*For the use only of Registered Medical Practitioners or a Hospital or a Laboratory*

**STIEPROX® LIQUID**

**Ciclopirox Olamine Liquid**

## QUALITATIVE AND QUANTITATIVE COMPOSITION

Ciclopirox olamine USP 1.5% w/w.

Ciclopirox olamine is a clear, yellow to light orange coloured, viscous liquid.

## PHARMACEUTICAL FORM

Shampoo.

## CLINICAL PARTICULARS

### Therapeutic Indications

*STIEPROX LIQUID* is indicated for the treatment of dandruff and seborrhoeic dermatitis of the scalp.

### Posology and Method of Administration

For topical application to the scalp only and adjacent areas.

For external use only.

***Adults and adolescents aged over 12 years***

*STIEPROX LIQUID* should be used two to three times a week. The hair should be wetted and sufficient shampoo applied to produce an abundant lather. The scalp and adjacent areas should be vigorously massaged with the fingertips. The hair should then be thoroughly rinsed and the procedure repeated for a second application. The shampoo should remain in contact with the scalp for a total contact time of 3-5 minutes over the two applications.

The recommended treatment period is 4 weeks.

A mild shampoo may be used in between applications of *STIEPROX LIQUID*.

***Children***

The safety and efficacy of ciclopirox olamine have not been established in children less than 12 years of age.

***Elderly***

No dose adjustment is required in the elderly.

***Renal impairment***

No dosage adjustment is required.

As there is limited percutaneous absorption of ciclopirox olamine following topical application, renal impairment is not expected to result in systemic exposure of clinical significance.

***Hepatic impairment***

No dosage adjustment is required.

As there is limited percutaneous absorption of ciclopirox olamine following topical application, hepatic impairment is not expected to result in systemic exposure of clinical significance.

**Contraindications**

No contraindications identified.

**Special Warnings and Special Precautions for Use**

*STIEPROX LIQUID* should be used with caution in patients with a known sensitivity or allergy to any ingredients.

Ciclopirox olamine may cause eye irritation. In case of accidental contact with the eyes, rinse with water.

Ciclopirox olamine may cause skin irritation. If irritation occurs and persists, treatment should be discontinued.

In rare instances, mainly in patients with chemically damaged (for example, due to hair dye), grey or white hair, a discolouration of the hair has been observed.

**Interaction with Other Medicaments and Other Forms of Interaction**

No data on drug interactions are available. Considering the low level of systemic absorption, drug interactions are unlikely to occur.

**Pregnancy and Lactation**

***Fertility***

Studies in animals given oral or subcutaneous ciclopirox olamine, did not reveal any impairment of fertility.

***Pregnancy***

The safety of ciclopirox olamine during human pregnancy has not been established. Studies in animals given oral or subcutaneous ciclopirox olamine did not reveal any developmental toxicity (*see Pre-clinical Safety Data*).

No effects during pregnancy are anticipated since systemic exposure is low.

***Lactation***

It is not known if ciclopirox olamine is excreted in human milk. Risk to the infant is likely to be low since systemic exposure is low.

Patients should be advised to ensure that any residual product is fully washed off the breast prior to breast-feeding.

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

Ciclopirox olamine is not known to exert an effect on the central nervous system following topical application. No effects are anticipated based on the adverse reaction profile.

**Undesirable Effects**

***Clinical trial data***

The following convention has been used for the classification of adverse reactions:
Very common ≥1/10
Common ≥1/100 to <1/10
Uncommon ≥1/1000 to <1/100
Rare ≥1/10000 to <1/1000
Very rare <1/10000

*Skin and subcutaneous tissue disorders*

| | |
|---|---|
| Common: | Application site irritation including, pruritus, burning sensation erythema* and application site rash* |

***Post-marketing data***

*Immune system disorders*

| | |
|---|---|
| Rare: | Application site hypersensitivity |

*Skin and subcutaneous tissue disorders*

| | |
|---|---|
| Rare: | Skin exfoliation*<br>Eczema<br>Alopecia*<br>Hair colour changes<br>Hair texture changes* |

*Since these effects are also symptoms of the underlying disease, it is expected that these adverse reactions would manifest as worsening of symptoms.

**Overdose**

***Symptoms and signs***

There is currently limited experience of accidental oral ingestion with ciclopirox olamine.

***Treatment of overdose***

Management should be as clinically indicated or as recommended by the national poisons centre, where available. There is no specific treatment for accidental oral ingestion of ciclopirox olamine. If accidental oral ingestion occurs, the patient should be treated supportively with appropriate monitoring as necessary.

**PHARMACOLOGICAL PROPERTIES**

**Pharmacodynamic Properties**

Pharmacotherapeutic group: Antifungals for topical dermatological use; ATC Code: D01AE14.

***Mechanism of action***

Ciclopirox olamine is a hydroxypyridone antifungal agent which is active *in vitro* inhibiting the growth of various fungal species including the yeast *Malassezia furfur* (formerly known as *Pityrosporum ovale* or *Pityrosporum orbiculare*). The latter has been implicated as a causative organism in dandruff and seborrhoeic dermatitis. Ciclopirox olamine also exhibits some anti-inflammatory activity.

***Pharmacodynamic effects***

Ciclopirox olamine 1.5% shampoo shows *in vivo* antifungal activity against *Malassezia* spp. A clinical study has shown that ciclopirox olamine 1.5% shampoo significantly reduced the count of *Malassezia furfur spp.* in samples obtained from the scalp of subjects with dandruff and/or seborrhoeic dermatitis.

Two active-comparator trials (S177-GB-01 and S177-GB-03) which included a total of 193 adults with either mild dandruff or moderate to severe dandruff or seborrhoeic dermatitis of the scalp showed that ciclopirox olamine 1.5% shampoo applied two times a week significantly reduced dandruff and scalp itch and improved the area×severity score and the global evaluation of clinical change from baseline, and was superior to placebo (S177-GB-03).

The efficacy of ciclopirox olamine 1.5 % shampoo applied three times a week was demonstrated in three randomized, double-blind, placebo-controlled trials in subjects aged 12 to 70 years with mild, moderate or severe dandruff or seborrhoeic dermatitis of the scalp. In a first study (S192-GB-04) with 258 subjects, ciclopirox olamine 1.5 % was compared with ciclopirox olamine 1.5 % + 3% salicylic acid, 3% salicylic acid only and placebo. The greatest improvement of dandruff occurred in the ciclopirox olamine 1.5% and the 1.5% ciclopirox olamine/3% salicylic acid groups. Ciclopirox olamine 1.5% and the 1.5% ciclopirox olamine/3% salicylic were also equally effective in seborrhoeic dermatitis. A significant reduction of the global clinical score for seborrhoeic dermatitis was observed in comparison with the placebo and salicylic acid groups. A second study (S177-GB-08) in 66 subjects confirmed the better efficacy (area×severity, clinical change compared to baseline, and subject's self assessment) of ciclopirox olamine 1.5% versus placebo. In a third trial (S177-FR-09) with 350 subjects ciclopirox olamine 1.5% shampoo was superior to placebo in reducing the area of scalp seborrhoeic dermatitis, the global change in comparison with baseline, and the patients' rating of itch, scaling and overall improvement.

**Pharmacokinetic Properties**

***Absorption***

The potential for clinically significant systemic absorption of ciclopirox olamine from a wash-off shampoo containing 1.5% ciclopirox olamine is expected to be low.

***Distribution***

Following oral administration of ciclopirox olamine to humans, affinity of ciclopirox olamine to serum proteins was found to be 96 ± 2% in the concentration range of 0.01 to 11.0 µg/mL.

***Metabolism***

The metabolic patterns after oral and dermal application are similar. Glucuronidation of ciclopirox olamine appears to be the major form of its metabolism.

***Elimination***

Following oral administration of ciclopirox olamine to humans, 96% of the administered dose is excreted within 12 hours. Ciclopirox olamine is excreted in urine with approximately 80% of an oral dose excreted as the glucuronide metabolite.

***Special patient populations***

*Children under 12 years old*

No data.

*Elderly*

See *section on Posology and Method of Administration.*

*Renal impairment*

See *section on Posology and Method of Administration.*

*Hepatic impairment*

See *section on Posology and Method of Administration.*

**Preclinical Safety Data**

***Carcinogenicity***

A dermal carcinogenic study in mice at concentrations of 1% and 5% ciclopirox olamine formulated in polyethylene glycol 400 applied to the intact skin, twice a week, for one year, followed by a six-month non-treatment period was conducted. No tumours were observed in any of the mice at the site of application. Overall incidence of neoplasms was similar among the treated and control groups. In addition, there is no evidence that ciclopirox olamine is carcinogenic following oral or subcutaneous administration to a number of animal species.

***Mutagenicity***

Ciclopirox olamine did not cause gene mutation or chromosomal damage in several bacterial mutagen assays or in two mammalian assays. In a battery of *in vitro* genotoxicity assays with ciclopirox free acid, one assay was weakly positive. The weight of evidence provided by the *in vitro* and *in vivo* assessments suggest that ciclopirox does not present a genotoxic hazard to humans.

***Reproductive Toxicology***

Reproductive studies in mice, rats, rabbits and monkeys, at doses of ciclopirox olamine 10 times that of a topical human dose, have revealed no significant evidence of impaired fertility or harm to the foetus. There is evidence that ciclopirox olamine crosses the placental barrier in animals.

## PHARMACEUTICAL PARTICULARS

### List of Excipients

Sodium lauryl ether sulphate 70%, Cocamidopropyl betaine, Disodium hydrogen phosphate dodecahydrate, Citric acid Anhydrous, Coconut diethanolamide, Hexylene glycol, Oleyl alcohol, Polysorbate 80, Polyquaternium-10, Fragrance Timotei AF17050, Citric Acid Anhydrous, Sodium Hydroxide, Purified water.

### Incompatibilities

No incompatibilities have been identified.

### Shelf Life

36 months.

The expiry date is indicated on the label and packaging.

### Special Precautions for Storage

Store in a cool place.

Do not freeze.

Keep out of reach of children.

### Nature and Specification of Container

HDPE bottle with cap in a carton.

**Instructions for Use / Handling**

For topical application on scalp only. For external use only.

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