New Zealand Data Sheet

1. Product Name

CANESTEN® EXTRA

Topical Cream

Clotrimazole 10 mg/g, Hydrocortisone acetate 11.2 mg/g

2. Qualitative and Quantitative Composition

CANESTEN EXTRA Antifungal Anti-Inflammatory Cream contains 10 mg/g of clotrimazole and 11.2 mg/g of hydrocortisone acetate (equivalent to 10 mg/g hydrocortisone) as active ingredients.

For a full list of excipients, see section 6.1.

3. Pharmaceutical Form

Cream – topical. A white to slightly yellowish cream.

4. Clinical Particulars

4.1 Therapeutic Indications

CANESTEN EXTRA cream is indicated for dermatophyte and yeast infections of the skin when inflammation is prominent. This includes conditions such as fungal infected dermatitis, intertrigo and Candida nappy rash.

4.2 Dose and Method of Administration

A small amount of CANESTEN EXTRA cream should be applied thinly and evenly with gentle rubbing to the affected area(s) twice daily. Use only until inflammation, itching and redness have subsided, and not for more than 7 days (unless directed by the doctor). Then use an antifungal-only cream such as CANESTEN Clotrimazole Anti-fungal Cream for 14 days after symptoms disappear to avoid recurrence of the infection.

Paediatric Population

The risk of systemic absorption, and hence systemic toxicity, is greater in children due to the higher permeation properties of the skin and a larger skin surface to body weight ratio than adults. Do not use on children under 2 years of age except on the advice of a doctor.

4.3 Contraindications

CANESTEN EXTRA cream is contraindicated in the following cases:

- hypersensitivity to the active substances or to any of the excipients listed in section 6.1
- use on broken skin
- diseases affecting the skin (such as acne, rosacea, perioral dermatitis, lues, tuberculosis, etc.)
- in or near the eyes
- viral skin diseases (e.g. herpes simplex, chicken pox, etc.)

- dermal vaccination reactions

4.4 Special Warnings and Precautions for Use

Because of its corticosteroid content, CANESTEN EXTRA cream should not be applied to large areas (more than 10% of the body surface) and/or under occlusive dressings (such as nappies and bandages) because this may increase absorption.

The effectiveness and safety of latex products such as condoms and diaphragms may be reduced by CANESTEN EXTRA cream 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 may occur only during treatment.

If an associated infection develops during use and does not respond to therapy, use should be discontinued until the infection is controlled.

Rebound of pre-existing dermatoses can occur with abrupt discontinuation after prolonged use of topical corticosteroid preparations

For external use only. Avoid contact with eyes. Do not swallow. Keep this medicine out of the reach of children.

Cetostearyl alcohol, which is an excipient in this medicine, may cause local skin reactions (e.g. contact dermatitis).

Hypothalamic-Pituitary Axis Suppression and Atrophic Striae

Long term corticosteroid use may increase the risk of hypothalamic-pituitary axis suppression, especially under occlusion. Use for longer than 4 weeks can cause atrophic striae and prolonged use on flexures and in intertriginous areas is undesirable.

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Paediatric Population

The risk of systemic absorption, and hence systemic toxicity, is greater in children due to the higher permeation properties of the skin and a larger skin surface to body weight ratio than adults. Do not use on children under 2 years of age except on the advice of a doctor.

4.5 Interactions with Other Medicinal Products and Other Forms of Interaction

Not known.

4.6 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 medicine on fertility. No data is available on the effects of topically applied hydrocortisone.

Pregnancy

Category A

[Category A: Medicines which have been taken by a large number of pregnant women and women of childbearing age without an increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.]

There is a limited amount of data from the use of clotrimazole or hydrocortisone in pregnant women. Animal studies with clotrimazole do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3 Preclinical Safety Data). Studies in animals have shown reproductive effects at high doses of corticosteroids after systemic use (see section 5.3 Preclinical Safety Data), and there is no animal data on the reproductive effects after topical use. As a precautionary measure, it is recommended not to apply CANESTEN EXTRA for a long period during pregnancy, particularly in the first three months, and it is preferable to avoid the use of CANESTEN EXTRA cream during the first trimester of pregnancy.

Lactation

Available pharmacodynamic/toxicological data in animals have shown excretion of clotrimazole and/or metabolites in milk after intravenous administration (see section 5.3 Preclinical Safety Data).

No data on hydrocortisone is available, but topically applied hydrocortisone is unlikely to cause systemic effects due to the low percutaneous penetration. However, cutaneous absorption may be increased under certain circumstances, such as with use of occlusive dressings, the degree of skin damage and the size of the treated area.

Breast-feeding should be discontinued during treatment with CANESTEN EXTRA cream.

4.7 Effects on Ability to Drive and Use Machines

CANESTEN EXTRA has no or negligible effects on the ability to drive or use machinery.

4.8 Undesirable Effects

The following adverse reactions have been identified during post-approval use of CANESTEN EXTRA cream. 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, dyspnoea, urticaria).

Skin and subcutaneous tissue disorders

Discomfort/pain, oedema, erythema, hypertrichosis, irritation, pruritus, rash, secondary infections and acneiform symptoms, skin atrophy, skin discolouration, skin striae, stinging/burning, teleangiectasis.

Post marketing

Topical steroid withdrawal syndrome
Eye disorders: vision blurred

Reporting of Suspected Adverse Reactions

Reporting suspected adverse reactions after authorisatio of the medicine is important. It allows contnued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

No reports are available on cases of overdosage with CANESTEN EXTRA cream.

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 favourable to absorption) or inadvertent oral ingestion. There is no specific antidote.

Excessive chronic exposure results in adverse systemic and dermal effects. In such cases, the use of topical corticosteroid should be discontinued, with consideration given to tapering the dose.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

Pharmacotherapeutic Group

Antifungals for topical use – imidazole and triazole derivates, combinations

ATC Code: D01A C20

CANESTEN EXTRA is a combination of clotrimazole and hydrocortisone.

Mechanism of Action

Clotrimazole

Clotrimazole acts against fungi by inhibiting ergosterol synthesis. Inhibition of ergosterol synthesis leads to structural and functional impairment of the fungal 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 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 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.

Hydrocortisone

Hydrocortisone is a weak corticosteroid with both glucocorticoid and to a lesser extent mineralocorticoid activity. As active ingredient in a topical cream it exerts antiphlogistic, antipruriginous, antiexudative and antiallergic effects.

Hydrocortisone - as other topically applied glucocorticoids - exerts an antiinflammatory, antiallergic, immunosuppressive, antimitotic (antiproliferative), antipruriginous, and vasoconstrictive effect on skin. Thus, in addition to the elimination of inflammation and pruritus, a normalization of keratinization, inhibition of excess fibroblast activity and epidermopoiesis, degradation of pathological metabolic products, and inhibition of acantholysis are achieved. However, this is not a curative therapy, but rather symptomatic treatment.

5.2 Pharmacokinetic Properties

Clotrimazole

Pharmacokinetic investigations after dermal application have shown that clotrimazole is practically not 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 0.01 µg/mL, reflecting that clotrimazole applied topically on the skin does not lead to measurable systemic effects or undesirable effects.

Hydrocortisone

Dermal absorption of hydrocortisone depends on the thickness and condition of the skin. In healthy skin no systemic effects of corticoids have been observed after local application.

However, in the case of inflamed or damaged skin, cutaneous absorption may be increased depending on the site of application, use of occlusive dressings, the degree of skin damage and size of the treated area. Systemic effects cannot be ruled out under such conditions.

An increase in the skin temperature or moisture content, e.g. in skin folds or under an occlusive dressing, also promotes absorption. In infants and small children the epidermal “barrier” is still poorly developed, which facilitates transcutaneous uptake of medicines. The occurrence of systemic effects depends partly on the dose and, to a much greater extent, on the duration of treatment.

More than 90% of the hydrocortisone absorbed is bound to plasma proteins. Hydrocortisone is metabolized in the liver and tissues, and the metabolites are excreted in the urine. The biological half-life is approximately 100 minutes.

No relevant absorption of hydrocortisone is expected after its use for a short period on limited skin inflammation areas.

5.3 Preclinical Safety Data

Clotrimazole

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 teratogenicity 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 medicine was secreted into milk at levels higher than in plasma by a factor of 10 to 20 at 4 hours after administration, followed by a decline to a factor of 0.4 by 24 hours.

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

Hydrocortisone

As an adrenocortical hormone, hydrocortisone is classified as relatively non-toxic for topical use. Teratogenic effects of high doses of corticosteroids such as cleft palate formation, growth retardation, and fetal mortality, etc. were observed after systemic use in animal studies; there are no data on teratogenic effects after dermal use.

Clotrimazole plus Hydrocortisone

Nonclinical data based on acute and repeated dose toxicity studies reveal no special hazard to humans. In a 90-day repeated dose dermal study, effects were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

6. Pharmaceutical Particulars

6.1 List of Excipients

CANESTEN EXTRA cream also contains benzyl alcohol, cetostearyl alcohol, triceteareth-4-phosphate, triglycerides medium chain, sodium hydroxide and purified water.

6.2 Incompatibilities

None

6.3 Shelf Life

36 months (3 years from date of manufacture)

6.4 Special Precautions for Storage

Store at or below 25ºC.

6.5 Nature and Contents of Container

CANESTEN EXTRA cream is a white to slightly yellowish cream filled into aluminium tubes with an inner lacquer and white polyethylene screw cap containing 15 g, 20 g or 30 g of cream (the 15 g and 20 g presentations are not marketed).

6.6 Special Precautions for Disposal and Other Handling

CANESTEN EXTRA should not be disposed of via wastewater or household waste. Ask a pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment

7. Medicine Schedule

Pharmacist Only Medicine

8. Sponsor

Bayer New Zealand Limited
Auckland
Free phone 0800 229 376
www.canesten.co.nz

9. Date of First Approval

11 August 2016

10. Date of Revision of Text

28 October 2021