Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Tioconazole 283mg/ml medicated nail lacquer

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml of product contains 283 mg of tioconazole.
For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Medicated nail lacquer
Tioconazole is a clear pale yellow solution for topical application.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Tioconazole is indicated for the topical treatment of nail infections due to susceptible fungi (dermatophytes and yeasts) and bacteria.

4.2 Posology and method of administration

Route of administration: Cutaneous use.

Posology

Adults: The solution should be applied to the affected nails and immediately surrounding skin every twelve hours using the applicator brush supplied.

The duration of treatment depends on the severity of the infection, the infectious microorganism and the location of the area to be treated.
Usually, the duration of treatment is up to six months, but may be extended to twelve months.

Use in the elderly: No special precautions are required. Use the adult dose.

Paediatric population: No special precautions are required. Use the adult dose.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Tioconazole is contra-indicated in individuals who have been shown to be hypersensitive to imidazole antifungal agents.

Use is contra-indicated during pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

Tioconazole is not for ophthalmic use.

4.5 Interaction with other medicinal products and other forms of interaction

None known.

4.6 Fertility, pregnancy and lactation

Pregnancy
In animal studies tioconazole was not teratogenic. At high doses it increased the incidence of renal abnormalities in rat embryos, but this effect was minor and transient and was not evident in weaned animals.

There is insufficient evidence as to the drug's safety in human pregnancy although absorption after topical administration is negligible. Because of the extensive duration of treatment required for nail infections, the use of Tioconazole is contra-indicated throughout pregnancy.

In case pregnancy is diagnosed for the person receiving the medicine, its use should be immediately discontinued.

Breast-feeding
It is unknown whether this drug is excreted in human milk. Because many drugs are excreted in human milk, nursing should be temporarily discontinued while Tioconazole is administered.

4.7 Effects on ability to drive and use machines

Tioconazole has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Tioconazole is well tolerated upon local application. The most common effect is local irritation (including local allergic reactions), usually seen during the first week of treatment and are transient and mild. Systemic allergic reactions are uncommon.

However, if a sensitivity reaction develops with the use of Tioconazole, treatment should be discontinued and appropriate therapy instituted.

The undesirable effects listed below were reported with frequencies corresponding to Common (≥1/100, ≤1/10), Uncommon (≥1/1000, <1/100), Rare (≥1/10,000 to <1/1,000), or Very rare (<1/10,000), Not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System Organ Class	**Frequency**	**Frequency**
Immune system disorders	Unknown	Allergic reaction
Nervous system disorders	Unknown	Paresthesia
Skin and subcutaneous tissue disorders	Unknown	Bullous eruption, dermatitis contact, dry skin, edema periorbital, nail disorder (including nail discoloration, periungual inflammation and nail pain), pruritis,skin irritation, skin exfoliation, urticaria
	Uncommon	Dermatitis, rash,
General disorders and administration site conditions	Common	Oedema peripheral
	Unknown	Pain

Anaphylactoid reactions have been reported in patients treated with other formulations than the dermatological preparation.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

No cases of overdosage with Tioconazole have been reported. Overdosage by topical application of tioconazole is unlikely because of negligible systemic absorption. In cases of overdose, treatment should be discontinued and symptomatic therapy instituted. In the event of excessive oral ingestion, gastrointestinal symptoms may occur. Appropriate means of gastric lavage should be considered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Imidazole and triazole derivatives; ATC-code: D01AC07.

Tioconazole is an imidazole derivative. It's chemical name is (RS)-1-[2-[(2-Chloro-3-thienyl)methoxy]-2-(2,4-dichlorophenyl)ethyl]-1H-imidazole and its molecular weight is 387.7. Tioconazole is a white or almost white, crystalline powder which is slightly soluble in water but very soluble in methanol, ethanol and chloroform.

Tioconazole is a broad spectrum antifungal agent that also has an antibacterial effect on a number of Gram-positive cocci (e.g. Stapphylococcus, Streptococcus species). It is active against commonly occurring dermatophyte and yeast-like fungal species. It is fungicidal in murine models vs. Candida spp., T. rubrum and T. mentacrophytes. In vitro it is fungicidal to pathenogenic dermatophytes, yeasts and other fungi. All dermatophytes and Candida spp. were inhibited by 6.25 or 12.5 mg/l respectively. It is also inhibitory vs. Staph. spp. and Strep. spp. at 100 mg/l or less.

5.2 Pharmacokinetic properties

Absorption
Absorption is rapid and extensive on oral administration to rats, monkeys and man, the major metabolite being a glucuronide conjugate of tioconazole. Tissue uptake in rat and monkey was highest in liver, kidney and intestinal tract with excretion in all species mainly in faeces.

Rat studies using oral, dermal and vaginal administration of C^{14} labelled tioconazole confirm significantly lower absorption via the topical route.

In man, oral formulations of tioconazole (500mg) gave plasma concentrations of 1300ng/ml. Topical administration of dermal cream 1% (20mg/day) for 28 days, or vaginal cream 2% (100mg/day) for 30 days gave negligible mean peak plasma levels, i.e. 10.1 and 11.5ng/ml respectively.

After single dose administration of tioconazole vaginal ointment 6.5% w/w (tioconazole 300mg) the mean peak plasma concentration was 18ng/ml in humans, achieved approximately 8 hours post dose.

5.3 Preclinical safety data

Tioconazole cream applied on rat and rabbit skin did not result in systemic toxicity in these animals. Mild topical reaction was observed.

Oral doses (200 mg/kg) did not affect behaviour in rats but 25 mg/kg i.v. produced dose-related respiratory distress, gasping, tremors and prostration. Slight but dose-related impairment of performance of mice on the rotating rod occurred from 25 mg/kg. Slight anti-cholinergic and anti-histamine (H1) activity was recorded in vitro but no effect on mice pupil size in vivo. Oral tioconazole prolonged alcohol and pentobarbital sleeping time at 150 and 37.5 mg/kg respectively.

In the anaesthetised cat i.v. tioconazole 2.5 - 10 mg/kg produced brief falls in blood pressure and increased heart rate, haematuria, tremors and twitches.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Undecylenic acid
Ethyl acetate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months
After first opening: 6 months

6.4 Special precautions for storage

Inflammable. Avoid heat and flame. Do not refrigerate. Keep the bottle tightly closed.

6.5 Nature and contents of container

Tioconazole is contained in an amber type III soda-lime silica glass bottle with a HDPE/LDPE screw cap fitted with a CE nylon brush applicator containing 12 ml.

6.6 Special precautions for disposal

No special requirements for disposal.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Creo Pharma Limited
Felsted Business Centre
Felsted, Dunmow
Essex CM6 3LY
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA1884/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 3rd September 2015

10 DATE OF REVISION OF THE TEXT

November 2016