

**Public Assessment Report**

**Decentralised Procedure**

**CICLOPIROX TERIX**

**8% nail lacquer**

**Applicant:**

**Terix Labs. Ltd**

**Italian Marketing Authorisation Number: 043229**

**European procedure number: IT/H/0385/001/DC**

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**Module 1**

**Information about the Initial Procedure**

|  |  |
| --- | --- |
| **Product Name** | **IT/H/0385/001/DC:**  Ciclopirox Terix |
| **Type of application** | Article 10.3 of Directive 2001/83/EC as amended |
| **Active Substance** | Ciclopirox |
| **Form** | Medicated nail lacquer |
| **Strength** | 8% |
| **MA Holder** | Terix Labs Ltd  6 Agias Elenis Str, Agias Elenis Building, office 43  1060 Nicosisa  Cyprus |
| **Reference Member State (RMS)** | IT |
| **Concerned Memember States (CMS)** | PL |
| **Procedure number** | IT/H/0385/001/DC |
| **Timetable** | End of procedure: Day 210 – 02/02/2015 |

Module 2

Summary of Product Characteristics

In accordance with Directive 2010/84/EU, the Italian version of the Summaries of Product Characteristics (SmPCs) for products granted Marketing Authorisations at a national level would be available on the AIFA website once the marketing Authorization will be granted.

Here is reported the English version of the SMPC approved at European level.

1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

1. **NAME OF THE MEDICINAL PRODUCT**

Ciclopirox Terix 8% w/w medicated nail lacquer

1. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

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

For the full list of excipients, see section 6.1.

1. **PHARMACEUTICAL FORM**

Medicated nail lacquer.

Clear, colourless to slightly yellow solution

1. **CLINICAL PARTICULARS**
2. **Therapeutic indications**

Treatment of fungal infections of the nails (Onychomycoses).

1. **Posology and method of administration**

Posology

Unless otherwise prescribed, Ciclopirox Terix is applied once daily to the affected nail in a thin layer.

The duration of the treatment depends on the severity of the infection, but should not exceed a treatment period of 6 months.

Paediatric population

The safety and efficacy of Ciclopirox Terix 8% w/w medicated nail lacquer in children have not yet been established.

Method of administration

Before the first application of Ciclopirox Terix, as much as possible of the affected part of the nail should be removed, for example with a pair of scissors and as much as possible of the hyperceratosic material should be removed with a nail file.

Throughout the application period the entire layer of lacquer should be removed once a week with a marketed nail polish remover. During this process too, as much hyperkeratotic material as possible should be removed from the nail plate, always with a nail file.

If, between one application and another the layer of lacquer is damaged, it is merely sufficient to reapply Ciclopirox Terix over the parts that have chipped off.

After each use, it is advisable to tightly close the cap of the bottle in order to prevent the drying up of the solution.

Do not allow the solution to come in contact with the neck of the bottle in order to prevent the cap from sticking.

1. **Contraindications**

Hypersensitivity to the active substance or to any of the excipients listed is section 6.1.  
Ciclopirox Terix is generally contraindicated during pregnancy and lactation (see also 4.6).  
Due to the lack of clinical experience, the product should not be used in the pediatric population.

1. **Special warnings and precautions for use**

The use, especially if it is prolonged, of products for topical use may give rise to sensitization phenomena or produce undesirable effects. In these situations the treatment should be discontinued and appropriate therapeutic measures taken.

Contact with the eyes and mucous membranes should be avoided.

Nail polish or other nail cosmetic products should not be used during treatment.

1. **Interaction with other medicinal products and other forms of interaction**

None known.

1. **Fertility, pregnancy and lactation**

Due to the lack of clinical experience, the administration of Ciclopirox Terix is contraidicated during pregnancy and lactation.

1. **Effects on ability to drive and use machines**

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

1. **Undesirable effects**

The frequency of possible side effects listed below is defined as:

Very common: 1/10

Common: 1/100 to <1/10

Uncommon: 1/1000 to <1/100

Rare: 1/10.000 to <1/1000

Very rare: <1/10.000

Not known: Frequency cannot be estimated from the available data.

General disorders and administration site conditions

In rare cases, allergic contact dermatitis may occur as a result of the contact of the product with the skin adjacent to the nail. Very rarely redness and flaking of the skin, can be observed.

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 the national reporting system [to be completed nationally].

**4.9 Overdose**

No casesof overdose have been reported.

1. **PHARMACOLOGICAL PROPERTIES**
2. **Pharmacodynamic properties**

Pharmaceutical group: antimicrobial agents for topical use.

ATC code: D01AE14

[tradename] is a medicine with topical antimycotic action. The active substance is ciclopirox, a hydroxypyridone derivative that has a broad spectrum of action and inhibitory activity against all pathogens species responsible for onychomycoses including: *Trichophytum rubrum, Epidermophytum floccosum, Candida albicans* and *Scopulariopsis brevicaulis*.

1. **Pharmacokinetic properties**

Ciclopirox penetrates the nail plate and reaches the pathogenic fungi within 48 hours of application and in 2-3 weeks of application there is, depending on the nail, a concentration gradient of the active substance.

1. **Preclinical safety data**

The LD50 (mg/kg) of ciclopirox is 238 (per os) and of 1321 (i.p) in mice and 2100-3200 (per os) and 663 (ip) in rats.

1. **PHARMACEUTICAL PARTICULARS**
2. **List of excipients**

Methoxyethene polymer with 2-butenedioic acid monobutyl ester, 1:1, ethyl acetate, isopropyl alcohol.

1. **Incompatibilities**

None known.

1. **Shelf life**

30 months

After first opening of the bottle: 6 months.

**6.4 Special precautions for storage**

This medicinal product does not require any special storage conditions.

1. **Nature and contents of container**

Ciclopirox Terix is presented in Type III amber glass bottles, sealed with a HD-PE screw cap, connected through a shank to an applicator brush. The brush applicator (CE mark) consists of LD-PE with brush hair of nylon secured in shaft with stainless steel.

Pack sizes: 3.3 ml and 6.6 ml.

Not all pack sizes may be marketed.

**6.6 Special precautions for disposal and other handling**

After use, it is advisable to carefully close the cap of the bottle in order to prevent the drying up of the solution.

Do not allow the solution to come in contact with the neck of the bottle in order to prevent the cap from sticking.

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

1. **MARKETING AUTHORISATION HOLDER**

[To be completed nationally]

1. **MARKETING AUTHORISATION NUMBER**

[To be completed nationally]

1. **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

[To be completed nationally]

1. **DATE OF REVISION OF THE TEXT**

[To be completed nationally]

Module 3

Package Leaflets

In accordance with Directive 2010/84/EU, the Italian version of the package leaflet for products granted Marketing Authorisations at a national level would be available on the AIFA website once the marketing Authorization will be granted.

Here is reported the English version of the PIL approved at European level.

1.3.1 Package leaflet: Information for the user

**Package leaflet: Information for the patient**

**Ciclopirox Terix 8% w/w medicated nail lacquer**

**Ciclopirox**

**Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.**

1. Keep this leaflet. You may need to read it again.
2. If you have any further questions, ask your doctor or pharmacist.
3. This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
4. If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

[**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**

Always use this medicine exactly as described in this leaflet or as your doctor, or pharmacist have told you.

1. Keep this leaflet. You may need to read it again.
2. Ask your pharmacist if you need more information or advice.
3. If you get any side effects, talk to your doctor, or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.
4. You must talk to a doctor if you do not feel better or if you feel worse after 6 months.]

[To be completed nationally]

**What is in this leaflet**

1. What Ciclopirox Terix is and what it is used for

2. What you need to know before you use Ciclopirox Terix

3. How to use Ciclopirox Terix

4. Possible side effects

5. How to store Ciclopirox Terix

6. Contents of the pack and other information

**1. What Ciclopirox Terix is and what it is used for**

Ciclopirox Terix 8% w/w is a medicated nail lacquer. It contains the active substance ciclopirox, which belongs to a group of medicines known as antifungals. Ciclopirox penetrates the nail plate and presents a fungicidal effect on all the major causative agents of fungal nail disease.

Ciclopirox Terix 8% w/w is used to treat fungal infections of the nails (Onychomycoses).

**2. What you need to know before you use Ciclopirox Terix**

**Do not use Ciclopirox Terix:**

* if you are allergic to ciclopirox or any of the other ingredients of this medicine (listed in section 6)
* in children due to insufficient experience in this age group up to now
* during pregnancy and lactation

**Warnings and precautions**

Talk to your doctor or pharmacist before using Ciclopirox Terix

The use, especially if it is prolonged, of products for topical use may give rise to sensitization phenomena or produce undesirable effects. In these situations the treatment should be discontinued and appropriate therapeutic measures taken. Contact with the eyes and mucous membranes should be avoided.

Do not use nail polish or other nail cosmetic products during treatment with Ciclopirox Terix.

**Children and adolescents**

Due to inadequate clinical experience, Ciclopirox Terix 8% w/w medicated nail lacquer should not be used in children.

**Other medicines and Ciclopirox Terix**

Tell your doctor or pharmacist if you are taking, or have recently taken any other medicines.

**Ciclopirox Terix** **with food, drink and alcohol**

Not applicable.

**Pregnancy, breast-feeding and fertility**

Ciclopirox Terix is generally contraindicated during pregnancy and lactation.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

**Driving and using machines**

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

**3. How to use Ciclopirox Terix** **8% w/w medicated nail lacquer**

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Unless otherwise prescribed, Ciclopirox Terix medicated nail lacquer is applied once daily to the affected nail in a thin layer.

Before the first application of Ciclopirox Terix, as much as possible of the affected part of the nail should be removed, for example with a pair of scissors and as much as possible of the hyperceratosic material should be removed with a nail file.

Throughout the application period the entire layer of lacquer should be removed once a week with a marketed nail polish remover. During this process too, as much hyperkeratotic material as possible should be removed from the nail plate, always with a nail file.

If, between one application and another the layer of lacquer is damaged, it is merely sufficient to reapply Ciclopirox Terix over the parts that have chipped off.

The duration of the treatment depends on the severity of the infection, but should not exceed a treatment period of 6 months.

After each use, it is advisable to tightly close the cap of the bottle in order to prevent the drying up of the solution.

Do not allow the solution to come in contact with the neck of the bottle in order to prevent the cap from sticking.

**If you use more Ciclopirox Terix** **than you should:**

No casesof overdose have been reported.

**If you forget to use Ciclopirox Terix**:

Do not use a double dose in order to make up for a forgotten one. Continue with treatment as recommended by your doctor or as explained at point 3 of this leaflet (How to use Ciclopirox Terix).

**If you stop using Ciclopirox Terix:**

If you stop treatment with Ciclopirox Terix before your nails are clear or their appearance is significantly improved and healthy nails have grown again, the fungi may not have disappeared. In this case, the condition of your nails can get worse again.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

**4. Possible side effects**

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The frequency of possible side effects listed below is defined as:

Very common: affects more than 1 user in 10.

Common: affects 1 to 10 of 100 users.

Uncommon: affects 1 to 10 users in 1,000.

Rare: affects 1 to 10 users in 10,000.

Very rare: affects less than 1 user in 10,000.

Not known: frequency cannot be estimated from the available data.

In rare cases allergic dermatitis has been observed when the skin surrounding the nail has came in contact with Ciclopirox Terix .In very rare cases redness and flaking have been observed.

Following the instructions contained in this leaflet reduces the risk of undesirable effects.

**Reporting of side effects**

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system [to be completed nationally]. By reporting side effects you can help provide more information on the safety of this medicine.

**5. How to store Ciclopirox Terix**

Keep this medicine out of the sight and reach of children.

This medicine does not require any special storage conditions.

After first opening use within 6 months. Keep the bottle tightly closed to avoid evaporation of the content.

Do not use this medicine after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.

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

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

**6. Contents of the pack and other information**

**What Ciclopirox Terix contains**

The active substance is Ciclopirox.

The other ingredients are methoxyethene polymer with 2-butenedioic acid monobutyl ester, 1:1, ethyl acetate, isopropyl alcohol.

**What Ciclopirox Terix** **looks like and contents of the pack:**

Ciclopirox Terix is a clear, colourless to slightly yellow solution presented in amber glass bottles with screw caps which are fitted with a brush.

Pack sizes are 3.3 ml and 6.6 ml.

Not all pack sizes may be marketed

**Marketing Authorisation Holder and Manufacturer**

**Marketing Authorization Holder**

[To be completed nationally]

{Name and address}

<{tel}>

<{fax}>

<{e-mail}>

**Manufacturer**

Doppel Farmaceutici S.R.L.

Via Martiri delle Foibe, 1

29016 Cortemaggiore (PC)

Italy

**This medicinal product is authorised in the Member States of the EEA under the following names:**

Italy: Ciclopirox Terix

Poland: Axopirox

**This leaflet was last revised in {MM/YYYY}.**

[To be completed nationally]

CE brush applicator

A035/3.3 ml pack

A071/6.6 ml pack

Module 4

Labelling

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**CARTON BOX**

**1. NAME OF THE MEDICINAL PRODUCT**

Ciclopirox Terix 8% w/w medicated nail lacquer

Ciclopirox

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each gr of medicated nail lacquer contains 80mg ciclopirox.

**3. LIST OF EXCIPIENTS**

Butyl ester of polyvinyl methylether/maleic anhydride copolymer, ethyl acetate, isopropyl alcohol.

**4. PHARMACEUTICAL FORM AND CONTENTS**

Medicated nail lacquer

3.3 ml

CE brush applicator (A035)

6.6 ml

CE brush applicator (A071)

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Read the package leaflet before use.

Cutaneous use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BESTORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**

**8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

This medicinal product does not require any special storage conditions.

After opening use within 6 months.

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

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

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

<[To be completed nationally]>

{Name and Address}

<{tel}>

<{fax}>

<{e-mail}>

**12. MARKETING AUTHORISATION NUMBER(S)**

<[To be completed nationally]>

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription.

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

<[To be completed nationally]>

|  |
| --- |
| **MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**  **LABEL** |

|  |
| --- |
| **1. NAME OF THE MEDICINAL PRODUCT** |

Ciclopirox Terix 8% w/w medicated nail lacquer

Ciclopirox

Cutaneous use

|  |
| --- |
| **2. METHOD OF ADMINISTRATION** |

|  |
| --- |
| **3. EXPIRY DATE** |

EXP

|  |
| --- |
| **4. BATCH NUMBER** |

Lot

|  |
| --- |
| **5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT** |

3.3 ml

6.6 ml

|  |
| --- |
| **6. OTHER** |

Module 5

Scientific discussion during the initial procedure

1. Introduction

Based on the review of the data on quality, safety and efficacy, the member states involved in the procedure considered that the applications for Ciclopirox Terix 8% medicated nail lacquer (MA No 043229; Procedure No IT/H/0385/001/DC) could be approved. This product is a prescription-only medicine indicated for the treatment of fungal infections of the nails (Onychomycoses).

This application was submitted using the Decentralised Procedure (DCP), with the Italy (IT) as Reference Member State (RMS) and Poland as Concerned Member State (CMS). This application was submitted under Article 10(3) of Directive 2001/83/EC, so called "Hybrid application”, as amended.

The drug product has been developed as the generic equivalent to Batrafen® nail lacquer 8% w/w, marketed by Sanofi-Aventis.

Ciclopirox Terix is a medicated nail laquer containing the active substance ciclopirox (ATC-code: D01AE14), it is indicated for the treatment of fungal infections of the nails (Onychomycoses).

Unless otherwise prescribed, Ciclopirox Terix is applied once daily to the affected nail in a thin layer.

The duration of the treatment depends on the severity of the infection, but should not exceed a treatment period of 6 months.

The Applicant demonstrates the essential similarity between test and reference product and in support of this decentralised procedure it submits a biowaiver.

The RMS has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these product types at all sites responsible for the manufacture and assembly of this product. For manufacturing sites within the Community, the RMS has accepted copies of current

manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

1. About the product

|  |  |
| --- | --- |
| **Proposed name of the medicinal product in the RMS** | Ciclopirox Terix |
| **Name of the drug substances (INN name):** | Ciclopirox |
| **Pharmaco-therapeutic group (ATC Code):** | D01AE14 |
| **Pharmaceutical form(s) and strength(s):** | Medicated nail lacquer |
| **Reference Number(s) for the Decentralised Procedure** | IT/H/0385/001/DC |
| **Reference Member State:** | IT |
| **ConcernedMemberStates:** | PL |
| **Marketing Authorisation Numbers** | AIC No: 043229 |
| **Name and address of the Authorization Holder** | Terix Labs Ltd  6 Agias Elenis Str, Agias Elenis Building, office 43  1060 Nicosisa  Cyprus |

1. Scientific Overview and discussion

III.1 Quality aspects

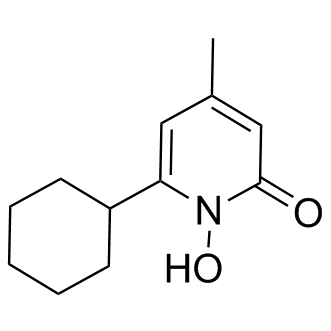
**ACTIVE SUBSTANCE – ciclopirox**

INN name: ciclopirox

|  |
| --- |
| **Chemical name:** 6-cyclohexyl-1-hydroxy-4-methyl-2(1H)-pyridone |
| **Systematic (IUPAC) name**: 6- cyclohexyl-1-hydroxy-4-methylpyridin-2(1H)-one |

**CAS Reg. No.:**  [29342-05-0]

**Structural formula:**



|  |
| --- |
| **Molecular formula:** C12H17NO2 |

**Relative Molecular mass:** 207.27

|  |
| --- |
| **Physical form:** White or yellowish white powder |
| **Solubility:** Slightly soluble in water, freely soluble in ethanol and methylene chloride  **Melting point:** 140°C - 145 °C |

The active substance is described in the relevant monograph of the European Pharmacopeia and a Certificate of Suitability has been issued.

Appropriate stability data have been generated, supporting a suitable retest period when the drug substance is stored in the proposed packaging.

**DRUG PRODUCT**

**Other Ingredients**

Other ingredients are: ethyl acetate, isopropyl alcohol, methoxyethene polymer with 2-butenedioic acid monobutyl ester, 1:1.

All the excipients, comply with the relevant Ph.Eur. monograph, except for the film forming agent methoxyethene polymer with 2-butenedioic acid monobutyl ester, 1:1.

The qualitative formulation was developed and each of the excipients was selected for its intended use based on development studies. They are included in the formulation at suitable levels and for recognized purposes.

All the excipients are free from any risk of TSE.

No genetically modified organisms (GMO) have been used in the preparation of these excipients.

**Pharmaceutical Development**

The establishment of the pharmaceutical equivalence was achieved by comparative studies (batches analysis) between batches of Ciclopirox Terix e Batrafen®.

Suitable pharmaceutical development data have been provided for this application.

**Manufacturing Process**

Satisfactory batch formula has been provided for the manufacture of the medicinal product, along with an appropriate description of the manufacturing process. The manufacturing process has been validatedon three industrial batches.

**Control of Finished Product**

The finished product specifications are satisfactory. Test methods have been described and adequately validated, as appropriate. However, the Applicant has provided a post-approval commitment to submit a variation aimed to introduce the detailed analytical method along with the relevant validation study for the benzene control within 1 month.

Batch data have been provided and comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

**Container Closure System**

Ciclopirox Terix nail lacquer 8% w/w is solution is packed into type III, amber glass bottles. Each bottle is sealed with a polyethylene stopper connected through a polyethylene shank to a hair brush made of black nylon.

Satisfactory specifications and statements of compliance to the current European regulations concerning materials in contact with foodstuff have been provided.

**Stability**

Finished product stability studies were performed in accordance to current guidelines on batches of finished product packed in the packaging proposed for marketing. Based on the results, a shelf-life of 30 months has been proposed and an in-use period of 6 months after first opening.

III.2 Non-clinical aspects

Ciclopirox nail lacquer 8 % w/w is hybrid application according to art. 10.3 2001/83/EC.

The pharmacodynamic, pharmacokinetic and toxicological properties of Ciclopirox are well known. As ciclopirox medicated nail lacquer 8% w/w, is the same type of solution as the innovator product, no further studies are required and the applicant has not provided any.

**Ecotoxicity/environmental risk assessment (ERA)**

The environmental risk assessment of Ciclopirox has followed the Guideline on the Environmental Risk Assessment of Medicinal Products for Human Use (Doc.Ref.EMEA/CHMP/SWP/4447/00).

III.3 Clinical aspects

## Introduction

Based on the review of the quality, safety and efficacy data, the Member States involved in the procedure have granted a marketing authorisation for Ciclopirox Terix 8% w/w medicated nail lacquer for the following therapeutic indication: treatment of fungal infections of the nails (Onychomycoses).

The application was made in accordance with Article 10(3) of Directive 2001/83/EC because “Ciclopirox Terix 8% medical nail lacquer”, is the hybrid form of the reference product “Batrafen 8% medical nail lacquer”, a locally applied and locally acting medicinal product.

Batrafen has been marketed by Sanofi –Aventis in Italy since November 1995.

## Pharmacokinetics

No new pharmacokinetics studies were performed.

## Pharmacodynamics

No new pharmacodinamic studies were performed.

## Clinical efficacy

This application is literature-based. No studies sponsored by the applicant have been undertaken to investigate the efficacy of Ciclopirox Terix.

As stated by current guidelines “A waiver of the need to provide equivalence data may be acceptable in the case of solutions, e.g. eye drops, nasal sprays or cutaneous solutions, if the test product is of the same type of solution (aqueous or oily), and contains the same concentration of the same active substance as the medicinal product currently approved. Minor differences in the excipient composition may be acceptable if the relevant pharmaceutical properties of the test product and reference product are identical or essentially similar”.

The Applicant demonstrated the essential similarity between test and reference products and in support of this decentralised procedure it submitted a biowaiver that has been judged admissible.

## Clinical safety

This application is literature-based. However, taking into account that the essential similarity between test and reference products has been demonstrated, the waiver provided, according to current guidelines, has been judged admissible.

**PHARMACOVIGILANCE SYSTEM AND RISK MANAGEMENT PLAN**

A summary of Pharmacovigilance System has been presented. As described by the applicant, it fulfills the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

The Applicant has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to ciclopirox.

- Summary table of safety concerns as approved in RMP version n. 1.3:



- Summary of Planned Risk Minimisation Activities as approved in RMP version n. 1.3:

Concerning the current RMP version n. 1.3, the proposed routine risk minimisation measures are evaluated as sufficient; as a consequence, no additional risk minimisation measures have been set in this RMP.

**SUMMARIES OF PRODUCT CHARACTERISTICS (Sm.PCs), PATIENT INFORMATION LEAFLETS (PILs) AND LABELLING**

The SmPCs, PILs and labelling are acceptable from a clinical perspective. The SmPCs are consistent with those for the originator products, where appropriate, along with current guidelines. The PILs are consistent with the details in the SmPCs and in-line with the current guidelines. The labelling is in-line with current guidance.

The packed leaflet has been evaluated via user consultation study in accordance with the requirements of articles 59(3) and 61(1) of directive 2001/83/EC. The language used for the purpose of the user testing PIL was English.

IV Overall conclusions and benefit-risk assessment

This Application is related to the request of the Applicant Terix Labs Ltd. for the Marketing Authorisation of a medicinal product containing Ciclopirox in medicated nail lacquer. The application was made in accordance with Article 10(3) of Directive 2001/83/EC because “Ciclopirox Terix 8% medicated nail lacquer”, is the hybrid form of the reference product “Batrafen 8% medicated nail lacquer”, a locally applied and locally acting medicinal product.

Batrafen has marketed by Sanofi-Aventis in Italy since November 1995.

The quality characteristics Ciclopirox Terix 8% medicated nail lacquer are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

However, the Applicant has provided a post-approval commitment to submit a variation aimed to introduce the detailed analytical method along with the relevant validation study for the benzene control within 1 month.

This application is literature-based. No studies sponsored by the applicant have been undertaken to investigate the efficacy and safety of Ciclopirox Terix.

The Applicant demonstrated the essential similarity between test and reference products and in support of this decentralised procedure it submitted a biowaiver, according to current guidelines.

The efficacy and safety profiles of ciclopirox are well known and no concerns are expected.

The SmPCs, PILs and labelling are satisfactory, and consistent with those for the reference products, where appropriate, along with current guidelines.

**BENEFITI RISK ASSESSMENT**

The quality of the product Ciclopirox Terix 8% medicated nail lacquer is acceptable, and no new non-clinical or clinical safety concerns have been identified.

A post-approval commitment for quality part has been provided by the Applicant.

The Applicant demonstrates the essential similarity between test and reference products and in support of this decentralised procedure it submits a biowaiver.

The benefit/risk balance is, therefore, considered to be positive.