Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Canesten Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of cream contains 10mg Clotrimazole equivalent to 1% w/w.

Excipients with known effect:
Cetostearyl alcohol 100mg in each gram of cream
Benzyl alcohol 20mg in each gram of cream

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream
A white oil-in-water type cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

A broad spectrum antifungal for use in the topical treatment of infections due to superficial dermatophytes, Candida species and other fungi sensitive to the anti-infective: Staphylococcus and Bacteroides. The drug has no effect on Lactobacilli.

4.2 Posology and method of administration

Canesten Cream should be applied to the affected area 2 or 3 times daily. To prevent relapse, treatment should be continued for at least two weeks after the disappearance of all signs of infection.

Patients should notify their physician if there is no improvement after 4 weeks of treatment.

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

All possibly infected areas should be treated at the same time.

This product contains cetostearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis). The product also contains benzyl alcohol which may cause allergic reactions and mild local irritation.

Avoid contact with eyes and do not swallow.

4.5 Interaction with other medicinal products and other forms of interaction

Laboratory tests have suggested that, when used together, this product may cause damage to latex contraceptives. Consequently the effectiveness of such contraceptives may be reduced. Patients should be advised to use alternative precautions for at least five days after using this product.

4.6 Fertility, pregnancy and lactation

Pregnancy:

There are limited data available from the use of clotrimazole in pregnant women. Animal studies with clotrimazole have shown reproductive toxicity at high oral doses (see section 5.3). At the low systemic exposures of clotrimazole following topical treatment, harmful effects are considered unlikely. Clotrimazole can be used during pregnancy, but only under the direction of a doctor or midwife.

Lactation:
There are no data on the excretion of clotrimazole into human milk. However, systemic absorption is minimal after administration and it is unlikely to lead to systemic effects. Clotrimazole may be used during lactation under medical supervision. If used topically on the nipple area, the area should be washed well before feeding child.

Fertility:
No human studies of the effects of clotrimazole on fertility have been performed, however, animal studies have not demonstrated any effects of the drug on fertility (See Section 5.3).

4.7 Effects on ability to drive and use machines

The medication has no or negligible influence on the ability to drive or use machinery.

4.8 Undesirable effects

The following adverse reactions have been identified during post-approval use of Clotrimazole. Because these reactions are reported voluntarily from a population of uncertain size, frequency cannot be estimated from the available data.

Immune system disorders: anaphylactic reactions, angioedema, hypersensitivity, Allergic reaction (ME) (with symptoms such as urticaria (ME), dyspnoea (PT), hypotension (PT) and syncope (PT)).

Skin and subcutaneous tissue disorders:
blister, dermatitis contact, erythema, paraesthesia, skin exfoliation, pruritus, rash, stinging skin /burning sensation skin.

General disorders and administration site conditions: application site irritation, application site reaction, oedema, pain.

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, Website: www.hpra.ie.

4.9 Overdose

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).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifungals for topical use – imidazole and triazole derivates.

ATC Code: D01A C01

Mechanism of Action
Clotrimazole acts against fungi by inhibiting ergosterol synthesis. Inhibition of ergosterol synthesis leads to structural and functional impairment of the cytoplasmic membrane.

Pharmacodynamic Effects:
Clotrimazole has a broad antimycotic spectrum of action *in vitro* and *in vivo*, which includes dermatophytes, yeasts, moulds, etc.

Under appropriate test conditions, the MIC values for these types of fungi are in the region of less than 0.062 – 8.0 microgram/ml substrate. The mode of action of clotrimazole is fungistatic or fungicidal depending on the concentration of clotrimazole at the site of infection. *In-vitro* activity is limited to proliferating fungal elements; fungal spores are only slightly sensitive.

In addition to its antimycotic action, clotrimazole also acts on, gram-positive microorganisms (streptococci/staphylococci/ Gardnerella vagiinalis) and gram-negative microorganisms (Bacteroides). It has no effect on Lactobacilli.

In vitro, clotrimazole inhibits the multiplication of Corynebacteria and gram-positive cocci – with the exception of enterococci – in concentrations of 0.5 – 10 microgram/ml substrate.

Primarily resistant variants of sensitive fungal species are very rare; the development of secondary resistance by sensitive fungi has so far only been observed in very isolated cases under therapeutic conditions.

5.2 Pharmacokinetic properties

Pharmacokinetic investigations after dermal application have shown that clotrimazole is minimally absorbed from the intact or inflamed skin into the human blood circulation. The resulting peak serum concentrations of clotrimazole were below the detection limit of 0.001µg/ml, suggesting that clotrimazole applied topically on the skin is unlikely to lead to measurable systemic effects or side effects.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction and development.

The local and systemic tolerance of clotrimazole in different dosage forms was assessed in subacute dermal studies in rabbits. There was no evidence of treatment-related local or systemic adverse effects in any of these studies.

The oral toxicity of clotrimazole has been well-studied.

Following a single oral administration, clotrimazole was slightly-to-moderately toxic in experimental animals, with LD50 values of 761 to 923 mg/kg bw for mice, 95 to 114 mg/kg bw for newborn rats and 114 to 718 mg/kg bw for adult rats, > 1000 mg/kg bw for rabbits, and > 2000 mg/kg bw for dogs and cats.

In repeated dose oral studies conducted in rats and dogs, the liver was found to be the primary target organ for toxicity. This was evidenced by an increase in serum transaminase activities and the appearance of liver vacuolation and fatty deposits starting at 50 mg/kg in the chronic (78-week) rat study and at 100 mg/kg in the subchronic (13-week) dog study.

Clotrimazole has been extensively studied in in vitro and in vivo mutagenicity assays, and no evidence of mutagenic potential was found. A 78-week oral dosing study of clotrimazole in rats did not show any carcinogenic effect.

In a rat fertility study, groups of FB30 rats received oral doses of clotrimazole up to 50 mg/kg bw, for 10 weeks prior to mating and either throughout a 3-week mating period (for males only) or, for females, until day 13 of gestation or 4-week postpartum. Neonatal survival was reduced in 50 mg/kg bw group. Clotrimazole at doses up to 25 mg/kg bw did not impair the development of the pups. Clotrimazole at all doses did not affect fertility.

No teratogencity effects were demonstrated in studies in mice, rabbits, and rats, given oral doses of up to 200, 180, and 100 mg/kg, respectively.

A study with 3 lactating rats administered 30 mg/kg clotrimazole intravenously showed that the drug was secreted into milk at levels higher than in plasma by a factor of 10 to 20 at 4 hrs after administration, followed by a decline to a factor of 0.4 by 24 hrs.

Given the limited systemic absorption of the drug after topical administration, no hazard is expected from the use of topical clotrimazole.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitan Stearate
Polysorbate 60
Cetyl Palmitate
Cetostearyl alcohol
Octyldodecanol
Benzyl alcohol
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Aluminium tubes with internal lacquer coating and HPDE screw-on caps containing a smooth white oil-in-water type cream supplied in 20g and 50g presentations.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

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.

6.6 Special precautions for disposal and other handling

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

7 MARKETING AUTHORISATION HOLDER

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10 DATE OF REVISION OF THE TEXT

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