



**CANESTEN AF BIFONAZOLE ONCE DAILY ATHLETES'S
FOOT CREAM**

PL 00010/0508

UKPAR

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CANESTEN AF BIFONAZOLE ONCE DAILY ATHLETES'S FOOT CREAM

PL 00010/0508

LAY SUMMARY

The MHRA granted BAYER PLC a Marketing Authorisation (licence) for the medicinal product Canesten AF Bifonazole Once Daily Athlete's Foot Cream (PL 00010/0508). This product is indicated for the treatment of athlete's foot.

Canesten AF Bifonazole Once Daily Athlete's Foot Cream contains Bifonazole. Bifonazole is one of a group of medicines called Imidazole antifungals, which are used to treat fungal infections.

This is a simple abridged reclassification application submitted by BAYER PLC under Article 10.c, an informed consent application cross referring to Canesten AF Once Daily Bifonazole Cream (PL 00010/0103). The applicant has confirmed that this product is pharmaceutically identical to the cross referenced product in terms of qualitative and quantitative composition of active ingredients and excipients.

This application is associated with a P to GSL reclassification application.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of Canesten AF Bifonazole Once Daily Athlete's Foot Cream being available on general sale outweigh the risks, hence a Marketing Authorisation has been granted.

**CANESTEN AF BIFONAZOLE ONCE DAILY ATHLETES'S
FOOT CREAM**

PL 00010/0508

SCIENTIFIC DISCUSSION

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INTRODUCTION

The UK granted a marketing authorisation for the medicinal product Canesten AF Bifonazole Once Daily Athlete's Foot Cream (PL 00010/0508) to BAYER PLC on 28th November 2007. The product is a general sale list (GSL) medicine indicated for the treatment of athlete's foot.

The application was submitted as simple abridged application according to article 10(c) of Directive 2001/83/EC, cross-referring to Canesten AF Once Daily Bifonazole Cream (PL 00010/0103).

This application is associated with a P to GSL reclassification application.

No new quality data were submitted nor was it necessary for this simple abridged 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.

This product contains 1% bifonazole as the active ingredient. Bifonazole is a broad spectrum imidazole antifungal agent.

PHARMACEUTICAL ASSESSMENT

1. INTRODUCTION

An application has been received from BAYER PLC to reclassify Canesten AF Bifonazole Once Daily Athlete's Foot Cream from Pharmacy (P) to General Sale List (GSL) for the treatment of athlete's foot. This product contains bifonazole 1%, and is indicated for the treatment of athlete's foot. The reclassification request is linked to a simple abridged application, also submitted by Bayer PLC.

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

Bifonazole cream has been licensed in the UK since 1986. It was first available as a prescription only medicine (POM), with a subsequent legal reclassification to pharmacy (P) medicine in 1997. The POM indication is the treatment of fungal skin infections due to dermatophytes, yeasts, moulds and other fungi infections include ringworm infections, athlete's foot, and pityriasis versicolor. The P product is indicated only for the treatment of athlete's foot.

It was not considered necessary to seek CHM's advice on this application prior to consultation, for the following reasons:

- Athlete's foot is a condition that has already been accepted as suitable for self-diagnosis and self-treatment by the patient.
- Bifonazole has a similar activity and side effect profile to clotrimazole, an imidazole antifungal drug already available on general sale for the treatment of athlete's foot.
- The product has been available as a Pharmacy medicine for some years and there is no evidence of antifungal resistance or misuse of the product.

Preclinical, pharmaceutical and clinical expert statements have been provided together with CVs showing the experts are appropriately qualified. The experts confirm that the products are identical in composition, manufacture and pharmaceutical characteristics to the respective reference product and that there are no toxicological or clinical issues.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The proposed name of the product is Canesten AF Bifonazole Once Daily Athlete's Foot Cream.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

The product contains the active ingredient bifonazole 1% w/w. It will be packaged into aluminium tube with tube sealing and inner lacquer and polythene screw cap with pack sizes of 15g, 20g, 25g, and 30g. The proposed shelf life is 5 years with no special storage conditions.

2.3 Legal status

The product will be a General Sale List (GSL) medicine.

2.4 Marketing authorisation holder/Contact Persons/Company

The proposed Marketing Authorisation holder is BAYER PLC, BAYER Healthcare Consumer Care Division, BAYER House, Strawberry Hill, Newbury, Berkshire, RG14 1JA, United Kingdom

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

2.5 Manufacturers

The proposed manufacturing sites are consistent with that registered for the cross-reference product and evidence of GMP compliance has been provided.

2.6 Qualitative and quantitative composition

The proposed compositions are consistent with the details registered for the cross-reference products.

2.7 Manufacturing process

The proposed manufacturing process is consistent with the details registered for the cross-reference products 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 products.

2.9 Drug substance specification

The proposed drug substance specification conformed to current Ph Eur monograph for bifonazole and was consistent with that of the reference product.

Current Ph Eur certificate of suitability for drug substance manufacturer has been provided to support the source of active substance. This manufacturer is in line with the reference product.

2.10 Bioequivalence / Bioavailability

No bioavailability and bioequivalence data are required to support this informed consent application as the proposed product is manufactured to the same formula utilising the same process. The finished product manufacturing site is also identical to that used by the reference product.

3. EXPERT REPORTS

The applicant has included detailed expert reports of the application. Signed declarations and copies of the experts' CVs are enclosed 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 names. The appearance of the product is identical to the cross-reference products.

5. SUMMARY OF PRODUCT CHARACTERISTICS

The proposed SmPC is consistent with the details registered for the cross-reference product, apart from those differences which are directly related to the reclassification.

6. PATIENT INFORMATION LEAFLET/BLISTER

PIL

The PIL is in compliance with current guidelines and user testing results have been submitted. 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.

The proposed artwork complies with the relevant statutory requirements.

7. CONCLUSIONS

The data submitted with the application are acceptable. A Marketing Authorisation should be granted.

PRECLINICAL ASSESSMENT

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

CLINICAL ASSESSMENT

With respect to the simple abridged application, no new clinical data have been supplied with this application and none are required for an application of this type. With respect to the reclassification application, new data have been submitted to establish the suitability of the product for GSL supply.

ASSESSMENT OF RECLASSIFICATION APPLICATION

1. ASSESSMENT OF SUITABILITY FOR GSL STATUS

Section 51 of the Medicines Act 1968 states that "GSL may be appropriate for medicines which can, with reasonable safety be sold or supplied otherwise than by or under the supervision of a pharmacist". "Reasonable safety" may be usefully defined as "Where the hazard to health and the risk of misuse and the need for special precautions in handling are small, and where wider sale would be a convenience to the purchaser".

1.1 Hazard to Health

1.1.1 Suitability of Indication for GSL Availability

Tinea pedis (athlete's foot) is an easily recognisable condition and is currently recognised as a suitable indication for OTC use. Other GSL products are available for these indications.

1.1.2 Safety

The safety profile of topical bifonazole is well established. The applicant has estimated that around 118 million patients have used bifonazole cream 1% worldwide since 1988. In the UK bifonazole cream has been marketed, as a Pharmacy product, between 2002 and 2004, and during that time approximately 51000 units have been sold.

There have been very few adverse drug reaction reports associated with topical bifonazole use. According to the latest Periodic Safety Update Report (PSUR), PSUR 8, only 9 reports were classified as serious and unlisted. These cases do not highlight a need for change in the risk : benefit ratio and no new issues of concern for the safety of the drug.

In addition there have been no reactions reported on ADROIT for all bifonazole containing products which, as stated by the MAH, provides considerable reassurance regarding the safety of this active ingredient.

<p>Assessor's Comment: <i>There are no issues regarding safety that need to be considered with regards to this reclassification application.</i></p>

1.1.3 Antifungal Resistance

A concern of making any antimicrobial agent more widely available is the risk of increasing resistance of susceptible micro organisms to the agent. This may be of particular concern where a substance is used topically as well as orally.

The applicant has considered this issue in detail as part of the clinical expert report. There have been some reports of resistance to azoles, but these have been almost exclusively confined to systemic use of fluconazole in specific clinical settings. There has been no evidence to date of acquired resistance to topical antifungals, including bifonazole.

Bifonazole is currently only used topically, therefore if there was a risk of organisms becoming resistant following topical use, this would not put patients at risk that later required systemic treatment for systemic mycoses.

One reason for organisms becoming resistant to antimicrobial agents is inadequate treatment of the infection, leading to re-infection or relapse. As this product is only applied once daily then compliance is likely to be greater over many other topical antifungal agents. Therefore eradication of the causal organism is more likely to occur.

Assessor's Comments: *There is no evidence of any resistance issues regarding the topical use of bifonazole that would affect this application.*

1.2 Risk of Misuse

As stated previously, athlete's foot is currently recognised as a suitable indication for GSL status. Patients are able to self diagnose athlete's foot as this condition is well known and well understood. Even if the cream is used for inappropriate conditions, such as psoriasis, dermatitis, erythrasma and bacterial toe cleft, there is no evidence that it would cause harm to the patient.

The patient information leaflet advises the patient that they should consult their doctor if there is no improvement in symptoms within 7 days. The patient is also advised that they should continue treatment for only two to three weeks. However, it is unlikely that treatment for longer than instructed would result in increased hazard.

Assessor's Comment: *The patient information leaflet (PIL) should be revised to include a more detailed description of the symptoms of athlete's foot to aid the patient in correct self-diagnosis. It should also include a statement that the patient should consult their doctor or pharmacist if they are unsure as to the cause of their infection.*

1.3 Need for Special Precautions in Handling

There are no requirements for special precautions in handling associated with topical bifonazole use.

1.4 Wider Sale would be a Convenience to the Purchaser

The majority of athlete's foot treatments are already purchased as GSL medicines. Widening the choice to include an additional product which is effective in treating this condition will be beneficial to sufferers. As this product only requires application once daily, compliance is likely to be good and thus there is greater chance that the infection will be cleared and relapse avoided.

2. DISCUSSION

Athlete's foot is a very common fungal infection which, whilst not serious, can be extremely uncomfortable for sufferers. It has been recognised for a number of years as a suitable indication for GSL status and can be easily recognised and self diagnosed.

Bifonazole is a highly effective antifungal agent which only requires administration once a day. This is likely to aid compliance and reduce the risk of incomplete treatment and occurrence of relapse.

The safety of this product is well established and the side effects are principally local reactions. This product has been available as Pharmacy medicine for a number of years now and there is no evidence of antifungal resistance or misuse of the product.

Label and leaflet instructions are clear, and the patients are advised to consult a doctor if there is no improvement within seven days. However, the PIL should be updated as mentioned above to ensure correct self diagnosis.

3. CONSULTATION

Consultation document ARM 40, which summarises the proposals for GSL supply of bifonazole 1% cream, was posted on the MHRA website on 12 February 2007. The deadline for comments was given as 26 March 2007.

Sixteen responses to consultation were received. Of the 16 responses, 3 supported the proposal, 5 supported it but expressed some concerns, 4 were opposed to it and 4 made no comment. A more detailed discussion of the responses follows.

3.1 General concerns

General concerns about the unsupervised sale of medicines were voiced by the Royal Pharmaceutical Society of Great Britain (RPSGB), the National Pharmacy Association (NPA), the Pharmaceutical Society of Northern Ireland and the Scottish Pharmaceutical General Council. These respondents consider that the issue of convenience is not of importance since there is an extensive network of pharmacies throughout the country. They consider that a patient seeking OTC treatment is best served by having access to a health professional, such as a pharmacist.

Assessor's comment

These arguments do not relate specifically to the product in question. The unsupervised supply of medicines through general sale outlets has been established for many years now.

3.2 Safety in use

The directions for use recommend a treatment period of 2 -3 weeks, and advise the patient to consult a doctor or pharmacist if there is no improvement in 7 days. The RPSGB are concerned that the length of treatment may cause problems of local irritation or hypersensitivity, and that there is no indication of how a patient may measure improvement.

Assessor's comment

The recommended length of treatment is broadly consistent with other OTC topical products containing an imidazole (clotrimazole, miconazole). The leaflet advises the patient to stop using the product if a rash occurs or the itching gets worse, i.e. if the patient experiences an allergic reaction. The leaflet also describes the symptoms that should improve within a few days and those that may take longer.

The RPSGB were concerned that symptoms of a more serious foot problem (such as cellulitis or cancer) may be overlooked or masked.

Assessor's comment

The leaflet advises the patient not to use the product unless they are sure that the condition they have is athlete's foot. It also advises the patient to consult a doctor or pharmacist if symptoms do not improve in 7 days. These warnings should help prevent masking of symptoms of a more serious condition. Other GSL products for treating athlete's foot have been available for some time without any apparent problems.

Two respondents were concerned that the 'Canesten' name, which was originally associated with the active ingredient clotrimazole, might lead to confusion and possible inappropriate use, if applied to a bifonazole-containing product.

Assessor's comment

'Canesten' has already been accepted as an 'umbrella' name, and is applied to products containing fluconazole, terbinafine or sodium citrate, as well as those containing clotrimazole. The proposed product name includes the word 'bifonazole' in order to provide some differentiation from other Canesten products. In the event that a bifonazole product was unintentionally used instead of a clotrimazole product, then it is unlikely that the patient would suffer harm since the action of the two drugs is very similar and both have similar indications for use.

3.3 Resistance

This was an issue raised by some respondents. One considered that, because bifonazole is an antimicrobial substance, its availability should be limited not increased; presumably this view was related to concerns about resistance. Another respondent commented on the absence of any reference to resistance in the consultation document. The British Society for Antimicrobial Chemotherapy considered that neither the product nor the setting had potential for serious harm; they did have concerns about resistance, however, and recommended that the MHRA review the available evidence relating to resistance prior to reclassifying bifonazole cream.

Assessor's comment

The consultation document did not discuss the issue of resistance and it is understandable that respondents may have thought that this aspect had not been considered at all. The clinical expert report, submitted as part of the reclassification application, discussed the issue in some depth. There have been some reports of resistance to azoles, but these have been almost exclusively confined to systemic use of fluconazole in specific clinical settings. There has been no evidence to date of acquired resistance to topical antifungals, including bifonazole. Bifonazole is currently only used topically, therefore if there was a risk of organisms becoming resistant following topical use, this would not put patients at risk that later required systemic treatment for systemic mycoses. The clinical expert concluded that acquired resistance is unlikely to emerge as a problem with topical bifonazole used to treat athlete's foot.

3.4 Product information

Some suggestions were made to improve the patient information leaflet:

- The patient should be advised not to use the product if unsure of the diagnosis
- The statement 'no special storage precautions are required' may lead to storage at extremes of temperature
- The self-help tips currently in the leaflet should be highlighted
- Typical symptoms of an allergic reaction should be given
- A clearer definition of 'intolerable' should be given

Assessor's comment

The leaflet already includes a warning not to use the product if unsure of the diagnosis; the warning could, however, be moved to the 'Do not use if' section for greater prominence. The statement, that there are no special storage precautions, is consistent with the SPC. The recommendations made in the last three bullet points above will be taken forward.

3.5 Miscellaneous

One respondent suggested that the medicine is ineffective. Another wished there to be a specific requirement that advertisements for the product state that further advice is available from the pharmacist.

Assessor's comment

Efficacy of bifonazole 1% cream in the proposed indication was established when the original product licence was granted. Regarding advertisements for the product, there is currently no requirement for GSL products to state that further advice is available from the pharmacist.

4. CONCLUSION

No new issues were identified during consultation. Canesten AF Bifonazole Once Daily Athlete's Foot Cream containing bifonazole 1% is considered suitable for supply as a GSL medicine for the treatment of athlete's foot in a maximum pack size of 30g.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The data for this application are consistent with those 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 application of this type.

EFFICACY

The applicant has confirmed that this product is pharmaceutically identical to the cross referenced product in terms of qualitative and quantitative composition of active ingredients and excipients.

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, with appropriate amendments to take into account the reclassification of the product.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Suitable justification has been provided for the reclassification of this product from Pharmacy (P) to General Sale List (GSL). GSL supply of the product is considered to be acceptably safe when supplied and used as recommended. 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.

STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the marketing authorisation application and the reclassification application on 14/12/2005.
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 05/01/2006.
3	Following assessment of the applications the MHRA requested further information on 26/10/2006, 20/11/06, 1/3/07, 23/3/07, 18/5/07, 8/6/07, 28/8/07 and 11/10/07.
4	The applicant responded to the MHRA's requests, providing further information on 6/11/06, 8/12/06, 6/3/07, 29/3/07, 1/6/07, 2/7/07, 13/8/07, 12/9/07 and 5/11/07.
5	A public consultation exercise (ARM 40) was carried out between 12/2/07 and 26/3/07.
6	The application was determined on 28/11/2007

SUMMARY OF PRODUCT CHARACTERISTICS

- 1 NAME OF THE MEDICINAL PRODUCT**
Canesten AF Bifonazole Once Daily Athlete's Foot Cream

- 2 QUALITATIVE AND QUANTITATIVE COMPOSITION**
The cream contains 1% w/w bifonazole.

- 3 PHARMACEUTICAL FORM**
A white cream.

- 4 CLINICAL PARTICULARS**
 - 4.1 Therapeutic indications**
Bifonazole is a broad spectrum antifungal agent.
Treatment of athlete's foot.
The preparation is not for vaginal use.

 - 4.2 Posology and method of administration**
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.

A physician or pharmacist should be consulted if symptoms do not improve within seven days.

 - 4.3 Contraindications**
History of hypersensitivity to imidazole antifungal agents or any of the excipients.
Treatment of infants with nappy rash.
Treatment of nail and scalp infections.

 - 4.4 Special warnings and precautions for use**
This product contains cetostearyl alcohol which may cause local skin reactions (e.g. contact dermatitis).

If unsure of the diagnosis, the patient should seek the advice of a doctor or pharmacist before using the product.

 - 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 a 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 (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

None

6.5 Nature and contents of container

Aluminium tubes containing 15g, 20g, 25g or 30g of cream.

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

Bayer plc, Trading as Bayer plc, Consumer Care Division

Bayer House

Strawberry Hill

Newbury

Berkshire

RG14 1JA.

8 MARKETING AUTHORISATION NUMBER(S)

PL 00010/0508

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28/11/2007

10 DATE OF REVISION OF THE TEXT

28/11/2007

PATIENT INFORMATION LEAFLET




Canesten[®] AF



Bifonazole
Once Daily
Athlete's Foot Cream
Bifonazole 1% w/w

PATIENT INFORMATION LEAFLET

**PLEASE READ THIS LEAFLET CAREFULLY
BEFORE USING CANESTEN[®] AF BIFONAZOLE
ONCE DAILY ATHLETE'S FOOT CREAM.**



Canesten AF Bifonazole Once Daily Athlete's Foot Cream contains Bifonazole. Bifonazole is one of a group of medicines called imidazole antifungals, which are used to treat fungal infections.

What is Canesten[®] AF Bifonazole Once Daily Athlete's Foot Cream?

This cream should only be used to treat athlete's foot.

What is Athlete's foot?

Athlete's foot is the common name for the fungal infection tinea pedis. It is caused by a group of fungi called dermatophytes. The name "athlete's foot" arose because this is an infection which is commonly, although not exclusively, suffered by people whose feet perspire or who use communal changing rooms.

Athlete's foot is highly contagious and infected skin shed on changing room floors or on towels can easily transfer the infection. The discomfort caused by the infection can be made worse by wearing shoes, particularly if they are made from synthetic materials which do not allow the feet to "breathe". The key triggers of athlete's foot include warmth, moisture and friction. The latter can damage the tissue allowing the fungus to take hold.

Tell-tale signs of athlete's foot are that the skin between your toes becomes flaky, itchy, red and inflamed. If you are unsure whether you have athlete's foot, seek the advice of your doctor or pharmacist.

When not to use Canesten[®] AF Bifonazole Once Daily Athlete's Foot Cream?

Do not use this cream if you have previously had an allergic reaction to bifonazole or another antifungal imidazole, or if you are allergic to any of the other ingredients in this product. An allergic reaction could be a rash or a very itchy skin. If you are unsure about this, ask your doctor or pharmacist.

Do not use this cream to treat nappy rash, vaginal infections, or nail and scalp infections.

Do not use this cream if you are unsure whether you have athlete's foot. Speak to your doctor or pharmacist first.

What special precautions should be taken?

If you are pregnant, trying for a baby or breast-feeding, tell your doctor before using the cream. If you have already informed your doctor, follow his/her instructions carefully.

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

When and how to use Canesten[®] AF Bifonazole Once Daily Athlete's Foot Cream?

- Before use, pierce the tube seal by inverting the cap over the end of the tube and press.
- Wash your feet and dry them thoroughly, especially between the toes, before applying the cream. Avoid excessive rubbing of the area to be treated.
- Apply the cream thinly and evenly over the affected area once a day and rub in gently. If possible, apply the cream at night before going to bed.
- Treatment should be continued for 2 - 3 weeks.

Some symptoms of athlete's foot, such as itching or soreness, should improve within a few days of treatment although symptoms such as redness and scaling may take longer to disappear.

Consult your doctor or pharmacist if symptoms do not improve within 7 days.

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

- Wash your socks, stockings or tights thoroughly in hot water to remove any shed skin or fungal spores.
- Wash your feet every day in warm, soapy water and dry thoroughly, especially between the toes but avoid excessive rubbing.
- Although your feet and toes will itch, do not scratch them. Scratching will damage the surface of the skin and cause the infection to spread further.
- Never share towels or bath mats.
- Change your socks, stockings or tights every day.

The cream is for external use only and should not be put in the mouth or swallowed. If it is swallowed accidentally, seek medical advice immediately. If the cream gets in your eyes accidentally, wash your eyes immediately and contact your doctor.

What should I do if I forget to use the cream?

Apply the cream as soon as possible and then continue the rest of your treatment as usual.

What side effects may I experience?

As with other medicines, the cream may cause side-effects in some people. You may experience a mild burning or irritation immediately after applying the cream. If this becomes unbearable, stop treatment and ask your doctor or pharmacist for advice.

If you experience a rash or the itching worsens soon after you start using the cream, stop using it and tell your doctor or pharmacist immediately as you may be allergic to this product.

If your symptoms get worse or persist, or you feel you are reacting badly to this medicine in any other way, consult your doctor or pharmacist.

How should I store my cream?

No special storage precautions are required.

Keep out of the reach and sight of children.

Do not use the cream after the expiry date which is printed on the end of the carton and on the end of the tube.

If you find that you still have this medicine after its expiry date, return it to your pharmacist, who will dispose of it properly.

Remember:

If you have any doubts about using your medicine correctly, seek the advice of your pharmacist.

What does Canesten® AF Bifonazole Once Daily Athlete's Foot Cream contain?

The cream contains 1% w/w of the active ingredient bifonazole. It also contains sorbitan stearate, polysorbate 60, cetyl palmitate, cetostearyl alcohol, 2-octyldodecanol, benzyl alcohol and water.

The cream comes in 15g, 20g, 25g and 30g tubes. Not all pack sizes may be marketed.

Marketing authorisation holder:

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

Manufacturer:

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

Date of preparation of leaflet: August 2007



Bayer

LABELLING

<p>Canesten® AF</p> <p>Bifonazole Once Daily</p> <p>Athlete's Foot Cream Bifonazole 1% w/w</p>  		
<p>Keep out of the reach and sight of children. No special storage precautions are required. Apply the cream thinly to the affected areas once daily and rub in gently, preferably at night before retiring, for two to three weeks. If no improvement is seen after 7 days consult your doctor or pharmacist.</p> <p>Bayer</p> <p>FOR EXTERNAL USE ONLY</p>	<p>One 15g tube of cream contains Bifonazole 1% w/w. It also contains sorbitan stearate, polysorbate 60, cetyl palmitate, cetostearyl alcohol, 2-octyldodecanol, benzyl alcohol and purified water.</p> <p>MA Holder: Bayer plc, Consumer Care Division, Newbury, Berkshire, RG14 1JA, U.K. PL 00010/0508</p> <p>15g</p>	<p>Expiry Date</p> <p>Batch No.</p> 



The flat label layout shows the following components:

- Top Panel:** Contains the product name 'Canesten® AF', 'Bifonazole Once Daily', 'Athlete's Foot Cream Bifonazole 1% w/w', the Bayer logo, and a footprint icon.
- Bottom Panel:** Contains the product name 'Canesten® AF', 'Bifonazole Once Daily', 'Athlete's Foot Cream Bifonazole 1% w/w', the Bayer logo, and a footprint icon.
- Back Panel:** Contains detailed usage instructions, a list of ingredients, and a barcode.
- Side Panel:** Contains the product name 'Canesten® AF', 'Bifonazole Once Daily', 'Athlete's Foot Cream Bifonazole 1% w/w', and the Bayer logo.
- Internal Panel:** Contains the Bayer logo, '15g', 'FOR EXTERNAL USE ONLY', and 'MA Holder: Bayer plc Consumer Care Division RG14 1JA, U.K. PL 00010/0508'.
- Bottom Left Panel:** Contains 'Keep out of the reach and sight of children. 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. Bayer'.
- Bottom Right Panel:** Contains 'Do not use this cream: If no improvement is seen after 7 days consult your doctor or pharmacist. Directions: Wash and dry the feet, then apply the cream thinly to the affected area once daily, preferably at night before retiring, for two to three weeks. If no improvement is seen after 7 days consult your doctor or pharmacist. Keep out of the reach and sight of children. Please read the enclosed leaflet carefully. Allergic to any of the other ingredients in this product. If you are unsure about this, ask your doctor or pharmacist. If you have previously had an allergic reaction to bifonazole or another antifungal imidazole, or if you are unsure whether you have Athlete's Foot, you should ask your doctor or pharmacist. * To treat vaginal infections. * To treat nail and scalp infections. * To treat nappy rash. * To treat athlete's foot, you should ask your doctor or pharmacist. © = Registered Mark of Bayer AG, Germany'.



<p>Canesten® AF</p> <p>Bifonazole Once Daily Athlete's Foot Cream Bifonazole 1% w/w</p>  		
<p>Keep out of the reach and sight of children. No special storage precautions are required. Apply the cream thinly to the affected areas once daily and rub in gently, preferably at night before retiring, for two to three weeks. If no improvement is seen after 7 days consult your doctor or pharmacist.</p> <p>Bayer</p> <p>FOR EXTERNAL USE ONLY</p>	<p>One 30g tube of cream contains Bifonazole 1% w/w. It also contains sorbitan stearate, polysorbate 60, cetyl palmitate, cetostearyl alcohol, 2-octyldodecanol, benzyl alcohol and purified water.</p> <p>MA Holder: Bayer plc, Consumer Care Division, Newbury, Berkshire, RG14 1JA, U.K. PL 00010/0508</p> <p>30g</p>	<p>Expiry Date</p> <p>Batch No.</p> 



Canesten® AF
Bifonazole
Once Daily
Athlete's Foot Cream
Bifonazole 1% w/w

Canesten® AF
Bifonazole
Once Daily
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Canesten® AF
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Once Daily
Athlete's Foot Cream
Bifonazole 1% w/w

30g

FOR EXTERNAL USE ONLY

Canesten® AF
MA Holder: Bayer plc Consumer Care Division RG14 1JA, U.K. PL 00010/0508

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

Directions: Wash and dry the feet, then apply the cream thinly to the affected area once daily preferably at night before retiring, for two to three weeks. If symptoms persist consult your doctor or pharmacist.
Keep out of the reach and sight of children. Please read the enclosed leaflet carefully.
If no improvement is seen after 7 days consult your doctor or pharmacist.
Do not use the cream:
• if you have previously had an allergic reaction to bifonazole or another antifungal imidazole, or if you are allergic to any of the other ingredients in this product. If you are unsure about this, ask your doctor or pharmacist.
• to treat vaginal infections.
• to treat nappy rash.
• to treat nail and scalp infections.
If you are unsure whether you have Athlete's Foot you should ask your doctor or pharmacist.

Expiry Date

Batch No.

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