

# Ciclopoli Nail Lacquer

Ciclopirox 8% nail lacquer

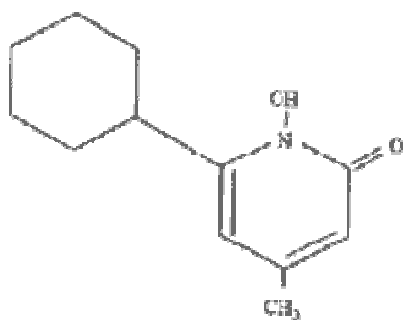
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## Presentation

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Ciclopoli Nail Lacquer contains 80mg/g (8%) of the active ingredient ciclopirox. Ciclopirox is 6-cyclohexyl-1-hydroxy-4-methyl-2-(1H) pyridone ( $C_{12}H_{17}NO_2$ ). MW: 207.3.

The chemical structure is shown below:



CAS 29342-05-0

Ciclopirox is a white to slightly yellowish-white, crystalline powder which is odourless to almost odourless. It is freely soluble in dichloromethane and ethanol 96%, very soluble in chloroform, soluble in ether and slightly soluble in water. The pKa value is 7.2.

Ciclopoli Nail Lacquer is a clear, colourless to slightly yellow solution.

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## Uses

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### **Actions**

Ciclopoli is a medicated nail lacquer for topical use on finger nails, toe nails and immediately adjacent skin (perionychium, hyponychium).

Pharmacotherapeutic group: Antimycotic for dermatologic use; ATC code: D01AE14

Ciclopoli 8% nail lacquer is a formulation based on a patented technology (ONY-TEC) for delivery of actives to nails. It is a hydro-alcoholic solution of hydroxypropyl chitosan, which has the following properties: good solubility in water, high plasticity, affinity to keratin and high compatibility with human tissues.

Ciclopoli 8% nail lacquer has a topic, anti-mycotic action. The active ingredient is ciclopirox (pyridone derivative). In vitro, ciclopirox has been shown to be both fungicidal and fungistatic as well as having sporicidal activity. Ciclopirox has activity against a broad spectrum of dermatophytes, yeasts, moulds and other fungi. For most dermatophytes (Trichophyton species, Microsporum species, Epidermophyton species) and yeasts (Candida albicans, other Candida species) the MIC falls within the range of 0.9 to 3.9 µg/ml.

After application on the nail surface, Ciclopoli 8% nail lacquer forms an invisible film, permeable to moisture and air, that adheres to the keratin structure of the nail allowing an easy and quick release of the active ingredient to the substrate.

### ***Pharmacokinetics***

Based on the ONY-TEC technology, Ciclopoli 8% nail lacquer has demonstrated good penetration properties through keratin. After application of the medicated nail lacquer to hornified tissues the active substance is immediately released and penetrates the nail. By achieving fungicidal concentrations at the site of infection, the active substance leads to irreversible binding to the fungal cell wall and this causes inhibition of the uptake of components needed for cellular synthesis and of the respiratory chain.

Since only a very small amount of ciclopirox is absorbed systemically, the drug exerts its activity particularly at the local level and the risk of possible interference with the normal body functions is negligible.

### ***Clinical Trials***

Ciclopoli 8% nail lacquer has been investigated in a long term clinical study in 467 patients with onychomycosis. It was a three arm study versus placebo (Ciclopoli 8% vehicle) and a commercially available formulation of ciclopirox 8% nail lacquer. All treatments were applied every day for 48 weeks to the infected nails. The patients were followed up for a further period of 12 weeks. As required by the different characteristics of the formulations, reference ciclopirox nail lacquer was removed once a week by means of solvents and nail filing, while Ciclopoli 8% and placebo (both water-soluble) simply by washing.

Efficacy data were available in 454 patients (ITT) and confirmed in 433 patients. (PP). Ciclopoli 8% nail lacquer showed a better efficacy compared to placebo and to reference ciclopirox. The better effect was evidenced on the primary endpoint "cure" rate (namely patients with negative mycology and 100% complete clear nail) and on the secondary endpoint "responder" rate (patients with negative mycology and ≥ 90% clear nail).

At weeks 48 and 52 the percentages of patients with complete cure and of responders, in the Ciclopoli 8% group, were consistently higher than in the reference ciclopirox group.

At week 60, i.e. 12 weeks after end of treatment, percentages of patients with complete cure and of responders, in the Ciclopoli 8% group, further increased compared to the reference group, being 119% higher for cure rate (statistically significant,  $p < 0.05$ ) and 66% higher for responder rate (statistically significant,  $p < 0.05$ ).

Ciclopoli nail lacquer showed a continuous increase in both efficacy endpoints during weeks 48, 52 and 60, differently from the reference product.

Tolerability at the application site was continuously monitored throughout the treatment period. Elicited signs/symptoms were recorded in a minority of patients in all treatment groups. Overall, signs or symptoms were more frequent with the reference ciclopirox product (8.6% signs and 16% symptoms) than with Ciclopoli 8% (2.8% signs and 7.8% symptoms). In placebo group, 7.2% signs and 12.4% symptoms were recorded. The most frequent sign recorded was erythema. This was observed by the Investigator in 2.8% of patients in Ciclopoli 8% group, and in 8.6% in reference group. Erythema was additionally reported by a further 2.1% of patients in the reference group. The most frequent symptom was burning. This was reported in 2.8% of patients in Ciclopoli 8% group and in 10.7% in reference group.

No fungal resistance to ciclopirox has so far been reported.

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## Indications

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Fungal infections of the nails, caused by dermatophytes, yeasts or moulds.

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## Dosage and Administration

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### ***Adults***

Unless otherwise directed, Ciclopoli 8% nail lacquer should be applied in a thin layer once a day on the affected nail/s after washing and drying. The medicated nail lacquer shall be applied over the entire nail plate, 5 mm of surrounding skin and, if possible under the free edge of the nail. Ciclopoli 8% nail lacquer needs about 30 seconds for drying. The treated nails should not be washed for at least six hours, therefore, application in the evening before going to bed is recommended. After that time, normal hygienic practices could be followed.

Ciclopoli 8% nail lacquer does not need to be removed by any solvent or abrasives (i.e. nail filing), it is sufficient to wash the nails. In case of unintentional removal by washing, Ciclopoli 8% nail lacquer can be applied again.

Regular removal of the nail free edge and any onycholytic material by nail clipping, is recommended.

Treatment should be continued until complete mycological and clinical cure is achieved and the healthy nail has grown again. Normally, complete cure of fingernails is achieved in about 6 months while for toenails it takes from 9 to 12 months.

The control of fungal culture should be done 4 weeks after the end of the treatment to avoid interference with culture results by possible residues of the active substance.

If the condition is refractory to therapy with Ciclopoli 8% nail lacquer and/or there is extensive involvement of one or several finger- and toenails, additional oral therapy shall be considered.

### ***Children***

Because of the lack of clinical experience, Ciclopoli Nail Lacquer is not recommended for use in children.

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## **Contraindications**

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Hypersensitivity to ciclopirox or any of the ingredients in the lacquer.

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## **Warnings and Precautions**

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In case of sensitisation, treatment should be discontinued and appropriate therapy instituted.

Ciclopoli 8% nail lacquer contains cetostearyl alcohol which may cause local skin reactions as for example irritative contact dermatitis.

### ***Use in pregnancy***

There are no clinical data on exposed pregnant women for ciclopirox. Animal studies have shown no direct or indirect harmful effect on pregnancy, embryonic development, development of the foetus and/or the birth. However, there are no adequate data on possible long term effects on postnatal development. Treatment with Ciclopoli 8% nail lacquer may only take place, if treatment is absolutely necessary, after the responsible doctor has carefully assessed the benefits against possible risks.

### ***Use in lactation***

It is unknown whether ciclopirox passes into breast milk in human. Treatment with Ciclopoli 8% nail lacquer may only take place, if treatment is urgently

necessary, after the responsible doctor has carefully assessed the benefits against possible risks.

### ***Use in children***

Safety and effectiveness in children below the age of 18 years have not been established, therefore, Ciclopoli Nail Lacquer is not indicated for use in children.

### ***Effects on Ability to Drive and Use Machines***

Ciclopoli 8% nail lacquer has no influence on the ability to drive and use machines.

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## **Adverse Effects**

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For the frequency of occurrence of side effects, the following phrases are used: very common ( $\geq 1/10$ ), common ( $\geq 1/100$  to  $< 1/10$ ), uncommon ( $\geq 1/1,000$  to  $< 1/100$ ), rare ( $\geq 1/10,000$  to  $< 1/1,000$ ), very rare ( $< 1/10,000$ ), not known (cannot be estimated from the available data).

No systemic adverse effects are expected. Reported signs and symptoms at the application site were mild and transient.

### General disorders and administration site conditions:

Very rare: erythema, scales, burning and itching at the application site.

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## **Interactions**

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Nil known.

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## **Overdosage**

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No overdosing has been reported with the use of this product.

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## **Pharmaceutical Precautions**

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Store below 25°C

Shelf life: 3 years

Store in the original container. The bottle should be kept tightly closed, to avoid evaporation of the contents. Store the bottle inside the carton to protect from light.

Do not store in a refrigerator. At temperatures below 15°C the medicated nail lacquer may gel. Light flocculation or formation of a light sediment may also occur which can be reversed by warming up to room temperature (25°C) through rubbing the bottle between hands till the solution is clear again (about one minute). This has no impact on product quality or performance.

The bottle should be capped when not in use. This product is flammable therefore contact with heat and open flame should be avoided.

Once the bottle has been opened Ciclopoli Nail Lacquer is stable for at least 6 months if stored as directed and protected from light.

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## **Medicine Classification**

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Pharmacist Only Medicine.

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## **Package Quantities**

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3.3 ml in a glass bottle, with screw cap, which are fitted with a brush.

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## **Further Information**

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### ***Preclinical safety data***

Preclinical data, up to a daily oral dose of 10 mg/kg from conventional repeated dose toxicity studies, revealed no evidence of any sort for toxicity as well as no evidence for genotoxicity or carcinogenicity. At a dosage of 5 mg/kg, a reduced fertility index in the rat was observed. No evidence for embryo-/foetotoxicity or teratogenicity was found in rats and rabbits. There is no evidence of any sort for peri- or postnatal toxicity, however possible long term effects on progeny have not been investigated. Ciclopoli 8% nail lacquer exhibited no irritation in studies on local tolerance in rabbits and guinea pigs.

The chitosan derivative contained in the formulation is free of tropomiosine and did not exhibit allergenic potential in patients with shellfish allergy.

Ciclopoli 8% nail lacquer contains the following excipients: Ethyl acetate, ethyl alcohol 96%, cetostearyl alcohol, hydroxypropylchitosan and purified water.

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## **Name and Address**

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**Date of Preparation**

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16 December 2010