A Division of Bayer East Africa Ltd

NAME OF THE MEDICINAL PRODUCT

Canesten

QUALITATIVE AND QUANTITATIVE COMPOSITION

(in terms of the active ingredient)

Qualitative composition in terms of the active ingredient(s) (INN):

all formulations: clotrimazole

Canesten cream: 1 g cream contains 10 mg clotrimazole

PHARMACEUTICAL FORM

Cutaneous cream

CLINICAL PARTICULARS

Therapeutic Indications

Cream:
Dermatomycoses caused by dermatophytes, yeasts, moulds, etc. (e.g. tinea pedum, tinea manuum, tinea corporis, tinea inguinalis, pityriasis versicolor, cutaneous candidiasis) and erythrasma.

In females fungal infections of the labia and adjacent areas , and in males inflammation of the glans and prepuce of the penis caused by yeast fungi (candidal vulvitis and candidal balanitis).

Posology and Method of Administration

Posology

To insure complete healing depending on the indication the treatment should be continued according to the indications as specified below (see 'Treatment duration') even if symptoms disappear.

Treatment duration

Dermatomycoses	3-4 weeks
Erythrasma	2-4 weeks
Pityriasis versicolor	1-3 weeks
Candida vulvitis and Candida balanitis	1-2 weeks

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

Clotrimazole cream:
The cream is applied thinly 2-3 times a day and gently rubbed in. A strip of cream (½ cm long) is enough to treat an area of about the size of the hand.

Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1

Special Warnings and Precautions for Use

Clotrimazole cream may reduce the effectiveness and safety of latex products such as condoms and diaphragms when applied on the genital area (women: labia and adjacent area of the vulva; men: prepuce and glans of the penis). The effect is temporary and occurs only during treatment.

Generally:
Keep medicine out of the reach of children. Avoid contact with eyes. Do not swallow.

Only for products containing cetostearyl alcohol:

Cetostearyl alcohol may cause local skin reactions (e.g. contact dermatitis).

Interactions with Other Medicinal Products and Other Forms of Interaction

None known.

Fertility, Pregnancy and Lactation

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.

Pregnancy:

There are limited amount of data from the use of clotrimazole in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of clotrimazole during the first trimester of pregnancy.

Lactation:

Available pharmacodynamic/toxicological data in animals have shown excretion of clotrimazole/metabolites in milk (for details see section 5.3). Breast-feeding should be discontinued during treatment with clotrimazole.

Effects on Ability to Drive and Use Machines

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

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, it is not always possible to reliably estimate their frequency.

Immune system disorders: allergic reaction (syncope, hypotension, dyspnea, urticaria)

Skin and subcutaneous tissue disorders: blisters, discomfort/pain, edema, erythema, irritation, peeling/exfoliation, pruritus, rash, stinging/burning

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. There is no specific antidote.

PHARMACOLOGICAL PROPERTIES

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.

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 µg/ml substrate. The mode of action of clotrimazole is primarily 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 vaginalis), and gram-negative microorganisms (Bacteroides).

In vitro clotrimazole inhibits the multiplication of Corynebacteria and grampositive cocci - with the exception of Enterococci - in concentrations of 0.5-10 µg/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.

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 0.001 µg/ml, suggesting that clotrimazole applied topically on the skin does is unlikely to lead to measurable systemic effects or side effects.

Preclinical Safety Data

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Mandatory:

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.

PHARMACEUTICAL PARTICULARS

List of Excipients

Sorbitan Stearate
Polysorbate 60
Cetyl palmitate
Cetostearyl Alcohol
Octyldodecanol
Benzyl alcohol
Purified water.

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Incompatibilities

None known

Special Precautions for Storage

Keep drug out of the reach of children.

Store at or below 30^0C

Nature and Contents of Container

Aluminium tubes of 20g each

Manufacturer

GP Grenzach Produktions GmbH
Emil-Barell-Str. 7
79639 Grenzach-Wyhlen
Germany

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04/10/2012