DAKTARIN GOLD 2% CREAM
PL 15513/0184

UKPAR

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LAY SUMMARY

The MHRA granted McNeil Products Limited Marketing Authorisation (licence) for the medicinal product Daktarin Gold 2% Cream on 1st April 2009. This product is indicated for the treatment of Athlete’s Foot, dhobie itch and sweat rash skin infections. The cream rapidly relieves the itching which these fungal infections cause. It also provides long lasting protection.

This product is a pharmacy (P) only medicine and contains ketoconazole, which works by destroying the fungi and yeasts that cause infection.

This application is a duplicate of a previously granted application for Nizoral Cream/Daktarin Gold (PL 00242/0107), which was originally approved to Janssen-Cilag Limited on 2nd December 1983.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Daktarin Gold 2% Cream outweigh the risks; hence a Marketing Authorisation has been granted.
SCIENTIFIC DISCUSSION

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INTRODUCTION

The UK granted McNeil Products Limited Marketing Authorisations for the medicinal product Daktarin Gold 2% Cream (PL 15513/0184) on 1st April 2009. The product is available on a Pharmacy (P) only licence.

The application was submitted as a simple abridged application according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC, cross-referring to Nizoral Cream/Daktarin Gold (PL 00242/0107), which was originally approved to Janssen-Cilag Limited on 2nd December 1983.

No new data were submitted nor were they necessary for this simple application, as the data is identical to that of the previously granted cross-reference product.

This suspension contains the active ingredients ketoconazole and is indicated for the treatment of the following mycotic infections of the skin: tinea pedis, tinea cruris and candidal intertrigo.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 15513/0184
PROPRIETARY NAME: Daktarin Gold 2% Cream
ACTIVE(S): ketoconazole
COMPANY NAME: McNeil Products Limited
LEGAL STATUS: P

1. INTRODUCTION
This is a simple, piggy back application for Daktarin Gold 2% Cream (PL 15513/0184) submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is McNeil Products Limited, Foundation Park, Roxborough Way, Maidenhead, Berkshire, SL6 3UG, United Kingdom.

The application cross-refers Nizoral Cream/Daktarin Gold (PL 00242/0107), which was originally approved to Janssen-Cilag Limited on 2nd December 1983.

The current application is considered valid.

2. MARKETING AUTHORITY APPLICATION FORM
2.1 Name(s)
The proposed name of the product is Daktarin Gold 2% Cream. The product has been named in-line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
The product contains ketoconazole. The finished product is packaged in an aluminium tube, inner lined with heat polymerised epoxyphenol resin with a latex coldseal ring at the end of the tube. The cap is made of polypropylene, calcium carbonate and glyceryl monostearate. The tubes come in sizes of 5g, 15g and 30g.

The proposed shelf-life (60 months) and storage conditions (Do not store above 25°C) are consistent with the details registered for the cross-reference product.

2.3 Legal status
On approval, the product will be available on a pharmacy (P) only licence.

2.4 Marketing authorisation holder/Contact Persons/Company
McNeil Products Limited, Foundation Park, Roxborough Way, Maidenhead, Berkshire, SL6 3UG, United Kingdom.

The QP responsible for pharmacovigilance is stated and their CV is included.

2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of GMP compliance has been provided.
2.6 Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size for each product is stated.

2.8 Finished product/shelf-life specification
The proposed finished product specification is in-line with the details registered for the cross-reference product.

2.9 Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10 TSE Compliance
No materials of animal or human origin are included in the product.
This information is consistent with the cross-reference product.

3. EXPERT REPORTS
The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts’ CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS
The proposed summary is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET/CARTON
The patient information leaflet has been prepared in-line with the details registered for the cross-reference product. The package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that they contain.
Labelling
The proposed artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In-line with current legislation, the applicant has also included the name of the product in Braille on the packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS
The data submitted with the application is acceptable. The grant of a Marketing Authorisation is recommended.
PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.
CLINICAL ASSESSMENT

No new clinical data have been supplied with this application and none are required for an application of this type.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The data for this application is consistent with that previously assessed for the cross-reference product and, as such, has been judged to be satisfactory.

PRECLINICAL
No new preclinical data were submitted and none are required for applications of this type.

EFFICACY
This application is identical to a previously granted application Nizoral Cream/Daktarin Gold (PL 00242/0107), which was originally approved to Janssen-Cilag Limited on 2nd December 1983.

No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with ketoconazole is considered to have demonstrated the therapeutic value of the compounds. The risk:benefit is, therefore, considered to be positive.
**STEPS TAKEN FOR ASSESSMENT**

1. The MHRA received the marketing authorisation application on 11\(^{th}\) March 2008.

2. Following standard checks and communication with the applicant the MHRA considered the application valid on 18\(^{th}\) March 2008.

3. Following assessment of the application, the MHRA requested further information relating to the quality dossiers on 6\(^{th}\) August 2008.

4. The applicant responded to the MHRA’s requests, providing further information on 19\(^{th}\) February 2009 for the quality sections.

5. The application was determined on 1\(^{st}\) April 2009.
DAKTARIN GOLD 2% CREAM
PL 15513/0184

STEPS TAKEN AFTER ASSESSMENT

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Daktarin Gold 2% Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Ketoconazole 2% w/w.
Excipients: Propylene glycol; Cetyl alcohol; Stearyl alcohol
For a full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM
Cream
White cream

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
For the treatment of the following mycotic infections of the skin: tinea pedis, tinea cruris and candidal intertrigo.

4.2 Posology and method of administration
For the treatment of tinea pedis (athlete’s foot) and tinea cruris (dhobie itch) and candidal intertrigo (sweat rash).

For tinea pedis, Daktarin Gold 2 % cream should be applied to the affected areas twice daily. The usual duration of treatment for mild infections is 1 week. For more severe or extensive infections (eg involving the sole or sides of the feet), treatment should be continued for 2–3 days after all signs of infection have disappeared to prevent relapse.

For tinea cruris and candidal intertrigo, apply cream to the affected areas once or twice daily until 2-3 days after all signs of infection have disappeared to prevent relapse. Treatment for up to 6 weeks may be necessary. If no improvement in symptoms is experienced after 4 weeks treatment, a doctor should be consulted.

Method of administration: Cutaneous use.

4.3 Contraindications
Daktarin Gold 2 % cream is contra-indicated in patients with a known hypersensitivity to any of the ingredients or to ketoconazole itself.

4.4 Special warnings and precautions for use
Not for ophthalmic use.
If a potent topical corticosteroid has been used previously in the treatment of seborrhoeic dermatitis, a recovery period of 2 weeks should be allowed before using Daktarin Gold 2 % cream, as an increased incidence of steroid induced skin sensitisation has been reported when no recovery period is allowed.

Propylene glycol may cause skin irritation. Cetyl alcohol and stearyl alcohol may cause local skin reactions (e.g. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction
None known.

4.6 Pregnancy and lactation
There are no adequate and well-controlled studies in pregnant or lactating women. To date, no other relevant epidemiological data are available. Data on a limited number of exposed pregnancies indicate no adverse effects of topical ketoconazole on pregnancy or on the health of the foetus/newborn child.
Animal studies have shown reproductive toxicity following oral administration of ketoconazole. (see Preclinical safety data, section 5.3). No effects on the breastfed newborn/infant are anticipated. See Pharmacokinetic properties, section 5.2..

4.7 Effects on ability to drive and use machines
None.

4.8 Undesirable effects
The safety of ketoconazole cream was evaluated in 1117 subjects who participated in 31 clinical trials. Each subject received at least one topical administration of ketoconazole cream.

Commonly observed adverse reactions to Ketoconazole cream in clinical trials were burning sensation, application site erythema and pruritus.

Including the above-mentioned adverse drug reactions (ADRs), the following table displays ADRs that have been reported with the use of ketoconazole cream from either clinical trial or postmarketing experiences. The displayed frequency categories use the following convention:

<table>
<thead>
<tr>
<th>Frequency Category</th>
<th>Very Common (≥1/10)</th>
<th>Common (≥1/100 to &lt;1/10)</th>
<th>Uncommon (≥1/1,000 to &lt;1/100)</th>
<th>Rare (≥1/10,000 to &lt;1/1,000)</th>
<th>Very rare (&lt;1/10,000)</th>
<th>Not Known (cannot be estimated from the clinical trial data)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Adverse Drug Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>General disorders and administration site conditions</td>
<td>Application site erythema; Application site pruritus</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Skin burning sensation; Bullous eruption; Dermatitis contact; Rash; Skin exfoliation; Sticky skin.</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Hypersensitivity.</td>
</tr>
</tbody>
</table>

4.9 Overdose
Exaggerated topical application may lead to erythema, oedema and a burning sensation, which will disappear upon discontinuation of the treatment.
If accidental ingestion of ketoconazole cream occurs, no special measures have to be taken.
5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic Group: Imidazole and triazole derivatives; ATC code: D01 AC08

Ketoconazole has a potent antimycotic action against dermatophytes and yeasts. Ketoconazole cream acts rapidly on the pruritus, which is commonly seen in dermatophyte and yeast infections. This symptomatic improvement often occurs before the first signs of healing are observed.

A study in 250 patients has shown that application twice daily for 7 days of ketoconazole 2% cream vs clotrimazole 1% cream for 4 weeks on both feet demonstrated efficacy in patients with tinea pedis (athlete’s foot) presenting lesions between the toes.

The primary efficacy endpoint was negative microscopic KOH examination at 4 weeks. Ketoconazole 2% treatment showed equivalent efficacy to 4 weeks clotrimazole 1% treatment. There was no evidence of relapse following treatment with ketoconazole cream at 8 weeks.

5.2 Pharmacokinetic properties
Plasma concentrations of ketoconazole were not detectable after topical administration of ketoconazole cream in adults on the skin. In one study in infants with seborrhoeic dermatitis (n = 19), where approximately 40 g of ketoconazole cream was applied daily on 40% of the body surface area, plasma levels of ketoconazole were detected in 5 infants, ranging from 32 to 133 ng/mL.

5.3 Preclinical safety data
Since ketoconazole administered topically as a cream is not systemically absorbed and does not produce detectable plasma concentrations, there is no specific relevant information.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
- Propylene Glycol
- Stearyl Alcohol
- Cetyl Alcohol
- Sorbitan Stearate
- Polysorbate 60
- Isopropyl Myristate
- Sodium Sulphite Anhydrous (E221)
- Polysorbate 80
- Purified Water

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
60 months.

6.4 Special precautions for storage
Do not store above 25°C.

6.5 Nature and contents of container
Tube made of 99.7% aluminum, lined on inner side with heat polymerised epoxyphenol resin with a latex coldseal ring at the end of the tube. The cap is made of 60% polypropylene, 30% calcium carbonate and 10% glyceryl monostearate.

Tubes of 5, 15 and 30g. Not all pack sizes may be marketed.

6.6 Special precautions for disposal
Not applicable.

7 MARKETING AUTHORISATION HOLDER
McNeil Products Limited
Foundation Park
Roxborough Way
Maidenhead
Berkshire
SL6 3UG
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 15513/0184

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
01/04/2009

10 DATE OF REVISION OF THE TEXT
01/04/2009
**Daktarin® GOLD 2% Cream**

- This medicine is used to treat Athlete’s Foot, Dohbie itch and sweat rash skin infections.
- This medicine is for use by adults and children of all ages.
- Do not use this medicine:
  - There are some people who should not use this medicine. To find out if you are one of them, see Section 2.
  - If you have ever had a bad reaction to any of the ingredients. See Section 6.
- Speak to your doctor:
  - If you suffer from any of the conditions mentioned in Section 2.
  - If you are taking any other medicines. See Section 2.
  - Follow the instructions on how to use this product carefully. See Section 3.

Now read this whole leaflet carefully before you use this medicine. Keep the leaflet: you might need it again.

### 1 What the medicine is for

Daktarin Gold 2% Cream is a medicine which is used to treat skin infections which may appear on the feet (Athlete’s Foot), in the groin area (Dohbie itch/tinea cruris) or between skin folds (Sweat Rash infected with a yeast infection ‘thrush’). The cream rapidly relieves the itching which these fungal infections cause. It also provides long lasting protection from Athlete’s Foot, as it will continue to work even after you have stopped using it.

The cream contains the active substance, ketoconazole, which works by destroying the fungi and yeasts that cause the infection. If you have Athlete’s Foot, the skin between your toes will be red and itchy. Your skin may flake and crack, and often the infection causes an unpleasant ‘cheesy’ smell. It is encouraged by moist, warm conditions and can be recognised by redness, irritation and itchiness between the toes.

Tinea cruris or Dohbie Itch is a fungal infection that occurs in the groin area and causes intense itching and inflammation (redness and soreness). In men, the skin of the scrotum is often affected.

### 2 Before using this medicine

This medicine is suitable for most adults and children but a few people should not use it. If you are in any doubt, talk to your doctor or pharmacist.

- **Do not use this medicine...**
  - If you have ever had a bad reaction to any of the ingredients.

If this applies to you, get advice from a doctor or pharmacist without using Daktarin Gold 2% Cream.

- **Talk to your doctor or pharmacist...**
  - If you are pregnant or breast-feeding.

- **If you are pregnant or breast-feeding**
  - Ask your doctor or pharmacist for advice before using this medicine if you are pregnant. You can use Daktarin Gold 2% Cream whilst breast-feeding. Do not apply directly to the breast while breast-feeding.

- **Special warnings about this medicine**
  - Do not let the cream get into your eyes.

### 3 How to use this medicine

Check the tables that follow to see how often to use.

- **Each tube of cream is sealed – unscrew the cap and use the cap to pierce the seal.**
- **For topical use only, which means it is applied directly to the affected area of skin.**
- **Do not use more often than the stated dose shown in the table.**

**How to apply the cream**

- Wash the infected area and dry it well. As many skin conditions are contagious, you should keep a towel and flannel for your own use and not share it so that you do not infect anyone else.
- Apply the cream onto the infected area and surrounding skin.
- Wash your hands carefully after applying the cream to avoid spreading the infection to other parts of the body or to other people. Similarly, clothing which comes into contact with the infected areas, such as socks, should be washed and changed frequently.

### 1 Adults and children of all ages

For Athlete’s foot (infections between the toes)

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and children of all ages</td>
<td>Rub the cream gently between the toes and surrounding area twice a day (morning and night) for 1 week.</td>
</tr>
</tbody>
</table>

- If Athlete’s Foot is more severe or extensive (e.g. affecting the sole or sides of the feet), continue to apply the cream to the affected areas for at least 2 to 3 days after signs of infection have cleared to prevent them coming back.
- If symptoms persist talk to your doctor.
### For Dhobie itch and Sweat Rash (Candidal Intertrigo)

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and children of all ages</td>
<td>Rub the cream into the affected area once or twice daily.</td>
</tr>
</tbody>
</table>

- Continue treatment for at least 2 to 3 days after signs of infection have cleared. Treatment may be necessary for up to 6 weeks. You may feel relief from symptoms quickly but it is important that you continue to use the cream as described to prevent them from coming back.
- If symptoms have not improved within 4 weeks talk to your doctor.

**If anyone has swallowed this product**
If anyone accidentally swallows Daktarin Gold 2% Cream, contact a doctor or your nearest Accident and Emergency department (Casuality), taking this leaflet and pack with you.

**If you forget to use the medicine**
If you forget to use a dose, use the next dose when needed. Do not use a double dose.

### 4 Possible side-effects

Daktarin Gold 2% Cream can have side-effects, like all medicines, although these don’t affect everyone and are usually mild.

If you experience any of the following, stop using the medicine and seek immediate medical help:
- Uncommon: (less than 1 in 100 but more than 1 in 1000 people are affected)
  - Localised eczema (dermatitis), skin rash, sticky skin, irritation, prickling sensation, inflammation, discomfort, dryness, bleeding or other reactions at the application site.
- Other effects:
  - Urticaria also known as hives, where the skin looks blotchy with white raised wheels (bumps) surrounded by redness.
  - If you experience any side-effects not included in this leaflet or are not sure about anything, talk to your doctor or pharmacist.

### 5 Storing this medicine

- Do not store above 25°C.
- Keep the product out of the reach and sight of children.
- Do not use your medicine after the date shown on the packaging.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

### 6 Further information

#### What's in this medicine?

- The active ingredient in 1 g of Daktarin Gold 2% Cream is: Ketoconazole 20 mg.
- Other ingredients are: Propylene glycol, stearyl alcohol, cetyl alcohol, sorbitan stearate, polysorbate 60, polysorbate 80, isopropyl myristate, sodium sulphite (E221) and purified water.

#### What the medicine looks like

Daktarin Gold 2% Cream is a white cream available in a 15 g tube.

**Product Licence holder:** McNeil Products Ltd, Maidenhead, Berkshire, SL6 3UG, UK.

**Manufacturer:** Janssen Pharmaceuticals NV, Turnhoutseweg 30, B2340, Beerse, Belgium.

This leaflet was revised December 2008. Daktarin is a registered trade mark.

### 7 Facts about Athlete’s Foot:

#### How do you catch Athlete's Foot?

It's extremely infectious so anyone can pick it up, especially people sharing communal changing rooms and showers.

Once the fungal spores have been transferred onto the feet, they thrive in the warm, moist areas between the toes. The skin soon becomes inflamed and itchy with flaking or cracking occurring. The infected flakes of skin are then shed onto the floor or into the socks and shoes by walking or friction.

Someone else will be easily infected if they step on these flakes, or if they share towels or footwear with someone who has already got Athlete’s Foot.

What is more, even if you've already got rid of your Athlete’s Foot, it’s very easy to re-infect yourself. The spores can live on or in your shoes or socks and if you don’t change them regularly, or treat them with antifungal powders or spray powders, the Athlete’s Foot soon returns.

#### How to prevent re-infection

If you want to avoid the vicious circle of re-infection, here are a few helpful hints:

- Spray inside your shoes and socks with fungicidal powder before putting them on.
- Don’t wear the same pair of shoes every day. This helps reduce the build-up of sweat which provides the moisture on which the fungus thrives.
- Avoid synthentic footwear. Choose cotton socks and leather shoes which allow your feet to breathe.
- Avoid sharing towels or footwear.
- Avoid walking barefoot in changing rooms.
- Dry thoroughly between your toes and keep toenails short as this reduces the number of places fungi can grow.
Daktarin® GOLD 2% Cream

Rapid itch relief and long lasting protection from ATHLETE’S FOOT
Also treats Dhobie Itch & infected Sweat Rash.

Directions: Wash the infected skin and dry well. For mild Athlete’s foot: apply to the affected area twice daily for one week. If your Athlete’s Foot is more severe or extensive: continue to apply the cream for at least 2-3 days after symptoms have cleared. For Dhobie Itch and Candidal Intertrigo: apply to the affected area for at least 2-3 days after symptoms have cleared. For further information please read enclosed leaflet. Keep all medicines out of reach and sight of children. Do not store above 25°C.

Ketoconazole 2% w/w. Also contains propylene glycol, cetyl and stearyl alcohol, sorbitan stearate, polysorbates 60 & 80, sodium sulphite (E221), isopropyl myristate, purified water.

FOR EXTERNAL USE ONLY 15g P

©denotes registered trademark

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