1. Name of the medicinal product

Batrafen Nail Lacquer

Active substance: ciclopirox

2. Qualitative and quantitative composition

1 g medicated nail lacquer contains 80 mg ciclopirox.
For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Medicated nail lacquer for application to the nails.

4. Clinical Pariculars

4.1 Therapeutic indications

For the treatment of fungal infections of the nails

4.2 Posology and method of administration

Dosage

Batrafen Nail Laquer is applied in a thin layer every other day in the first month, at least twice weekly in the second month and once a week from the third month onwards.

Method of administration

As much as possible of the destroyed nail material should be removed before the start of treatment with Batrafen Nail Laquer, for example with scissors or with the enclosed disposable nail files.

Unless directed otherwise, Batrafen Nail Laquer is applied in a thin layer to the diseased nail every other day in the first month. In this way, the nail is saturated with the active substance.

In the second month of treatment, application can be reduced to at least twice weekly and to once a week from the third month of treatment onwards.

Throughout the application period the entire layer of lacquer is removed once a week with alcohol swabs. During this process too, as much as possible of the affected nail material should be removed with disposable nail files.

If in the meantime the layer of lacquer becomes damaged, it is sufficient to paint over the chipped areas again with Batrafen Nail Laquer.

Do not use nail polish or other nail cosmetic products on the treated nails.

Duration of administration

The duration of use depends on the severity of the infection, but should not exceed a treatment period of 6 months.

In this period, the pathogens of the nail fungal infection are generally killed off. The doctor will decide whether it is necessary to continue treatment.

Pediatric Patients

Based on the safety profile in adults, Batrafen Nail Laquer is considered safe for use in children twelve years and older. No clinical trials have been conducted in the pediatric population.

4.3 Contraindications

Hypersensitivity to the active substance ciclopirox or to any of the excipients listed in 6.1..

The use of Batrafen Nail Laquer in children under 12 years old and during pregnancy and lactation is not indicated because of lack of clinical experience.

4.4 Special warnings and precautions for use

So far there is no relevant clinical experience with patients with insulin dependent diabetes or who have diabetic neuropathy. The risk of removal of the unattached, infected nail, by the health care professional and trimming by the patient should be carefully considered before prescribing to patients with a history of insulin dependent diabetes mellitus or diabetic neuropathy.

Caution is advised in patients who
• Are immunocompromised (e.g., received an organ transplant, were HIV positive etc.) or had a history of immunosupression
• Require medication to control epilepsy
• Use or require topical corticosteroids on a repeated monthly basis
• Use steroid inhalers on a regular basis
Since ciclopirox has not been studied in those populations.

Do not light a cigarette or come into contact with fire until the preparation has completely dried.

4.5 Interaction with medicinal products and other forms of interaction

Not known.

4.6 Pregnancy and lactation

The use of Batrafen Nail Laquer during pregnancy and lactation is not indicated because of a lack of clinical experience.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

The incidences of undesirable effects are based on the following categories:
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Immune system disorder

Rare: Allergic contact dermatitis.

Skin and subcutaneous tissue disorders
Very rare: Reddening and desquamation where Batrafen Nail Laquer has come into contact with skin adjacent to the nail,

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulations by using an online form
http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifungals for dermatological use, antifungals for topical use, ATC code: D01AE14.

In vitro, ciclopirox has been shown to be both fungicidal and fungistatic as well as having sporicidal activity.

Study results on the mechanism of action indicate that the fungicidal effect of ciclopirox is based on inhibition of the cellular uptake of vital cell constituents, while at the same time the efflux of other essential cell components is induced.

Ciclopirox olamine accumulates strongly in the interior of the fungal cell, where it is irreversibly bound to certain structures and organelles such as the cell wall, cell membrane, mitochondria, ribosomes and microsomes.

No evidence of metabolisation of ciclopirox olamine by the fungal cell has been found.

Comparative studies have shown that ciclopirox and ciclopirox olamine have the same type of antimicrobial effect for a relevant spectrum of dermatomycosis pathogens

5.2 Pharmacokinetic properties

Penetration of ciclopirox from the nail lacquer into excised onychomycotic human fingernails

Release of the radiolabelled active substance (^{14}C) from the nail lacquer and penetration into excised onychomycotic nails produces tissue concentrations in the deeper nail layers equivalent to 2 to 10 times the minimum inhibitory concentration for relevant pathogens in onychomycoses within 24-48 hours.

In vivo studies on the penetration of ciclopirox from the nail lacquer into healthy human fingernails

As the conditions in excised nails provide only a very limited reflection of the in vivo situation, penetration of ciclopirox from the lacquer into the nail plate of healthy fingernails was studied. The presence of the active substance was detected by means of a biotest (inhibition of the growth of Candida pseudotropicalis). This test revealed sufficient tissue concentrations of ciclopirox in various layers of the nail plate to totally inhibit growth of the test pathogen. The increase in the diffusion gradient to steady state was achieved in 14 days. In addition, distribution of the active substance throughout the entire nail plate was relatively homogeneous, at least in the distal portion. This study showed that the ciclopirox that penetrates the nail plate remains microbiologically active.

No data are available on absorption through the nail plate and systemic uptake of ciclopirox, but this should be well below a value of 1.3% (dermal absorption).

There is no evidence to suggest that the toxicological data obtained for ciclopirox olamine cannot be extrapolated to the use of ciclopirox.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Isopropyl alcohol , Ethylacetate , Poly (Buthylhydrogenmaleate, Methoxyethylene) (1:1)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.
Once the bottle has been opened, Batrafen Nail Laquer has a shelf life of 6 months provided it is stored correctly.

6.4 Special precautions for storage

Store below 25°C
Keep the bottle in the outer carton in order to protect from light.

6.5 Nature and contents of container

Glass bottles with screw cap and inserted brush.
Bottle containing 3g medicated nail lacquer.

6.6 Special precautions for disposal and other handling

To prevent the solution from drying up, Batrafen Nail Laquer should be tightly sealed after use.
To prevent the screw cap from sticking to the bottle, avoid spilling solution on the screw thread.

7. MANUFACTURER

Sanofi Aventis, Frankfurt am Main, Germany

8. MARKETING AUTHORISATION HOLDER

Sanofi-Aventis Israel ltd. P.O.B. 8090 Netanya 4250499.

The format of this leaflet was determined by the Ministry of Health and its content was checked and approved on 06/2019

Batr-Lacquer-13