporum*, *Epidermophyton*

Moulds: *Alternaria*, *Hendersonula*, *Scopulariopsis*

Dematiacea: *Cladosporium*, *Fonsecaea*, *Wangiella*

Dimorphic Fungi: *Coccidioides*, *Histoplasma*, *Sporothrix*

With the exception of some *Actinomyces*, bacteria are not sensitive to amorolfine. *Propionibacterium acnes* is only slightly sensitive.

In rats, progressive cataract formation was seen after high oral doses (40 and 60 mg/kg/day in 26- and 13- week studies, respectively). Females were more affected than males. In both sexes, further deterioration occurred during the recovery period. Cataract formation also became apparent after 26 weeks in dogs treated orally with 40 mg/kg/day. The mechanism of cataract formation is unknown.

Additional data from a study in pigmented rats with dermal application of 0.25% amorolfine cream indicated neither a direct cataractogenic nor a co-cataractogenic potential. The systemic exposure of the rats during this study resulted in plasma concentrations 7 to 10 fold greater than expected in humans.

Pharmacokinetics

Amorolfine from nail lacquer penetrates and diffuses through the nail plate.

In one clinical study, patients being treated for a large number of infected nails tended to have measurable levels of amorolfine between 0.1 and 0.5 ng/mL whereas other patients have levels below the level of quantification (0.1 ng/mL). In this study, nails were not filed before application of the lacquer. One patient consistently had greater than 0.5 ng/mL (maximum 1.05 ng/mL).

Indications

Onychomycosis caused by dermatophytes, yeasts and moulds.

Dosage and Administration

The patient should apply the nail lacquer to affected finger or toenails once or twice weekly as follows:

1. Before the first application of LOCERYL nail lacquer, it is essential that the affected areas of nail (particularly the nail surfaces) should be filed down as thoroughly as possible using the nail file supplied. The surface of the nail should then be cleaned and degreased using a cleaning pad (as supplied). Before repeat application of LOCERYL nail lacquer, the affected nails should be filed down again as required, and in any case they must first be cleaned with a cleaning pad to remove any remaining lacquer.

Caution: Nail files used for affected nail must not be used for healthy nails.

2. With one of the reusable spatulas supplied, apply the nail lacquer to the entire surface of the affected nails. For each nail to be treated, dip the spatula into the nail lacquer without wiping off any of the lacquer on the bottle neck. After use, clean the spatula as well as the neck of the bottle with the same cleaning pad used before for nail cleaning. Immediately after application, the bottle should be tightly closed. Allow the nails to dry.

When working with organic solvents (thinners, white spirit, etc) wear impermeable gloves in order to protect the LOCERYL lacquer on the nails.

Treatment should be continued without interruption until the nail is regenerated and the affected areas are finally cured. The required duration of treatment depends essentially on intensity and localisation of the infection. In general, it is six months for fingernails. Longer periods are probably required for toenails.

Cosmetic lacquers, artificial nails, or occlusive dressings should not be used during treatment with LOCERYL nail lacquer.

Clinical efficacy has not been demonstrated in severe onychomycosis (involving the lunula) for amorolfine 5% nail lacquer when used alone.

Contraindications

LOCERYL nail lacquer must not be reused by patients who have shown hypersensitivity to the treatment.

Since there are no data on the use of LOCERYL in pregnant and lactating women, the use of LOCERYL nail lacquer should be avoided during pregnancy and lactation.

Warnings and Precautions

Occasionally, a slight transient burning sensation in the area of the nails was observed after application of nail lacquer. The application of lacquer to skin areas surrounding the nails should be avoided.

Use in Pregnancy

Category B3

Exposure of pregnant rats and rabbits to systemic amorolfine (≥ 10 mg/kg/day orally) resulted in increased resorptions (embryotoxicity). The significance of these findings to human embryotoxicity is not known. There are no data on the use of amorolfine in pregnant women.

Use in Lactation

In a peri- and postnatal study in rats, an increased mortality of newborn pups was observed at 10 mg/kg/day orally. There is no information on whether amorolfine passes into human breast milk. There are no data on the use of amorolfine in lactating women.

Use in Children

Owing to the lack of clinical experience available to date, children – particularly young children and infants – should not be treated with amorolfine.

Carcinogenicity and Genotoxicity

No animal carcinogenicity studies have been conducted on amorolfine. Amorolfine was not shown to be genotoxic in a standard battery of assays for gene mutations and chromosomal changes.

Adverse Effects

Of the 502 patients treated with amorolfine nail lacquer monotherapy, 3 (0.6%) experienced local adverse events such as itching and erythema. Of the 172 patients evaluated for safety in the combination group during the monotherapy period, 3 (1.8%) experienced the following adverse reactions: pruritis and vesicles (1), periungual scaling (1) and nail discolouration (1). In a sensitisation study involving 122 subjects, about one-tenth of patients experienced delayed hypersensitivity skin reactions.

Rare cases of nail disorder (nail discolouration, brittle nails (onychhorrexia) or broken nails) have been reported during treatment with LOCERYL nail lacquer. However these reactions may also be linked to the onychomycosis itself.

Very Rarely ($\leq 1/10000$) burning sensation and contact dermatitis.

Interactions

There are no known interactions.

Overdosage

No information is available concerning overdosage in humans.

Pharmaceutical Precautions

Store below 30°C.

Keep out of reach of children.

Medicine Classification

Pharmacy Medicine.

Package Quantities

Nail lacquer (5%) 5mL.

The package contains in addition: 30 cleaning pads impregnated with 70% isopropyl alcohol in foil packets, 10 spatulas and 30 nail files.

Further Information

Clinical Trials

Clinical efficacy of amorolfine has been demonstrated in three main multicentre studies in around 700 patients. The percentage of clinical responders (cure / improvement) ranged from 70% to 80% in all three studies.

In an open, comparative, randomised clinical study conducted in 340 patients with severe infections involving mainly toenails, clinical efficacy has been demonstrated when amorolfine 5% nail lacquer was applied twice weekly in conjunction with griseofulvin 500mg twice daily for the first 2 months of a 12 month treatment course. The reduction in treatment with griseofulvin decreased the risk of intolerance to griseofulvin. Clinical efficacy has not been demonstrated in severe onychomycosis (involving the lunula) for amorolfine 5% nail lacquer when used alone.

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