Ciclopirox Topical Solution, 8% (Nail Lacquer)

For use on fingernails and toenails and immediately adjacent skin.

Not for use in eyes.

DESCRIPTION

Ciclopirox Topical Solution, 8% (Nail Lacquer) contains a synthetic antifungal agent, ciclopirox. It is intended for topical use on the fingernails and toenails and immediately adjacent skin of fingernail and toenail disorders which have been determined by the physician to be due to a susceptible fungus.

Ciclopirox is a molecule in which a cyclohexyl ring is linked to a hydroxy group and a methyl group by a methylene group as follows:

\[
\text{Ciclopirox} = \text{CH}_2\text{CH}_2\text{OH} - \text{C}\left(\text{CH}_3\right)\text{CH}_2\text{OH}
\]

The chemical name for ciclopirox is 6-cyclohexyl-1-hydroxy-4-methyl-2-picolinic acid. The molecular weight of ciclopirox is 207.27. The CAS Registry Number is [29342-10-1].

Pharmacology

The penetration of the Ciclopirox Topical Solution, 8%, (Nail Lacquer), to the nail plate is dependent on the susceptibility of the pathogen, the thickness of the nail plate, and whether the nail is healthy or diseased. Ciclopirox Topical Solution, 8%, (Nail Lacquer), penetrates the nail to a depth of approximately 0.4 mm. As demonstrated, ciclopirox Topical Solution, 8%, (Nail Lacquer), demonstrated penetration up to a depth of approximately 0.4 mm. As demonstrated, ciclopirox Topical Solution, 8%, (Nail Lacquer), demonstrated penetration up to a depth of approximately 0.4 mm. As demonstrated, ciclopirox Topical Solution, 8%, (Nail Lacquer), demonstrated penetration up to a depth of approximately 0.4 mm.

In vitro studies have shown that ciclopirox inhibits the activity of keratinases present in dermatophytes and yeasts. Viable counts of T. mentagrophytes, T. rubrum, and T. verrucosum were reduced by 99.99% when exposed to 0.05% ciclopirox. In multiple species of dermatophytes, catalase activity is reduced by 99% in the presence of ciclopirox. In vitro studies show that ciclopirox inhibits the activity of keratinases present in dermatophytes and yeasts. Viable counts of T. mentagrophytes, T. rubrum, and T. verrucosum were reduced by 99.99% when exposed to 0.05% ciclopirox. In multiple species of dermatophytes, catalase activity is reduced by 99% in the presence of ciclopirox.

No studies have been conducted to determine whether ciclopirox might reduce the efficacy of systemic antifungal agents for onychomycosis. However, ciclopirox Topical Solution and systemic antifungal agents for onychomycosis are used concurrently in patients with moderate to severe mycosis.

DOSAGE AND ADMINISTRATION

Ciclopirox Topical Solution, 8%, (Nail Lacquer) is intended for use on the fingernail and toenail and immediately adjacent skin. Treatment should be performed by professionals trained in treatment of nail disorders or by the patient under the supervision of a health care provider.

CLINICAL PHARMACOLOGY

Patients with systemic antifungal agents for onychomycosis should be treated with ciclopirox Topical Solution and systemic antifungal agents for onychomycosis concurrently.

Pharmacokinetics

The pharmacokinetics of ciclopirox Topical Solution and ciclopirox oligamine were investigated using various in vitro and in vivo infection models. One in vivo study evaluated the penetration of ciclopirox Topical Solution (0.05% in a lipid vehicle) through normal and diseased skin in vivo. The compound is excreted as either glucuronide or acetylglucuronide. After oral administration of ciclopirox, approximately 90% of the radioactivity is excreted within 12 hours of administration. Ninety percent of the rectally excreted radioactivity was in the form of unchanged ciclopirox. The penetration of ciclopirox into the nail plate, as determined in 3 patients with dermatophytes onychomycosis, after application of Ciclopirox Topical Solution, 8%, (Nail Lacquer) was noted to start on day 3 and reach a peak level of 90% of the dose by day 10. In this study, ciclopirox levels peaked over 12:00:00. Random serum concentrations of ciclopirox reached peak levels within 20 minutes of the first dose of ciclopirox. Three percent of the radioactivity was excreted within 12 hours of administration. Ninety percent of the rectally excreted radioactivity was in the form of unchanged ciclopirox.
Ciclopirox Topical Solution, 8%, (Nail Lacquer), should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The teratogenicity of Ciclopirox Topical Solution, 8%, (Nail Lacquer), was assessed by evaluating the effect of oral administration of ciclopirox olamine in animals on the development of their offspring. In pregnant rabbits (at the dose level of 12 weeks following the end of treatment are presented below. Note that post-treatment efficacy assessments were scheduled to become pregnant, had a history of immunosuppression used only.

<table>
<thead>
<tr>
<th>Week 48</th>
<th>Active Vehicle</th>
<th>Active Vehicle</th>
<th>Active Vehicle</th>
<th>Active Vehicle</th>
</tr>
</thead>
<tbody>
<tr>
<td>112</td>
<td>112</td>
<td>118</td>
<td>118</td>
<td></td>
</tr>
</tbody>
</table>

The results of the 92 studies of Ciclopirox Topical Solution, 8%, (Nail Lacquer), are summarized in Table 1. The number of patients in the five studies compared to vehicle. In a separate study of the photosensitizing potential of ciclopirox olamine, 3% (3/327) and vehicle (4/328).

In two studies for the endpoint “almost clear” (≤ 10% nail involvement and negative mycology), statistical significance was demonstrated in one of two studies. These results are consistent with the clinical efficacy data of ciclopirox olamine 8% solution for the treatment of onychomycosis of the great toenails without lunula involvement treated with ciclopirox olamine 8% solution (Nail Lacquer).

In a 6-month drug-free observation period prior to necropsy revealed no specific effects on fertility or other reproductive parameters in the treated males. In the presence of an increased skin penetration potential is anticipated in this clinical trials with use of Ciclopirox Topical Solution, 8%, (Nail Lacquer), it is recommended to be used by women of reproductive potential who can be adequately counseled regarding the potential for fetal exposure. There is no evidence of genetic toxicity. There were no differences observed in the genotoxicity tests performed with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. The following in vitro genotoxicity tests have been conducted with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. In an in vivo transformation assay (negative). In an in vivo transformation assay (negative). In a 6-month drug-free observation period prior to necropsy revealed no specific effects on fertility or other reproductive parameters in the treated males.

There were no differences observed in the genotoxicity tests performed with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. The following in vitro genotoxicity tests have been conducted with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. In an in vivo transformation assay (negative). In an in vivo transformation assay (negative). In a 6-month drug-free observation period prior to necropsy revealed no specific effects on fertility or other reproductive parameters in the treated males.

There were no differences observed in the genotoxicity tests performed with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. The following in vitro genotoxicity tests have been conducted with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. In an in vivo transformation assay (negative). In an in vivo transformation assay (negative). In a 6-month drug-free observation period prior to necropsy revealed no specific effects on fertility or other reproductive parameters in the treated males.

There were no differences observed in the genotoxicity tests performed with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. The following in vitro genotoxicity tests have been conducted with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. In an in vivo transformation assay (negative). In an in vivo transformation assay (negative). In a 6-month drug-free observation period prior to necropsy revealed no specific effects on fertility or other reproductive parameters in the treated males.

There were no differences observed in the genotoxicity tests performed with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. The following in vitro genotoxicity tests have been conducted with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. In an in vivo transformation assay (negative). In an in vivo transformation assay (negative). In a 6-month drug-free observation period prior to necropsy revealed no specific effects on fertility or other reproductive parameters in the treated males.

There were no differences observed in the genotoxicity tests performed with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. The following in vitro genotoxicity tests have been conducted with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. In an in vivo transformation assay (negative). In an in vivo transformation assay (negative). In a 6-month drug-free observation period prior to necropsy revealed no specific effects on fertility or other reproductive parameters in the treated males.

There were no differences observed in the genotoxicity tests performed with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. The following in vitro genotoxicity tests have been conducted with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. In an in vivo transformation assay (negative). In an in vivo transformation assay (negative). In a 6-month drug-free observation period prior to necropsy revealed no specific effects on fertility or other reproductive parameters in the treated males.

There were no differences observed in the genotoxicity tests performed with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. The following in vitro genotoxicity tests have been conducted with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. In an in vivo transformation assay (negative). In an in vivo transformation assay (negative). In a 6-month drug-free observation period prior to necropsy revealed no specific effects on fertility or other reproductive parameters in the treated males.

There were no differences observed in the genotoxicity tests performed with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. The following in vitro genotoxicity tests have been conducted with ciclopirox olamine alone (negative; negative) in Chinese hamster bone marrow cells. In an in vivo transformation assay (negative). In an in vivo transformation assay (negative). In a 6-month drug-free observation period prior to necropsy revealed no specific effects on fertility or other reproductive parameters in the treated males.