# CANESTEN BIFONAZOLE GEL

**PL 00010/0617**

## UKPAR

### TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lay Summary</td>
<td>2</td>
</tr>
<tr>
<td>Scientific discussion</td>
<td>3</td>
</tr>
<tr>
<td>Steps taken for assessment</td>
<td>11</td>
</tr>
<tr>
<td>Steps taken after authorisation – summary</td>
<td>12</td>
</tr>
<tr>
<td>Summary of Product Characteristics</td>
<td>13</td>
</tr>
<tr>
<td>Product Information Leaflet</td>
<td>16</td>
</tr>
<tr>
<td>Labelling</td>
<td>18</td>
</tr>
</tbody>
</table>
LAY SUMMARY

The MHRA granted Bayer plc a Marketing Authorisation (licence) for the medicinal product Canesten Bifonazole Gel on 6th July 2009. This product, to be available as a pharmacy medicine, contains the active substance bifonazole. Bifonazole belongs to a group of medicines called imidazoles and is an antifungal agent that fights the cause of fungal skin infections.

Canesten Bifonazole Gel is used for the treatment of athlete’s foot.

This application is a duplicate of a previously granted application for Canesten Bifonazole (PL 00010/0104), which was originally granted to Bayer plc on 14th February 1986.

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

TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>4</td>
</tr>
<tr>
<td>Pharmaceutical assessment</td>
<td>5</td>
</tr>
<tr>
<td>Preclinical assessment</td>
<td>8</td>
</tr>
<tr>
<td>Clinical assessment</td>
<td>9</td>
</tr>
<tr>
<td>Overall conclusions and risk benefit assessment</td>
<td>10</td>
</tr>
</tbody>
</table>
INTRODUCTION

The MHRA granted Bayer plc a Marketing Authorisation (licence) for the medicinal product Canesten Bifonazole Gel on 6th July 2009. This product, to be available as a pharmacy medicine, contains the active substance bifonazole.

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 Canesten Bifonazole (PL 00010/0104), which was originally granted to Bayer plc on 14th February 1986.

No new data were submitted nor was it necessary for this simple application, as the data are identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no PAR was generated for it.

Bifonazole is a broad spectrum imidazole antifungal agent, which is effective against dermatophytes, yeasts, moulds and other fungi.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 00010/0617
PROPRIETARY NAME: Canesten Bifonazole Gel
ACTIVE(S): Bifonazole
COMPANY NAME: Bayer plc
LEGAL STATUS: P

1. INTRODUCTION
This is a simple, piggy back application for Canesten Bifonazole Gel, submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Bayer plc, Consumer Care Division, Bayer House, Strawberry Hill, Newbury, Berkshire, RG14 1JA.

The application cross-refers to Canesten Bifonazole (PL 00010/0104), which was originally granted to Bayer plc on 14th February 1986.

The current application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM
2.1 Name(s)
The proposed name of the product is Canesten Bifonazole Gel. 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 bifonazole, equivalent to 1% w/w. The finished product is packaged in collapsible aluminium tubes containing either 15g or 50g of product, and aluminium laminated tubes containing 20g of product. The proposed shelf-life (60 months) and storage conditions (there are no specific storage instructions) are consistent with the details registered for the cross-reference product.

2.3 Legal status
On approval, the product will be available as a pharmacy medicine (legal status P).

2.4 Marketing authorisation holder/Contact Persons/Company
Bayer plc, Consumer Care Division, Bayer House, Strawberry Hill, Newbury, Berkshire, RG14 1JA.

The QP responsible for pharmacovigilance is stated and his 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 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 were used in the manufacture of 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
PIL
The patient information leaflet has been prepared in-line with the details registered for the cross-reference product.

PIL user testing has been submitted and the results indicate that the PIL 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 it contains.

Carton and blister
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 outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.
7. CONCLUSIONS
The data submitted with the application are 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 are consistent with that previously assessed for the cross-reference product and as such have been judged to be satisfactory.

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

EFFICACY
This application is identical to a previously granted application for Canesten Bifonazole (PL 00010/0104), which was originally approved to Bayer plc on 14th February 1986.

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 bifonazole is considered to have demonstrated the therapeutic value of the compound. The risk:benefit is, therefore, considered to be positive.
CANESTEN BIFONAZOLE GEL
PL 00010/0617

STEPS TAKEN FOR ASSESSMENT

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 23/09/2008.</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 26/09/2008.</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application the MHRA requested further information on 23/02/2009.</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 12/06/2009.</td>
</tr>
<tr>
<td>5</td>
<td>The application was determined on 06/07/2009.</td>
</tr>
</tbody>
</table>
**CANESTEN BIFONAZOLE GEL**  
**PL 00010/0617**

**STEPS TAKEN AFTER ASSESSMENT**

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

1 NAME OF THE MEDICINAL PRODUCT
Canesten Bifonazole Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Bifonazole 1% w/w
For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Gel
A clear, colourless gel.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Bifonazole is a broad spectrum imidazole antifungal agent.
It is indicated for the treatment of athlete’s foot.
The preparation is not for vaginal use.

4.2 Posology and method of administration
For cutaneous use.
The gel should be thinly applied and rubbed into the affected areas once daily, preferably at night before retiring, for two to three weeks.
The affected areas should be washed and dried thoroughly before the gel is applied.

4.3 Contraindications
History of hypersensitivity to imidazole antifungal agents or any of the excipients. Treatment of infants with nappy rash.

4.4 Special warnings and precautions for use
None stated.

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

4.6 Pregnancy and lactation
After oral administration to animals at high doses, bifonazole was not teratogenic, but embryotoxic and foetotoxic effects were observed. Bifonazole gel for topical administration should not normally be used in pregnancy. As no information is available on the effect of bifonazole on lactation, it should not be used in nursing mothers.

4.7 Effects on ability to drive and use machines
None known.

4.8 Undesirable effects
Skin reactions (usually transient slight irritation, reddening, peeling or burning) occur frequently (more than 1.0%). The development of contact dermatitis has been reported infrequently (more than 0.1%). These side-effects are reversible after discontinuation of the treatment.
Very rarely, systemic hypersensitivity reactions may occur.
4.9 Overdose
In the event of accidental oral ingestion, routine measures such as gastric lavage should be performed as soon as possible after ingestion.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
ATC code: D01AC10 Antifungals for Topical Use

Bifonazole is a broad spectrum imidazole antifungal agent. It is effective against dermatophytes, yeasts, moulds and other fungi.

5.2 Pharmacokinetic properties
After a single application (topical) of 15.2mg [14C] bifonazole cream, and subsequent occlusion for six hours, 0.6±0.3% of the dose was absorbed. The absorption rate was approximately 0.008mg/100cm² per hour. In inflamed skin these values were higher by a factor of four. Similar results were obtained after the application of bifonazole as a 1% solution.

Plasma levels up to 16ng/ml were obtained in babies with nappy rash after a single 5g application of the cream.

After intravenous administration of 0.016mg/kg [14C] bifonazole, tissue uptake was rapid. Bifonazole is, however, rapidly metabolised with only 30% of an intravenous dose remaining unaltered 30 minutes post-dose.

Elimination of the metabolites is biphasic (T½ of eight and 50 hours). Within five days of administration 45% of the administered dose has been excreted renally, with 40% being eliminated via the liver and bile (faeces).

5.3 Preclinical safety data
Toxicological studies showed good local tolerability. However, for bifonazole cream and solution slight skin irritant effects were observed which could be attributed to the additives 2-octyl dodecanol (cream) and isopropyl myristate (solution), respectively. There were no indications of changes caused specifically by the active substance, and no signs of any systemic effects were observed. Studies on reproductive toxicity showed no evidence of teratogenic activity, however embryotoxic effects were seen in rabbits at high oral doses (30mg/kg bodyweight). Bifonazole had no influence on fertility and showed no mutagenic properties.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Emulgin B3
Cetiol HE
Isopropyl isostearate
Lactic acid
Ethanol
Benzyl alcohol
Purified Water

6.2 Incompatibilities
None known.

6.3 Shelf life
60 months.

6.4 Special precautions for storage
This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container
Collapsible aluminium tubes containing 15g or 50g of gel. Aluminium-laminated tubes containing 20g of gel.
6.6 Special precautions for disposal
None.

7 MARKETING AUTHORISATION HOLDER
Bayer plc
Consumer Care Division
Bayer House
Strawberry Hill
Newbury
Berkshire
RG14 1JA.

8 MARKETING AUTHORISATION NUMBER(S)
PL 00010/0617

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
06/07/2009

10 DATE OF REVISION OF THE TEXT
06/07/2009

11 DOSIMETRY (IF APPLICABLE)

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)
Read all of this leaflet carefully because it contains important information for you.

This medicine is available without prescription. However, you still need to use Canesten Bifonazole Gel carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve.
- If you have any unusual effects after using this product, tell your doctor or pharmacist.

IN THIS LEAFLET
1. What is Canesten Bifonazole Gel and what is it used for?
2. Before you use Canesten Bifonazole Gel
3. How to use Canesten Bifonazole Gel
4. Possible side effects
5. How to store Canesten Bifonazole Gel
6. Further information

1. WHAT IS CANESTEN® BIFONAZOLE GEL AND WHAT IS IT USED FOR?

Canesten Bifonazole Gel is used to treat athlete's foot.
If unsure whether you have athlete's foot, seek the advice of your doctor or pharmacist.
The active substance in Canesten Bifonazole Gel is bifonazole. Bifonazole belongs to a group of medicines called imidazoles and is an antifungal agent which fights the cause of fungal skin infections.

2. BEFORE YOU USE CANESTEN® BIFONAZOLE GEL

Do not use Canesten® Bifonazole Gel:

- If you are allergic (hypersensitive) to bifonazole or any of the other ingredients of Canesten Bifonazole Gel (see section 6, Further information).
- To treat nappy rash, if your baby has nappy rash, seek your doctor's advice for a suitable treatment.

Before using Canesten® Bifonazole Gel, see your doctor if:

- You have ever had an allergic reaction to any antifungal product.

Pregnancy and breast-feeding:

Do not use Canesten Bifonazole Gel if you are pregnant or breast-feeding.

3. HOW TO USE CANESTEN® BIFONAZOLE GEL

If Canesten Bifonazole Gel has been prescribed for you by your doctor, follow any instructions he/she may have given you. If you purchased this product without a prescription, follow these directions closely:

- Before use, pierce the tube seal by inverting the cap over the end of the tube and press.
- Before applying the gel, your feet should be washed and dried thoroughly, especially between the toes.
- The gel should be applied thinly and evenly to the affected areas once daily, preferably at night before going to bed, and rubbed in gently.
- Treatment should be continued for 2-3 weeks.
- It may help to use an antifungal dusting powder as well. Ask your doctor or pharmacist to recommend one.

The symptoms of athlete's foot, such as itching or soreness, should improve within a few days of treatment although signs such as redness and scaling may take longer to disappear. If symptoms persist, consult your doctor.

Canesten® Bifonazole Gel is for external use only.
Do not put the gel in your mouth or swallow it.
If the gel is swallowed accidentally, tell your doctor straight away or contact the Accident and Emergency Department of your nearest hospital.
If you accidentally get gel in your eyes or mouth, wash immediately with water and contact your doctor.

If you forget to use Canesten® Bifonazole Gel:
Apply the gel as soon as possible and then continue the rest of your treatment as usual.

You can help the treatment to work if you follow these simple self-help tips:

- Although the infected area will itch, try not to scratch. Scratching will damage the surface of the skin and cause the infection to spread further.
- Keep the affected skin areas clean.
- Pay particular attention to drying the skin, including between the toes, but avoid excessive rubbing.
- Do not share towels, bath mats, etc. with other people as you could spread the infection to them.
- Always wash your hands after treating the infection to prevent it from spreading.
- Wash your socks, stockings and tights thoroughly in hot water to remove any shed skin or fungal spores.
- Change your footwear daily if possible.
4. POSSIBLE SIDE EFFECTS
Like all medicines, Canesten Bifonazole Gel can cause side effects, although not everybody gets them. As with all medicines, some people may be allergic to the gel. If you are allergic, a reaction will occur soon after you start using it. If you experience an allergic reaction, stop using Canesten Bifonazole Gel and tell your doctor straight away or contact the Accident and Emergency Department of your nearest hospital. Signs of an allergic reaction may include:
- Rash.
- Swallowing or breathing problems.
- Swelling of your lips, face, throat or tongue.
- Weakness, feeling dizzy or faint.
- Nausea.

After you apply the gel, you might experience the following symptoms:
- Slight irritation or burning.
- Reddening of the skin.
- Peeling.

If this is intolerable, stop treatment and see your doctor as soon as possible.

Canesten Bifonazole Gel may cause a local skin irritation which can be very similar to the symptoms of the infection. If any of your symptoms gets worse, stop treatment and see your doctor as soon as possible. These symptoms may include:
- Burning, pain or itching.
- Redness.
- Rash.
- Swelling.

If you experience any of the above effects or react badly to the gel in any other way not listed in this leaflet, tell your doctor or pharmacist immediately.

5. HOW TO STORE CANESTEN® BIFONAZOLE GEL
Keep out of the reach and sight of children.
This product should be stored in the original carton. Do not use Canesten Bifonazole Gel after the expiry date which is stated at one end of the carton and on the end of the tube of gel. The expiry date refers to the last day of that month.

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 Canesten® Bifonazole Gel contains:
- The active substance is bifonazole at a strength of 1% w/w.
- The other ingredients are emulgin B3, cetiol H E, isopropyl isostearate, lactic acid, ethanol, benzyl alcohol and purified water.

What Canesten® Bifonazole Gel looks like and contents of the pack:
Canesten Bifonazole Gel is available in tubes containing 15g, 20g and 50g of a clear colourless gel.

Marketing Authorisation Holder:
Bayer plc, Consumer Care Division, Bayer House, Strawberry Hill, Newbury, Berkshire RG14 1LA, UK.

Manufacturer:
Kern Pharma S.L., Poligon Industrial Colon II, Calle Venus 72, 08228 Terrassa, Spain.

Remember: If you have any doubts about using Canesten® Bifonazole Gel correctly, seek the advice of your doctor or pharmacist.

Further information about fungal infections:
Fungal infections are very common and affect many people. One of the most common fungal skin infections is athlete's foot (Tinea pedis). It is caused by a contagious fungus which thrives in warm, moist environments. The fungus that causes athlete's foot usually lives harmlessly on our skin and in our environment. The natural balance that normally keeps it under control can be upset by factors such as damp moist conditions. This could happen, for example, through regularly wearing training shoes that keep the feet hot and sweaty. Since this fungus is contagious, it can also often be picked up in changing rooms.

Tell-tale signs of athlete's foot are that the skin becomes itchy, red and inflamed. Sporty people or those who work in a warm, damp environment, tend to be more likely to catch this condition.

For UK residents only: if you have any questions or would like more information, call our Canesten Advice Line on 0845 758 5030. Calls charged at local rate. This leaflet was last revised in August 2008.

Canesten is a registered trademark of Bayer AG, Germany.

Bayer
CANESTEN BIFONAZOLE GEL
PL 00010/0617
LABELLING
Canesten®

Bifonazole Gel

Effective treatment for Athlete’s Foot

Please read the enclosed leaflet carefully before use.
The affected areas should be washed and dried thoroughly
before the gel is applied. The gel should be thinly applied and
rubbed into the affected areas once daily, preferably at night
before retiring, for two to three weeks.
If symptoms persist consult your doctor.
The gel contains Bifonazole 1% w/w.
It also contains emuolin B3, cetol HE, isopropyl isostearate,
lactic acid, ethanol, benzyl alcohol and purified water.
Keep out of the reach and sight of children.
Store in the original carton. No special storage precautions
are required.

Bayer

15g

MA Holder:
Bayer plc
Consumer Care Division
Newbury, Berkshire
RG14 1JL, U.K.

For external use only

PL 00010/0617
Please read the enclosed leaflet carefully before use.
The affected areas should be washed and dried thoroughly
before the gel is applied. The gel should be thinly applied
and rubbed into the affected areas once daily, preferably at
night before retiring, for two to three weeks.
If symptoms persist consult your doctor.
The gel contains Bifonazole 1% w/w.
It also contains emulgin B3, cetiol HE, Isopropyl Isostearate,
lactic acid, ethanol, benzyl alcohol and purified water.
Keep out of the reach and sight of children.
Store in the original carton. No special storage precautions
are required.
Canesten®

Bifonazole Gel

Effective treatment for Athlete’s Foot

Please read the enclosed leaflet carefully before use.
The affected areas should be washed and dried thoroughly
before the gel is applied. The gel should be thinly applied and
rubbed into the affected areas once daily, preferably at night
before retiring, for two to three weeks.
If symptoms persist consult your doctor.
The gel contains Bifonazole 1% w/w.
It also contains emuigin B3, cetiol HE, isopropyl isostearate,
lactic acid, ethanol, benzyl alcohol and purified water.
Keep out of the reach and sight of children.
Store in the original carton. No special storage
precautions are required.

Bayer
50g
MA Holder:
Bayer plc
Consumer Care Division
Newbury, Berkshire
RG14 1JA, U.K.
PL 00010/0617