

Ciclopirox Nail Varnish

Ciclopirox 8%w/w Topical Solution

Presentation

Ciclopirox Nail Varnish is a clear, colourless to pale yellow solution supplied in a glass bottle with a brush for ease of application. Each gram of Ciclopirox Nail Varnish contains 80 mg of ciclopirox.

Uses

Actions

Ciclopirox is a synthetic, broad spectrum anti-fungal agent that inhibits the growth of dermatophytes, yeasts and moulds. Ciclopirox is the free acid of ciclopiroxolamine and has an identical spectrum of activity to ciclopiroxolamine.

The mechanism of action has been investigated using both *in vitro* and *in vivo* models. It appears to exert its anti-fungal and anti-bacterial activity principally by causing intracellular depletions of essential substrates e.g. amino acids and/or ions e.g. potassium. The exact mechanism is not known. But it seems depletion results from inhibition of transmembrane transport of these substances into cells. One *in vitro* study has suggested that ciclopirox acts by chelation of the polyvalent cations (Fe^{3+} or Al^{3+}) resulting in the inhibition of the metal-dependent enzymes that are responsible for the degradation of peroxides within the fungal cell. The clinical significance of this observation is not known. Ciclopirox does not appear to inhibit synthesis or cause lysis of the yeast cell wall.

Ciclopirox is fungistatic and fungicidal against a wide range of fungi and yeast. The MIC of ciclopirox for 34 of 35 fungal and yeast strains were between 0.89-3.9 $\mu\text{g/mL}$ (*in vitro*). For *Trichophyton metagrophytes* the MIC was 7.8 $\mu\text{g/mL}$. Ciclopirox has also been shown to be active against a number of pathogenic gram positive and gram negative bacteria e.g. *E. coli*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, relevant *Staphylococcus* and *Streptococcus* species, *Mycoplasma* species, *Trichomonas vaginalis* and Actinomyces. Most strains tested were in the range 7.7-31.3 $\mu\text{g/mL}$.

Pharmacokinetics

As demonstrated in pharmacokinetic studies in animals and man, ciclopiroxolamine is rapidly absorbed after oral administration and completely eliminated in all species via faeces and urine. Most of the compound is excreted either unchanged or as glucuronide with glucuronidation being the main metabolic pathway.

Systemic absorption of ciclopirox was determined in patients with dermatophytic onychomycoses after application of ciclopirox 8% topical solution to all 20 fingers and toes once daily for 6 months. Random serum concentrations and 24 hour urinary excretion of ciclopirox were determined approximately every 4 weeks during treatment and 4 weeks post-treatment. Ciclopirox serum levels ranged from 12-80 ng/mL with total urine levels ranging between 49-4685 ng/mL. One month after ending treatment, serum and urinary levels of ciclopirox were below the limit of detection.

Combined results from 2 vehicle controlled studies showed ciclopirox peak serum levels in the range 10.0-24.6 ng/mL in 24 of 66 (36%) evaluable patients. The Nail Varnish was applied once daily to all toenails and affected fingernails over a 48 week period. 11 patients also concomitantly used ciclopiroxolamine 1% cream.

In vitro studies have evaluated the penetration and anti-fungal activity of ciclopirox lacquer. Healthy volunteers applied the lacquer to finger or toenails once daily for up to 45 days with the lacquer being removed once per week. After 7-14 days there was a high level of biological activity at all depths of the nail increasing to a plateau by 30 days in fingernails and 10-45 days in toenails. The concentrations were significantly higher than those needed to inhibit the growth of dermatophytes that cause onychomycosis.

In vitro studies also indicate that after application of Ciclopirox topical solution 8%, ciclopirox penetrates nails to a depth of about 0.4 mm. Ciclopirox applied to toenails 0.6-1.29 mm thick showed penetration of 0.02-0.04% of the applied dose. After treatment every 3 days for 30 days penetration was 0.01-0.07% of the applied dose. Ciclopirox the nail plate building up a gradient within 14 days of application depending upon nail condition. Penetration by ciclopirox seems to be dependent upon the structure and thickness of the nail, with penetration increasing according to the extent of mycotic infection.

Nails with infection involvement of less than 60% of the nail plate at the start of treatment, have a 4-5 times greater chance of clear regrowth compared to nails showing a higher involvement. 100% clearance rates have been shown in cases of 30% nail plate involvement. When more than 60% of the nail plate is involved clear regrowth may be reduced to a clinical improvement of approximately 30%.

Indications

The treatment of fungal infections of the nails caused by dermatophytes, yeasts and moulds.

Dosage and Administration

Before starting treatment, remove any loose nail or nail material using nail clippers or nail file and the remaining diseased nail roughened with a nail file..

Apply a thin layer of Ciclopirox Nail Varnish to the affected nail(s) every second day for 1 month then twice per week for 4 weeks, then once per week.

Allow the varnish to dry (approximately 30 seconds) before putting on socks or stockings. After applying the varnish, wait 8 hours before taking a bath or shower.

Each week remove the entire coating of varnish using a commercial nail polish remover. The nail should be trimmed using clippers and/or nail files before reapplying Ciclopirox Nail Varnish. If the coating of varnish is damaged in the meantime, it is sufficient to paint over the chipped areas again with Ciclopirox Nail Varnish.

The duration of application depends upon the severity of the infection. Do not use for longer than 6 months except on medical advice.

Ciclopirox Nail Varnish is not indicated for use in children or adolescents aged under 18 years.

Contraindications

Hypersensitivity to ciclopirox or any of the excipients used in this product.

Ciclopirox Nail Varnish should not be used during pregnancy or while breast feeding.

Warnings and Precautions

Do not use Ciclopirox Nail Varnish near the eyes or genital areas. Do not take it orally. It is for use on the nails only. Ciclopirox Nail Varnish is a known eye irritant and care should be taken to ensure that the patient does not transfer the product to the eyes by touching them after applying the varnish to their fingernails.

If a reaction indicating sensitivity or chemical irritation occurs while using Ciclopirox Nail Varnish, treatment should be discontinued and appropriate therapy instituted. There is no relevant clinical experience with patients with a history of immunosuppression e.g. extensive, persistent or unusual distribution of dermatomycoses, extensive seborrheic dermatitis, recent or recurring herpes zoster or persistent herpes simplex, who are immunocompromised e.g. HIV infected patients, transplant patients or have diabetic neuropathy. These patients should be carefully evaluated as to the suitability of Ciclopirox Nail Varnish for use in the treatment of fungal infection.

Commercial/cosmetic nail varnishes should not be worn while treating nails with Ciclopirox Nail Varnish as there is no clinical experience with the efficacy of Ciclopirox Nail Varnish when used with these other nail varnishes.

In clinical studies no overall differences were observed between elderly and younger patients but a greater sensitivity in some older patients cannot be ruled out.

Use during Pregnancy and Lactation

Category B3.

There are no adequate or well controlled studies of topically applied ciclopirox in pregnant women. Ciclopirox Nail Varnish should only be used during pregnancy if the potential benefit to the mother outweighs the potential risk to the foetus.

Animal studies have not indicated any significant foetal malformations but the relevance of this to humans is unknown.

It is not known if ciclopirox is excreted in human milk. Ciclopirox Nail Varnish should only be used by nursing mothers if the potential benefit to the mother outweighs the potential risk to the child.

Effects on ability to drive and use machines

Ciclopirox Nail Varnish is unlikely to have any effect on a person's ability to drive or operate machinery.

Adverse Effects

Ciclopirox Nail Varnish is generally well tolerated. Where Ciclopirox Nail Varnish has come into contact with skin adjacent to the nail, a light reddening or scaling of the skin has been noted in a few cases.

The most frequent adverse effects are local and dermatological effects. They are rarely severe enough to require discontinuance of the medication.

The most frequent adverse effects are periungual erythema and erythema of the proximal nail fold. These effects occurred in 5% and 1% of patients receiving the medication and the varnish vehicle respectively.

Nail disorders e.g. ingrown toenails, irritation, discolouration and changes in shape have been reported.

Application site reactions and/or burning of the skin have been reported as has contact dermatitis.

Worsening of clinical symptoms may occur in some patients.

Interactions

None known..

Overdosage

Should too much Ciclopirox be used or it is used inappropriately provide symptomatic treatment. However no relevant systemic effects are expected if Ciclopirox Nail Varnish is applied to large areas or used too frequently.

Pharmaceutical Precautions

Store below 25 °C. Protect from heat, light and moisture.

Make sure the product is tightly closed after use. To prevent the cap sticking to the bottle, do not allow the product to get on the threads on the bottle neck.

Product remains stable for at least 6 months after opening if stored as directed.

Medicines Classification

Pharmacist Only Medicine

Package Quantities

Bottles of 3.3 mL or 6.6 mL with application brush.

Further Information

Ciclopirox also contains isopropyl alcohol, ethyl acetate and butyl monoester of poly(methylvinyl ether/maleic acid. Ethyl acetate and isopropyl alcohol are solvents that evaporate after application. They are flammable therefore the product should not be used near a naked flame.

An applicator brush is supplied with the product.

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Date of Preparation

2 March 2010