

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

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

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The cream contains 1% w/w bifonazole.

Excipients with known effect:

Cetostearyl alcohol 100mg in each gram of cream
Benzyl alcohol 20mg in each gram of cream.

For excipients see section 6.1.

3 PHARMACEUTICAL FORM

A white cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

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). The cream also contains benzyl alcohol which may cause allergic reactions and mild local irritation.

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

Patients with a history of hypersensitivity reactions to other imidazole antifungal agents (e.g. econazole, clotrimazole, miconazole) must take bifonazole-containing products with caution.

4.5 Interaction with other medicinal products and other forms of interaction

Limited data suggest that an interaction between topical bifonazole and warfarin may be possible, leading to increases in INR. If bifonazole is used in a patient on warfarin therapy they should be appropriately monitored.

Closer monitoring may be required in cases of occlusion and/or application to a large surface area or to broken and damaged skin.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no clinical data from the use of bifonazole in pregnant women. Studies in animals have shown reproductive toxicity at high oral doses (see section 5.3) however these effects should not be anticipated at the low systemic exposures observed following topical bifonazole administration (see section 5.2).

Bifonazole should only be used during pregnancy after an evaluation by a doctor of the benefit to the patient and the risk to the fetus.

Lactation

It is unknown whether bifonazole is excreted in human breast milk after topical application.

Bifonazole is excreted in milk after intravenous administration in animals (see section 5.3).

A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue bifonazole therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

During the lactation period bifonazole should not be applied to the chest area.

Fertility

Preclinical studies gave no evidence that bifonazole can impair male or female fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Bifonazole cream has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

- Immune system disorders

Very rarely, systemic hypersensitivity reactions may occur.

The following adverse drug reactions are based on spontaneous reports, thus the frequency of individual events is not known (cannot be estimated from data).

- General disorders and administration site conditions

Administration site pain, oedema peripheral (at administration site)

- Skin and subcutaneous tissue disorders

Dermatitis contact, dermatitis allergic, erythema, pruritus, rash, urticaria, blister, skin exfoliation, eczema, dry skin, skin irritation, skin maceration, skin burning sensation

These side effects are reversible after discontinuation of the treatment.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at:

www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

No risk of acute intoxication is seen as it is unlikely to occur following a single dermal application of an overdose (application over a large area under conditions favorable to absorption) or inadvertent oral ingestion.

However, in the event of accidental oral ingestion, routine measures such as gastric lavage should be performed only if clinical symptoms of overdose become apparent (e.g. dizziness, nausea or vomiting). Gastric lavage should be carried out only if the airway can be protected adequately.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifungals for dermatological use – Bifonazole

ATC Code: D01A C10

Bifonazole is an imidazole derivative with a broad antimycotic spectrum, which includes dermatophytes, yeasts, moulds and other fungi such as *Malassezia furfur*. It is also effective against *Corynebacterium minutissimum*.

Bifonazole exerts its anti-fungal action by inhibiting the biosynthesis of ergosterol on two different levels. Inhibition of ergosterol synthesis leads to structural and functional impairment of the cytoplasmic membrane.

The resistance situation for bifonazole is favourable. Primary resistant variants of sensitive fungal species are very rare. Investigations so far did not provide any evidence of a development of secondary resistance in primarily sensitive strains.

5.2 Pharmacokinetic properties

Absorption

Bifonazole penetrates well into infected skin layers. 6 hours after administration concentrations in the various skin layers reach from 1000 µg/cm³ in the top layer of the epidermis (stratum corneum) to 5 µg/cm³ in the stratum papillare. All concentrations determined are thus within a range of reliable antimycotic activity.

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

Elimination of the metabolites is biphasic (T_½ 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 of topical formulations. With bifonazole cream and solution slight skin irritant effects were observed which could be attributed to the excipients 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.

Preclinical data on oral dosage forms reveal no special hazards for humans based on conventional studies of single dose toxicity and genotoxicity. Effects on the liver (enzyme induction, fatty degeneration) were observed in repeated dose toxicity studies with oral administration but only at exposures in excess of the maximum human exposure indicating little relevance to clinical use. No carcinogenicity studies were performed with bifonazole.

In reproduction toxicology studies in rats and rabbits, oral doses of 30 mg/kg body weight resulted in embryotoxicity including lethality. In the rats, bifonazole at oral doses up to 100 mg/kg body weight was not embryotoxic, but a retarded skeletal development in the fetuses was observed at the dose of 100 mg/kg. This fetal effect on the skeletal development can be considered as a secondary effect resulting from the maternal toxicity (a reduction in body weight).

Given the low absorption of the active ingredient via the skin these results have little relevance to clinical use. In a study of lactating rats treated with radioactively labelled bifonazole (10 mg/kg body weight intravenous), approximately 3.2% of the dose was excreted in the milk. In another study of radioactively labelled bifonazole, it was found that intravenously administered bifonazole (10mg/kg body weight) passes through the placental barrier in rats.

No impairment of male or female fertility was observed in rats at oral doses up to 40 mg/kg body weight.

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
400 South Oak Way
Reading
RG2 6AD

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

27/11/2020