8X Cream (Ciclopirox Olamine USP 1% w/w)

To be sold by retail on the prescription of a Registered Medical Practitioner only.

Qualitative and Quantitative Composition

Each gm contains:

Ciclopirox Olamine USP..... 10 mg

Benzyl Alcohol IP..... 10 mg

(As Preservatives)

In a cream base ..... q.s.

Dosage Form and Strength

Topical Cream, 1% w/w

Clinical Particulars

Therapeutic Indications

8X Cream is indicated for the topical treatment of the following dermal infections: tinea pedis, tinea cruris, and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, and *Microsporum canis*; candidiasis (moniliasis) due to *Candida albicans*; and tinea (pityriasis) versicolor due to *Malassezia furfur*.

Posology and Method of Administration

Gently massage **8X Cream** into the affected and surrounding skin areas twice daily, in the morning and evening. Clinical improvement with relief of pruritus and other symptoms usually occurs within the first week of treatment. If a patient shows no clinical improvement after four weeks of treatment with **8X Cream**, the diagnosis should be redetermined. Patients with tinea versicolor usually exhibit clinical and mycological clearing after two weeks of treatment.

Contraindications

8X Cream is contraindicated in individuals who have shown hypersensitivity to any of its components.

Special Warnings and Precautions for Use

8X Cream is not for ophthalmic use.

Keep out of reach of children.

Precautions

If a reaction suggesting sensitivity or chemical irritation should occur with the use of **8X Cream**, treatment should be discontinued and appropriate therapy instituted.

Information for Patients

The patient should be told to:

1. Use the medication for the full treatment time even though symptoms may have improved and notify the physician if there is no improvement after four weeks.
2. Inform the physician if the area of application shows signs of increased irritation (redness, itching, burning, blistering, swelling, or oozing) indicative of possible sensitization.
3. Avoid the use of occlusive wrappings or dressings.

Drug Interactions

No information.

Use in Special Populations

Pregnant Women

Teratogenic Effects: Pregnancy Category B

There are no adequate or well-controlled studies in pregnant women. Therefore, **8X Cream** should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactating Women

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when **8X Cream** is administered to a nursing woman.

Pediatric Patients

Safety and effectiveness in pediatric patients below the age of 10 years have not been established.

Effects on Ability to Drive and Use Machines

No information.

Undesirable Effects

In all controlled clinical studies with 514 patients using Ciclopirox Cream and in 296 patients using the vehicle cream, the incidence of adverse reactions was low. This included pruritus at the site of application in one patient and worsening of the clinical signs and symptoms in another patient using ciclopirox cream and burning in one patient and worsening of the clinical signs and symptoms in another patient using the vehicle cream.

If you experience any side-effects, talk to your doctor or pharmacist or write to drugsafety@cipla.com. You can also report side effects directly via the national pharmacovigilance program of India by calling on 1800 180 3024 or you can report to Cipla Ltd on 18002677779.

By reporting side-effects, you can help provide more information on the safety of this product.

Overdose

No information.

Pharmacological Properties

Ciclopirox olamine is administered topically and is distributed to the stratum corneum, epidermis, hair follicles, sebaceous glands, and dermis. Topical ciclopirox also penetrates into fingernails and toenails.

Mechanism of Action

Ciclopirox is a hydroxypyridone antifungal agent that acts by chelation of 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.

Pharmacokinetic Properties

Pharmacokinetic studies in men with tagged ciclopirox solution in polyethylene glycol 400 showed an average of 1.3% absorption of the dose when it was applied topically to 750 cm^2 on the back followed by occlusion for 6 hours. The biological half-life was 1.7 hours and excretion occurred via the kidney. Two days after application only 0.01% of the dose applied could be found in the urine. Fecal excretion was negligible. Penetration studies in human cadaverous skin from the back, with Ciclopirox Cream with tagged ciclopirox showed the presence of 0.8 to 1.6% of the dose in the stratum corneum 1.5 to 6 hours after application. The levels in the dermis were still 10 to 15 times above the minimum inhibitory concentrations.

Autoradiographic studies with human cadaverous skin showed that ciclopirox penetrates into the hair and through the epidermis and hair follicles into the sebaceous glands and dermis, while a portion of the drug remains in the stratum corneum. Draize Human Sensitization Assay, 21-Day Cumulative Irritancy study, Phototoxicity study, and PhotoDraize study conducted in a total of 142 healthy male subjects showed no contact sensitization of the delayed hypersensitivity type, no irritation, no phototoxicity, and no photo-contact sensitization due to Ciclipirox Cream.

Nonclinical Properties

Carcinogenesis, Mutagenesis, Impairment of Fertility

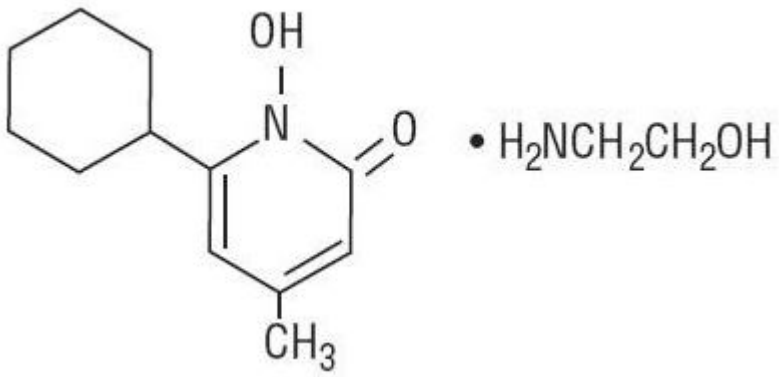
A 104-week dermal carcinogenicity study in mice was conducted with ciclopirox cream applied at doses up to 1.93% (100 mg/kg/day or 300 mg/m^2 /day). No increase in drug related neoplasms was noted when compared to control. The following *in vitro* genotoxicity tests have been conducted with ciclopirox: evaluation of gene mutation in the Ames Salmonella and *E. coli* assays (negative); chromosome aberration assays in V79 Chinese hamster lung fibroblast cells, with and without metabolic activation (positive); chromosome aberration assays in V79 Chinese hamster lung fibroblast cells in the presence of supplemental Fe3+, with and without metabolic activation (negative); gene mutation assays in the HGPRT-test with V79 Chinese hamster lung fibroblast cells (negative); and a primary DNA damage assay (i.e., unscheduled DNA synthesis assay in A549 human cells) (negative). An *in vitro* cell transformation assay in BALB/c 3T3 cells was negative for cell transformation. In an *in vivo* Chinese hamster bone marrow cytogenetic assay, ciclopirox was negative for chromosome aberrations at a dosage of 5000 mg/kg body weight. A combined oral fertility and embryofetal developmental study was conducted in rats with ciclopirox olamine. No

effect on fertility or reproductive performance was noted at the highest dose tested of 3.85 mg/kg/day ciclopirox (approximately 1.2 times the maximum recommended human dose based on body surface area comparisons).

Description

Ciclopirox Cream contains a synthetic, broad-spectrum, antifungal agent ciclopirox (as ciclopirox olamine). The chemical name is 6-cyclohexyl-1-hydroxy-4-methyl-2(1*H*)-pyridone, 2-aminoethanol salt.

The CAS Registry Number is 41621-49-2. The chemical structure is:



Chemical formula: $C_{14}H_{24}N_2O_3$

Molecular weight: 268.357 g/mol

ATC code: D01AE14

Pharmacotherapeutic group: Antifungal

Pharmaceutical Particulars

Incompatibilities

Not applicable

Shelf Life

Please see manufacturing date and expiry date printed on pack. Do not use the product after the expiry date which is stated on the packaging. The expiry date refers to the last day of that month.

Packaging Information

8X Cream.....Available in tube of 30g

Storage and Handling Instructions

Store at a temperature not exceeding 30°C. Keep all medicine out of reach of children.

Patient Counselling Information

What is 8X Cream?

- **8X Cream** is a prescription medicine used to treat fungal infections of the skin.

How should I use 8X Cream?

- Use **8X Cream** exactly as your healthcare provider tells you to use it. Your healthcare provider will tell you how much, where and when to apply **8X Cream**.

Do not use 8X Cream if you:

- are allergic to ciclopirox, or any of the ingredients in **8X Cream**

What is the most important information I should know about 8X Cream?

- Use the medication for the full treatment time even though symptoms may have improved and notify the physician if there is no improvement after four weeks.
- Inform the physician if the area of application shows signs of increased irritation (redness, itching, burning, blistering, swelling, or oozing) indicative of possible sensitization.
- Avoid the use of occlusive wrappings or dressings.

What are the possible side effects of 8X Cream?

- Itching at the site of application, burning, worsening of clinical signs and symptoms are possible side effects of **8X Cream**.

> If you experience any side-effects, talk to your doctor or pharmacist or write to drugsafety@cipla.com. You can also report side effects directly via the national pharmacovigilance program of India by calling on 1800 180 3024 or you can report to Cipla Ltd on 18002677779. By reporting side-effects, you can help provide more information on the safety of this product.

Details of Manufacturer

BDR Pharmaceuticals International Pvt. Ltd.

At: Plot No.16, Pharmacity, Selaqui,

Dehradun, Uttarakhand- 248 011

Details of Permission or License Number with Date

44/UA/LL/2009

Date of Revision

16/12/2019