Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Canespor 10 mg/g Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains bifonazole 1% w/w. 1 g of cream contains 10 mg bifonazole.

Excipient(s) with known effect
Cetostearyl alcohol 100 mg/g
Benzyl alcohol 20mg/g

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream

White cream

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Canespor 10mg/g Cream is indicated in adults for the treatment of tinea pedis including treatment of an exposed nailbed following keratolytic removal of the nail.

4.2 Posology and method of administration

Posology

To achieve a lasting cure, treatment with Canespor Cream must be carried out reliably and over an adequate period. The usual periods of treatment are summarized in the table below:

Indication	**Duration of treatment**
Tinea pedis (Athlete's Foot))	3 weeks
Antimycotic treatment of the nail bed after keratolytic removal of the nail	4 weeks

Paediatric population

Canespor Cream should only be used on infants and children under medical supervision.

Method of administration

Canespor Cream is used once a day, preferably in the evening, before retiring. It should be applied thinly to the affected skin area and rubbed in gently.

A small amount of cream is generally sufficient to treat an area of about the size of the palm of hand.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

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

Antimycotic treatment of the skin of the nail bed with Canespor Cream can only be carried out after keratolytic removal of the infected nail.

If symptoms worsen or persist after the recommended duration of treatment, medical advice should be sought.

This product contains benzyl alcohol which may cause mild local irritation.

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

Patients on warfarin therapy should be monitored when bifonazole is used concomitantly (see section 4.5)

Diabetic patients should seek medical advice before using Canespor Cream due to the potential risk of a more severe course of infection.

Do not use occlusive bandages in the affected skin area after the application of Canespor 10mg/g Cream.

Absorption of orally administered imidazole antimycotics may lead systemic toxicity. Studies with bifonazole suggest a low level of absorption after topical application to healthy skin. The preparation should only be used with care on areas of denuded or broken skin.

Avoid contact with the eyes. Do not swallow.

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 Canespor Cream is used in a patient on anticoagulant therapy, such as warfarin, caution should be exercised and the anticoagulant effect should be monitored (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of bifonazole in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). Canespor cream is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding
It is unknown whether bifonazole is excreted in human milk.
Available pharmacodynamic/ toxicological data in animals have shown excretion of bifonazole/metabolites in milk (for details see 5.3). A risk to newborns/infants cannot be excluded. Canespor 10 mg/g Cream should not be used during breast-feeding.

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

Canespor Cream has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

Frequencies of side-effects observed in clinical studies are defined according to the MedDRA frequency convention: very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000); very rare (< 1/10,000), not known (frequency cannot be estimated from the available data). The adverse reactions designated as frequency 'not known' have been identified during post-approval use of bifonazole. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency.

General disorders and administration site conditions
Uncommon: localized oedema (peripheral)
Not known: administration site pain

Immune system disorders
Not known: allergic dermatitis/hypersensitivity

Skin and subcutaneous tissue disorders
Very common: burning skin/burning sensation.
Uncommon: erythema, eczema, (skin) irritation and pruritus.

Not known: dermatitis contact, rash, urticaria, blister, skin exfoliation, dry skin, skin maceration.

These side effects are generally 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Absorption of orally administered imidazole antimycotics may lead to systemic toxicity. Studies with bifonazole suggest a low level of absorption after topical application to healthy skin. The preparation should only be used with care on areas of denuded or broken skin.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifungals for topical use – imidazole and triazole derivatives ATC code: D01AC10.

Bifonazole is an imidazole derivative which is active against fungi such as dermatophytes.

Bifonazole exerts its anti-fungal action by inhibiting the biosynthesis of ergosterol on two different levels, thereby distinguishing bifonazole both from other azole derivatives and from other anti-fungals which act only on a single level. 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/cm^3 in the top layer of the epidermis (stratum corneum) to 5 μg/cm^3 in the stratum papillare.

Pharmacokinetic investigations after topical application to intact human skin have shown that only a small amount of bifonazole is absorbed (0.6-0.8% of the dose); the resulting serum concentrations were usually below the detection limit (i.e. < 1 ng/mL). Higher absorption was observed after application to inflamed skin (2-4% of the respective dose).

5.3 Preclinical safety data

Preclinical data 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. Both *in vitro* and *in vivo* tests for detection of gene mutation did not demonstrate genotoxic activity.

In reproduction toxicology studies in 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 effects resulting from the maternal toxicity (a reduction in body weight). Given the low absorption of the active ingredient via the skin, the relevance of these findings to clinical use is unknown. No impairment of male or female fertility was observed in rats at oral doses up to 40 mg/kg body weight.

Bifonazole passes through the placental barrier in rats. A study with lactating rats administered bifonazole intravenously showed that the drug was secreted into milk.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Cetostearyl alcohol
Cetyl palmitate
Octyldodecanol
Polysorbate 60
Purified water
Sorbitan stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.
After opening, Canespor Cream can be used for up to 16 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 tube with inner lacquer (epoxy phenolic resin) and polyethylene (PE) screw cap. A membrane is also included to guarantee the first opening of the tube.

Pack sizes of 20 g or 30 g

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Bayer Limited
The Atrium
Blackthorn Road
Dublin 18
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1410/083/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9th March 2018

10 DATE OF REVISION OF THE TEXT