

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Onytec 80mg/g medicated nail lacquer

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One gram of medicated nail lacquer contains 80 mg of ciclopirox.

Excipient with known effect:

One gram of solution of medicated nail lacquer contains 10 mg cetostearyl alcohol and 730 mg ethanol.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Medicated nail lacquer. Clear, colourless to slightly yellowish solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Mild to moderate fungal infections of the nails caused by dermatophytes, yeasts and moulds, without nail matrix/lunula involvement.

Onytec 80 mg/g medicated nail lacquer is indicated in adults.

4.2 Posology and method of administration

Posology

Paediatric population

The safety and efficacy of Onytec in children and adolescents below 18 years of age have not yet been established. No data are available.

Method of administration:

Cutaneous use

For topical use on fingernails, toenails and immediately adjacent skin (perionychium, hyponychium).

Unless otherwise directed, Onytec nail lacquer is applied in a thin layer once a day on the affected nail/s after careful 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. Onytec 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.

Onytec 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, Onytec 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 healthy nail has grown again. Normally, treatment duration of fingernails is for about 6 months while for toenails it is about 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 active substance.

Being a topical treatment, no different posology is necessary for special population groups.

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

4.3 Contraindications

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

Children and adolescents below 18 years of age due to insufficient experience in this age group.

4.4 Special warnings and precautions for use

Mild to moderate onychomycosis is defined as fungal infection affecting up to 75% of the nail surface, involvement of up to 5 nails, without involvement of nail matrix/lunula.

In case of severe onychomycosis and of predisposing factors, such as diabetes and immune disorders, the addition of a systemic therapy should be considered.

Duration of disease, extent of infection (involvement of the nail plate) and nail thickness (>2mm may indicate matrix involvement, and keratinaceous debris) may influence results of therapy.

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

Patients with a history of diabetes, immune disorders, peripheral vascular disease, injury, painful or seriously damaged nails, skin conditions such as psoriasis or any other chronic skin condition, oedema, breathing disorders (Yellow nail syndrome) should seek medical advice prior to commencing treatment.

The risk of removal of the unattached, infected nail, by the health care professional or during cleaning by the patient should be carefully considered for patients with a history of insulin dependent diabetes mellitus or diabetic neuropathy.

Contact with the eyes and mucous should be avoided.

The medicated nail lacquer is for external use only.

Nail polish or other nail cosmetic products should not be used on the treated nails.

Onytec contains cetostearyl alcohol which may cause local skin reactions (e.g. contact dermatitis).

The bottle should be capped when not in use.

This medicine contains 730 mg alcohol (ethanol) in each g of solution. It may cause a burning sensation on damaged skin.

This product is flammable. Keep away from heat and open flame.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interaction studies have been performed. However, after application as recommended, the systemic bioavailability of ciclopirox is below 2%, an amount which is considered as negligible, thus no interactions are foreseen at systemic level.

4.6 Fertility, pregnancy and lactation

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 (see section 5.3). As the systemic exposure to ciclopirox is negligible, the use of Onytec nail lacquer may be considered during pregnancy, if necessary.

Breast feeding:

It is unknown whether ciclopirox or its metabolites are excreted in human milk but at therapeutic doses of Onytec nail lacquer no effects to the newborn/infants are anticipated.

Fertility:

No fertility studies have been performed in humans. A reduced fertility index in the rat was observed following oral administration (see section 5.3). This animal data are of negligible clinical relevance due to the low systemic exposure to ciclopirox following therapeutic treatment with Onytec

4.7 Effects on ability to drive and use machines

Onytec has no influence on the ability to drive and use machines.

4.8 Undesirable effects

For the frequency of occurrence of undesirable 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).

General disorders and administration site conditions:

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

Not known: rash, eczema, allergic dermatitis, also beyond the application site.

(Transient) nail discolouration (this reaction can also be attributed to the onychomycosis itself).

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 HPRC Pharmacovigilance, Website: www.hpra.ie.

4.9 Overdose

Onytec is for topical use. No overdose has been reported with the use of this product. In the event of accidental oral ingestion, an appropriate method of gastric emptying may be used.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifungals for dermatological use; Other antifungals for topical use; ATC code: D01AE14

Onytec nail lacquer is an original, patented formulation of ciclopirox based on hydroxypropyl chitosan for delivery of the active ingredient to nails.

Onytec 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 $\mu\text{g/ml}$.

Table of susceptibility (strains relevant to illness)

| | |
|---------------|--|
| Dermatophytes | <i>Trichophyton rubrum</i> <i>Trichophyton mentagrophytes</i> <i>Trichophyton spp</i> <i>Microsporum canis</i> <i>Epidermophyton floccosum</i> |
| Yeasts | <i>Candida albicans</i> <i>Candida parapsilosis</i> |
| Moulds | <i>Scopulariopsis brevicaulis</i> <i>Aspergillus spp</i> <i>Fusarium solani</i> |

Clinical efficacy and safety

Onytec nail lacquer has been investigated in a long term clinical study in 467 patients with onychomycosis, compared to placebo 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. All the efficacy assessments were done on a target great toenail.

Table of the results at the end of follow-up (week 60)

| End-point | Onytec nail lacquer | Placebo | EU Reference product |
|----------------------------|---------------------|---------|----------------------|
| complete "cure"* | 12.7% | 1.3% | 5.8% |
| "responders"# | 28.7% | 14.7% | 17.3% |
| "improvement" [§] | 46.5% | 34.7% | 39.7% |

| | | | |
|--|-------|-------|-------|
| | | | |
| Decrease of diseased nail [‡] | 36.3% | 16.2% | 21.8% |

* conversion to negative of both KOH microscopy and fungal culture, and 100% healthy appearing target great toenail

[#] conversion to negative of both KOH microscopy and fungal culture, and decrease of diseased nail area to $\leq 10\%$ (including zero) of total as assessed by the blinded Evaluator

[§] patients with at least 20% decrease of diseased nail area, as assessed by the blinded Evaluator, at the end of treatment versus baseline and conversion to negative KOH and culture

[‡] Decrease of diseased nail area to $\leq 10\%$ of total as assessed by the blinded Evaluator

Onytec nail lacquer showed a better efficacy compared to placebo and to reference ciclopirox. A better effect was evidenced on the primary endpoint "cure" rate and on the key secondary endpoint "responder" rate, being 119% higher than the reference for cure rate (statistically significant, $p < 0.05$) and 66% higher for responder rate (statistically significant, $p < 0.05$). In the clinical study no drug-related systemic adverse event was recorded.

Tolerability at the application site was continuously monitored throughout the treatment period. Signs and symptoms recorded were 2.8% and 7.8%, respectively, in the Onytec group; 8.6% signs and 16% symptoms were recorded in the reference group and 7.2% signs and 12.4% symptoms were recorded in placebo group. The most frequent sign recorded was erythema (2.8% in the Onytec group and 8.6% in the reference group). The most frequent symptom was burning (2.8% in the Onytec group and 10.7% in the reference group).

A further second randomized long-term clinical study was conducted on 137 onychomycotic patients. It was a randomized, two arms, 48-week study, comparing Onytec nail lacquer daily applied with a marketed formulation of 5% amorolfine nail lacquer on acrylate basis given twice a week.

All the efficacy variables (study endpoints) were evaluated on a target great toenail.

The study has attained its primary objective, i.e. Onytec nail lacquer, after 12 weeks of treatment, was not inferior to amorolfine 5% in the culture conversion to negative: conversion to negative of culture 78.3% for Onytec nail lacquer vs. 64.7% amorolfine 5% nail lacquer, meaning a difference of 13.6% between the treatments (95% confidence interval [-1.4; 28.5]).

At weeks 48 the percentages of patients with complete cure rate, treatment success/responder rate and mycological cure in the Onytec group, were consistently higher than in the reference group:

Table: results at the end of treatment (week 48)

| End-points | Onytec nail lacquer | 5% amorolfine nail lacquer | Difference (%) | 95 % confidence interval for the difference |
|--------------------------------|---------------------|----------------------------|----------------|---|
| Complete cure rate* | 35.0% | 11.7% | 23.3** | 8.8; 37.9 |
| Treatment success [#] | 58.3% | 26.7% | 31.7** | 14.9; 48.4 |
| Mycological cure [§] | 100% | 81.7% | 18.3** | 8.5; 28.1 |

* conversion to negative of both KOH microscopy and fungal culture, and 100% healthy target great toenail, as assessed by the blinded evaluator

[#] conversion to negative of both KOH microscopy and fungal culture, and decrease of diseased nail area to $\leq 10\%$ of total as assessed by the blinded evaluator

[§] conversion to negative of both KOH microscopy and fungal culture

** $p < 0.001$

In this clinical study, too, no drug-related systemic adverse event was recorded.

Onytec nail lacquer was well tolerated in terms of local and general adverse reactions. Signs of irritation were only found in 2.06% of the Onytec nail lacquer group at the skin surrounding the treated nails.

5.2 Pharmacokinetic properties

Onytec nail lacquer has demonstrated good penetration properties through keratin. 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.

A very small amount of ciclopirox is absorbed systemically ($< 2\%$ of the applied dose and the blood levels in a long term study were 0.904 ng/ml (n=163) and 1.144 ng/ml (n=149) after 6 and 12 months of treatment, respectively. This shows that the drug exerts its activity particularly at the local level and the risk of possible interference with the normal body functions is negligible.

5.3 Preclinical safety data

Preclinical data up to a daily oral dose of 10 mg ciclopirox/kg revealed no special hazard for humans based on conventional studies of repeated dose toxicity, genotoxicity and carcinogenic potential. In reproduction studies in rats and rabbits no embryo-/fetotoxicity or teratogenicity was found. At the oral dose of 5 mg/kg, a reduced fertility index in the rat was observed. There was no evidence for peri- or postnatal toxicity, however possible long term effects on progeny have not been investigated. Onytec 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethyl acetate
Ethanol (96%)
Cetostearyl alcohol
Hydroxypropyl-chitosan
Purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

After first opening the bottle: 6 months

6.4 Special precautions for storage

Keep the bottle in the outer carton, in order to protect from light. Do not refrigerate or freeze.

After first opening the container: Keep the bottle tightly closed to avoid evaporation of the content.

For storage conditions after first opening of the medicinal product, see section 6.3

This product is flammable. Keep away from heat and open flame.

At temperature 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.

6.5 Nature and contents of container

Clear glass bottles with polypropylene screw caps which are fitted with a brush.

Pack sizes: 3.3 ml, 6.6 ml.

Not all pack sizes may be marketed

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Polichem S.A.
50, Val Fleuri
L-1526 Luxembourg
Luxembourg

8 MARKETING AUTHORISATION NUMBER

PA1005/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28th September 2012
Date of latest renewal: 14th March 2017

10 DATE OF REVISION OF THE TEXT

November 2022