

Data Sheet

CANESTEN[®] PLUS

Topical Cream

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

Product Description

CANESTEN PLUS Clotrimazole and Hydrocortisone Cream contains 10 mg/g of clotrimazole and 11.2 mg/g of hydrocortisone acetate as active ingredients. CANESTEN PLUS cream also contains benzyl alcohol, cetostearyl alcohol, tricetareth-4-phosphate, triglycerides medium chain, sodium hydroxide and purified water.

Pharmacology

Pharmacotherapeutic group

CANESTEN PLUS cream is a combination of clotrimazole, which is an imidazole derivative, and hydrocortisone acetate, which is a glucocorticoid. Clotrimazole is a broad spectrum antimycotic.

Mechanism of Action

Clotrimazole

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

Hydrocortisone

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

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 0.062-4 (-8) 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 - as for other topically applied glucocorticoids - exerts an anti-inflammatory, immunosuppressive, antimitotic (antiproliferative), antipruriginous, and vasoconstrictive effect on skin. Thus, it provides symptomatic treatment of inflammation and pruritus associated with minor skin irritations and rashes.

Pharmacokinetic Properties

Clotrimazole

Pharmacokinetic investigations after dermal application have shown that only a small amount of clotrimazole (< 2% of the dose) is absorbed. 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 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. Children are more susceptible to transcutaneous uptake of medicines because they have a greater area-to-body mass ratio. 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 needs to be expected after its use for a short period on limited skin inflammation areas.

Preclinical Safety Data

Clotrimazole

Toxicological studies in different animals with local or intravaginal application showed good local and vaginal tolerability. Preclinical data reveal no special hazard for humans based on conventional studies of single and repeated dose toxicity, genotoxicity and toxicity to reproduction.

Hydrocortisone

As an adrenocortical hormone, hydrocortisone is classified as relatively non-toxic on topical use. So far there is no evidence of any reproduction toxicity for corticoids used topically in accordance with the instructions. Teratogenic effects of high doses of glucocorticosteroids such as cleft palate formation, growth retardation, etc. are known after systemic use in animal studies; there are no data on teratogenic damage after dermal use. Years of therapeutic experience in man with topical use of hydrocortisone have not yielded any evidence of teratogenicity.

Indications

CANESTEN PLUS 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.

Contraindications

CANESTEN PLUS cream is contraindicated in the following cases:

- hypersensitivity to any of the ingredients

- 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
- dermal vaccination reactions

Precautions

For external use only. CANESTEN PLUS cream should not be applied in the eyes.

Because of its corticosteroid content, CANESTEN PLUS cream should not be applied:

- to large areas (more than 10%) of the body surface
- for a long period during pregnancy particularly in the first three months
- under occlusive dressing due to increased absorption.

If hypersensitivity reactions occur, use should be discontinued.

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

Interactions with Latex

The effectiveness and safety of latex products such as condoms and diaphragms may be reduced by CANESTEN PLUS 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.

Use in Pregnancy

Category A

While controlled clinical studies in pregnant women do not exist, epidemiological investigations give no indication that harmful effects on the mother and child should be anticipated when CANESTEN PLUS cream is used during pregnancy. It is recommended not to apply CANESTEN PLUS cream for a long period during pregnancy, particularly in the first three months. CANESTEN PLUS cream should only be used in the first 3 months of pregnancy after first consulting a doctor.

[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.]

Use in Lactation

Although systemic absorption following topical administration is low, there is no information on whether or not CANESTEN PLUS cream is excreted in breast milk. Caution should be exercised when this product is administered to nursing mothers and it should not be applied on the breasts.

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.

Use in Children

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.

Bandages and some nappies may act as an occlusive dressing and may increase systemic absorption.

Ability to Drive and Use Machines

No effects on ability to drive and use machines have been observed.

Interactions with other Medicines

Not known.

Adverse Reactions

Skin reactions (such as hypersensitivity reactions e.g. burning, stinging, oedema or redness) can occur occasionally.

Particularly after use on large areas (more than 10% of the body surface) and/or after long-term use (longer than 2-4 weeks) or under occlusive conditions, local skin alterations such as skin atrophy, teleangiectasis, hypertrichosis, striations, hypopigmentation, secondary infection and acneiform symptoms may occur.

Dosage

A small amount of CANESTEN PLUS 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.

Overdosage

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

For overdosage, treatment should be symptomatic and supportive. In the case of oral overdose, emesis or activated charcoal is not usually indicated unless multiple ingestions are suspected.

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.

Presentation and Storage Conditions

CANESTEN PLUS cream is a white to slightly yellowish cream filled in tubes containing 15 g, 20 g or 30 g of cream.

Storage

Store below 25°C.

Medicine Classification

Pharmacist Only Medicine

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