

**CANESTEN BIFONAZOLE CREAM  
PL 00010/0616**

**UKPAR**

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**CANESTEN BIFONAZOLE CREAM**  
**PL 00010/0616**

**LAY SUMMARY**

The MHRA granted Bayer plc a Marketing Authorisation (licence) for the medicinal product Canesten Bifonazole Cream on 6th July 2009. This product, to be available as a prescription-only 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 Cream is used to treat fungal skin infections, such as ringworm, athlete's foot and fungal sweat rash.

This application is a duplicate of a previously granted application for Mycospor Cream (PL 00010/0103), which was originally granted to Bayer plc on 11<sup>th</sup> 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 Cream outweigh the risks; hence a Marketing Authorisation has been granted.

**CANESTEN BIFONAZOLE CREAM  
PL 00010/0616**

**SCIENTIFIC DISCUSSION**

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## **INTRODUCTION**

The MHRA granted Bayer plc a Marketing Authorisation (licence) for the medicinal product Canesten Bifonazole Cream on 6th July 2009. This product, to be available as a prescription-only 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 Mycospor Cream (PL 00010/0103), which was originally granted to Bayer plc on 11<sup>th</sup> 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 00010/0616

**PROPRIETARY NAME:** Canesten Bifonazole Cream

**ACTIVE(S):** Bifonazole

**COMPANY NAME:** Bayer plc

**E.C. ARTICLE:** Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC

**LEGAL STATUS:** POM

### **1. INTRODUCTION**

This is a simple, piggy back application for Canesten Bifonazole Cream, 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 Mycospor Cream (PL 00010/0103), which was originally approved to Bayer plc on 11<sup>th</sup> 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 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 bifonazole, equivalent to 1% w/w. The finished product is packaged in aluminium tubes containing either 15g or 50g 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 prescription-only medicine (legal status POM).

#### **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 Mycospor Cream (PL 00010/0103), which was originally approved to Bayer plc on 11<sup>th</sup> 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 CREAM  
PL 00010/0616**

**STEPS TAKEN FOR ASSESMENT**

|   |   |
|---|---|
| 1 | The MHRA received the marketing authorisation application on 05/09/2008.  |
| 2 | Following standard checks and communication with the applicant the MHRA considered the application valid on 10/09/2008. |
| 3 | Following assessment of the application the MHRA requested further information on 23/02/2009.                           |
| 4 | The applicant responded to the MHRA's requests, providing further information on 12/06/2009.                            |
| 5 | The application was determined on 06/07/2009.   |

**CANESTEN BIFONAZOLE CREAM  
PL 00010/0616**

**STEPS TAKEN AFTER ASSESSMENT**

| <b>Date submitted</b> | <b>Application type</b> | <b>Scope</b> | <b>Outcome</b> |
|-----------------------|-------------------------|--------------|----------------|
|                       |                         |              |                |
|                       |                         |              |                |
|                       |                         |              |                |
|                       |                         |              |                |
|                       |                         |              |                |

# CANESTEN BIFONAZOLE CREAM

## PL 00010/0616

### SUMMARY OF PRODUCT CHARACTERISTICS

#### 1 NAME OF THE MEDICINAL PRODUCT

Canesten Bifonazole Cream

#### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The cream contains 1% w/w bifonazole.

For full list of excipients, see section 6.1.

#### 3 PHARMACEUTICAL FORM

Cream

A white cream.

#### 4 CLINICAL PARTICULARS

##### 4.1 Therapeutic indications

Bifonazole is a broad spectrum antifungal agent.

It is indicated for the treatment of fungal skin infections due to dermatophytes (e.g. Trichophyton species), yeasts (e.g. candida species), moulds and other fungi. These include ringworm (tinea) infections, athlete's foot, pityriasis versicolor.

The preparation is not for vaginal use.

##### 4.2 Posology and method of administration

For cutaneous use.

The cream 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 cream 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 cream 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,  $0.6 \pm 0.3\%$  of the dose was absorbed. The absorption rate was approximately 0.008mg/100cm<sup>2</sup> 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 ( $T_{1/2}$  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-octyldodecanol (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**

Sorbitan stearate  
Polysorbate 60  
Cetyl palmitate  
Cetostearyl alcohol  
2-Octyldodecanol  
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**  
Aluminium tubes containing 15g and 50g of cream.
- 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 00010/0616
- 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)**

# Canesten®



## Bifonazole Cream

Bifonazole 1% w/w

**Read all of this leaflet carefully because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not give it to anyone else under any circumstances.
- If you have any unusual effects after using this product, tell your doctor.

### IN THIS LEAFLET

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

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

Canesten Bifonazole Cream is used to treat fungal skin infections such as ringworm, athlete's foot and fungal sweat rash.

The active substance in Canesten Bifonazole Cream 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 CREAM

**Do not use Canesten® Bifonazole Cream:**

- If you are allergic (hypersensitive) to bifonazole or any of the other ingredients of Canesten Bifonazole Cream (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 Cream, see your doctor if:**

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

**Important information about some of the ingredients:**

This product contains cetostearyl alcohol which may cause local skin irritation (e.g. rash, itching or redness).

**Pregnancy and breast-feeding:**

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

### 3. HOW TO USE CANESTEN® BIFONAZOLE CREAM

Unless directed otherwise by your doctor, 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 cream, the infected skin should be washed and dried thoroughly, especially between the toes if the feet are infected.
- The cream 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, depending on the type of infection.
- If you have athlete's foot, it may help to use an antifungal dusting powder as well. Ask your doctor or pharmacist to recommend one.

The symptoms of skin infection, 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 Cream is for external use only:**

**Do not put the cream in your mouth or swallow it.**

If the cream is swallowed accidentally, tell your doctor straight away or contact the Accident and Emergency Department of your nearest hospital.

If you accidentally get cream in your eyes or mouth, wash immediately with water and contact your doctor.

**If you forget to use Canesten® Bifonazole Cream:**

Apply the cream 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, 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.

**If you have athlete's foot:**

- Remember to dry the skin between the toes thoroughly.
- 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 Cream can cause side effects, although not everybody gets them.

As with all medicines, some people may be allergic to the cream. If you are allergic, a reaction will occur soon after you start using it. If you experience an allergic reaction, stop using Canesten Bifonazole Cream 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 cream, 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 Cream 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 cream in any other way not listed in this leaflet, tell your doctor immediately.

#### 5. HOW TO STORE CANESTEN® BIFONAZOLE CREAM

**Keep out of the reach and sight of children.**

This product should be stored in the original carton.

Do not use Canesten Bifonazole Cream after the expiry date which is stated at one end of the carton and on the end of the tube of cream. 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 Cream contains:**

- The active substance is bifonazole at a strength of 1% w/w.
- The other ingredients are sorbitan stearate, polysorbate 60, cetyl palmitate, cetostearyl alcohol, 2-octyldodecanol, benzyl alcohol, and purified water.

*See Section 2 'Important information about some of the ingredients' for cetostearyl alcohol advice.*

#### What Canesten® Bifonazole Cream looks like and contents of the pack:

Canesten Bifonazole Cream is available in tubes containing 15g and 50g of white cream.

#### Marketing Authorisation Holder:

Bayer plc, Consumer Care Division, Bayer House, Strawberry Hill, Newbury, Berkshire RG14 1JA, UK.

#### Manufacturer:

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

**Remember: This medicine has been prescribed for you. Do not give it to anyone else under any circumstances.**

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

#### Further information about fungal infections:

Fungal infections are very common and affect many people. Some of the most common fungal skin infections include athlete's foot, ringworm and sweat rash. There are two main types of fungal infection:

- The tinea group, also known as dermatophytes.
- The candida group, also known as yeasts.

The tinea group includes athlete's foot and ringworm, both of which are easily spread by contact. 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. Ringworm is usually passed on from animals to children. Ringworm is not actually a worm; its name comes from the circular worm-like shape that it forms on the skin. The main symptom for both is an itchy, scaly and irritating rash.

The candida group can be responsible for conditions such as sweat rash. Sweat rash can appear anywhere on the body, but is more likely to occur where folds of skin rub against each other, such as: under the breasts, under arms, around the groin and on the back. Candida is a yeast-like fungus that usually lives harmlessly on our skin. However, the natural balance that normally keeps it under control can be upset by factors such as sweating, tight or synthetic clothing and cosmetic preparations such as bath additives. When levels of the yeast increase, the skin can develop the following symptoms: persistent burning and itching, soreness and a variety of patches or blemishes as well as a softened and soggy appearance.

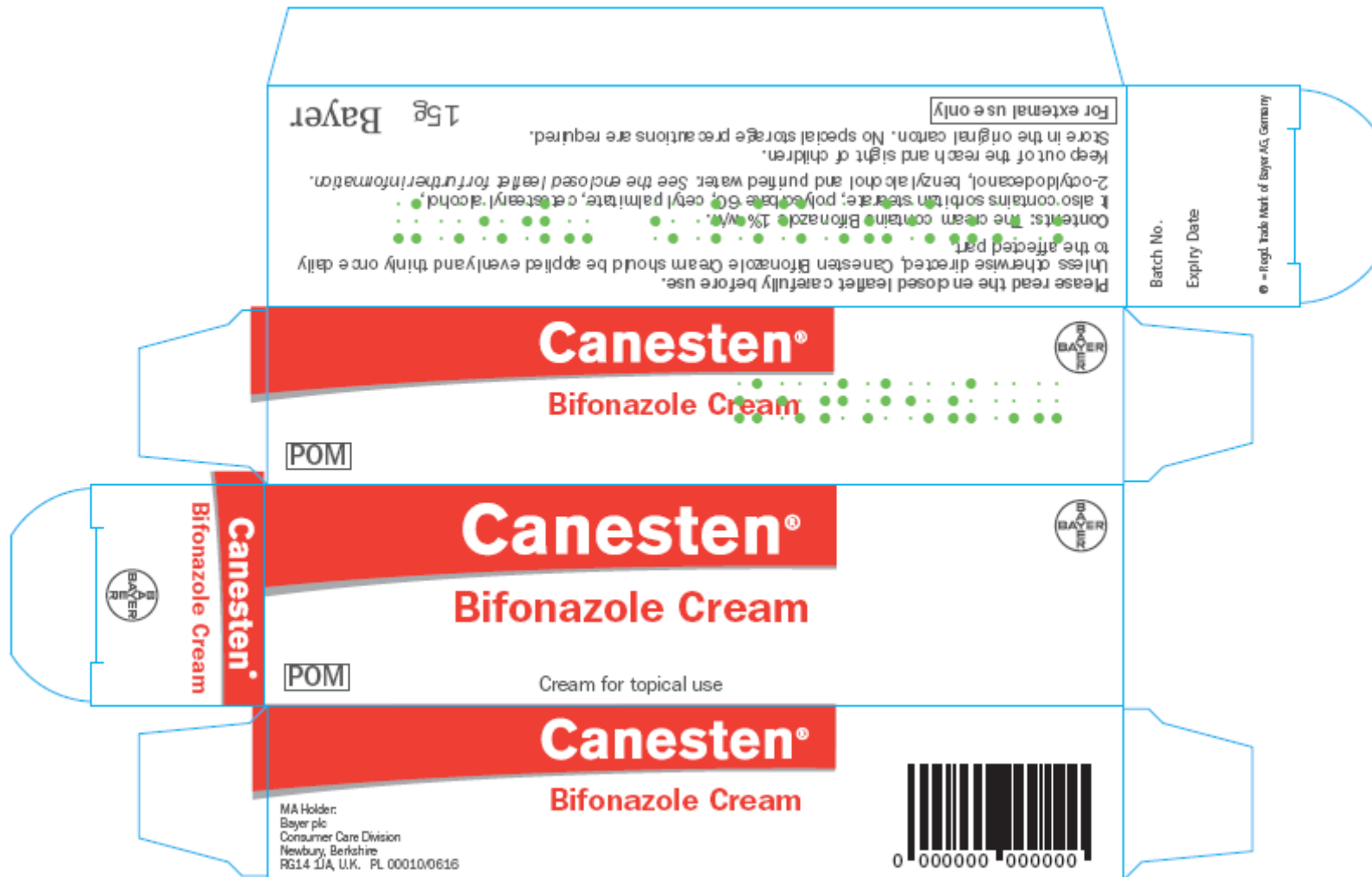
For UK residents only: if you have any questions or would like more information, call our Canesten Advice Line on 0845 758 5030. Calls charged at local rate.

This leaflet was last revised in August 2008.

Canesten is a registered trademark of Bayer AG, Germany.

**Bayer**

**CANESTEN BIFONAZOLE CREAM  
PL 00010/0616  
LABELLING**





# Canesten®

## Bifonazole Cream

Please read the enclosed leaflet carefully before use. Unless otherwise directed, Canesten Bifonazole Cream should be applied evenly and thinly once daily to the affected part.

Keep out of the reach and sight of children. Store in the original carton. No special storage precautions are required.

Contents: The cream contains Bifonazole 1% w/w. It also contains sorbitan stearate, polysorbate 60, cetyl palmitate, cetostearyl alcohol, 2-octyldodecanol, benzyl alcohol and purified water. See the enclosed leaflet for further information.

For external use only **POM**

**Bayer**

15g

MA Holder:  
Bayer plc  
Consumer Care Division  
Newbury, Berkshire  
RG14 1JA, U.K.  
PL 00010/0616



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Batch No. Expiry Date

# Canesten®

## Bifonazole Cream

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For external use only

**POM**

**Bayer**

50g

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RG14 1JA, U.K.  
PL 00010/0616



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