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CUTIVATE™

GlaxoSmithKline

Fluticasone-propionate

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of CUTIVATE Cream 0.05% contains 500 micrograms of fluticasone propionate (micronised) HSE.

PHARMACEUTICAL FORM

Cream

CLINICAL PARTICULARS

Indications

TREATMENT OF INFLAMMATORY DERMATOSES

CUTIVATE Cream is indicated for adults, children and infants aged three months and over for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses such as:

- Eczema including atopic, infantile, and discoid eczemas
- Prurigo nodularis
- Psoriasis (excluding widespread plaque psoriasis)
- Neurodermatoses including lichen simplex
- Lichen planus
- Seborrhoeic dermatitis
- Contact sensitivity reactions
- Discoid lupus erythematosus
- An adjunct to systemic steroid therapy in generalised erythroderma
- Insect bite reactions
- Prickly heat

REDUCTION OF RISK OF RELAPSE

CUTIVATE Cream is indicated for the reduction of the risk of relapse of chronic recurrent atopic eczema once an acute episode has been treated effectively.

Dosage and Administration

TREATMENT OF INFLAMMATORY DERMATOSES

For adults, children and infants aged three months and over, apply a thin film of CUTIVATE Cream to the affected skin areas once or twice daily (see Warnings and Precautions).

REDUCTION OF RISK OF RELAPSE

Once an acute episode has been treated effectively, application frequency should be reduced to once daily application, twice weekly, without occlusion. Application should be continued to all previously affected sites or to known sites of potential relapse. This regime should be combined with routine daily use of emollients. The condition must be re-evaluated on a regular basis (see Warnings and Precautions).

Contraindications

- Rosacea.
- Acne vulgaris.
- Perioral dermatitis.
- Primary cutaneous viral infections (e.g., herpes simplex, chickenpox).
- Hypersensitivity to any of the ingredients.
- Perianal and genital pruritus.
- The use of CUTIVATE Cream is not indicated in the treatment of primary infected skin lesions caused by infection with fungi or bacteria.
- Dermatoses in infants under three months of age, including dermatitis and napkin eruptions.

Warnings and Precautions

Prolonged application of high doses to large areas of body surface, especially in infants and small children, might lead to adrenal suppression. Children and infants have a greater surface area to body weight ratio compared with adults. Therefore, in comparison with adults, children and infants may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity. Care should be taken when using CUTIVATE Cream to ensure the amount applied is the minimum that provides therapeutic benefit.

The face, more than other areas of the body, may exhibit atrophic changes after prolonged treatment

with potent topical corticosteroids. This must be borne in mind when treating such conditions as psoriasis, discoid lupus erythematosus and severe eczema.

If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye so as to avoid the risk of local irritation or glaucoma.

Topical steroids may be hazardous in psoriasis for a number of reasons, including rebound relapses, development of tolerances, risk of generalised pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin. If used in psoriasis careful patient supervision is important.

Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy and systemic administration of antimicrobial agents.

Bacterial infection is encouraged by the warm, moist conditions induced by occlusive dressing, and so the skin should be cleansed before a fresh dressing is applied.

Overt suppression of the HPA-axis (morning plasma cortisol less than 5 microg/dL) is very unlikely to result from therapeutic use of CUTIVATE Cream unless treating more than 50% of an adult's body surface and applying more than 20 g per day.

CUTIVATE Cream contains the excipient imidurea which releases traces of formaldehyde as a breakdown product.

Formaldehyde may cause allergic sensitization or irritation upon contact with the skin.

Interactions

None reported.

Pregnancy and Lactation

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however, administration of fluticasone propionate during pregnancy should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus.

The excretion of fluticasone propionate into human breast milk has not been investigated.

When measurable plasma levels were obtained in lactating laboratory rats following subcutaneous administration there was evidence of fluticasone propionate in the milk.

However plasma levels in patients following dermal application of fluticasone propionate at recommended doses are likely to be low.

Effects on Ability to Drive and Use Machines

None reported.

Adverse Reactions

Adverse events are listed below by system organ class and frequency. Frequencies are defined as:

very common:	≥1 in 10
common:	≥1 in 100 and <1 in 10
uncommon:	≥1 in 1,000 and <1 in 100
rare:	≥1 in 10,000 and <1 in 1,000
very rare:	<1/10,000 including isolated reports.

Very common, common and uncommon events were generally determined from clinical trial data. The background rates in placebo and comparator groups were not taken into account when assigning frequency categories to adverse events derived from clinical trial data, since these rates were generally comparable to those in the active treatment group. Rare and very rare events were generally derived from spontaneous data.

Infections and infestations

Very rare: Secondary infection.

Secondary infection, particularly when occlusive dressings are used or when skin folds are involved have been reported with corticosteroid use.

Immune system disorders

Very rare: Hypersensitivity.

If signs of hypersensitivity appear, application should stop immediately.

Endocrine disorders

Very rare: Features of hypercortisolism.

Prolonged use of large amounts of corticosteroids, or

treatment of extensive areas, can result in sufficient systemic absorption to produce the features of hypercortisolism. This effect is more likely to occur in infants and children, and if occlusive dressings are used.

In infants, the napkin may act as an occlusive dressing (see Warnings and Precautions).

Vascular disorders

Very rare: Dilation of superficial blood vessels.

Prolonged and intensive treatment with potent corticosteroid preparations may cause dilation of the superficial blood vessels.

Skin and subcutaneous tissue disorders

Very rare: Thinning, striae, hypertrichosis, hypopigmentation, allergic contact dermatitis, exacerbation of dermatoses, pustular psoriasis.

Local burning and pruritus have been reported, however in clinical trials the incidence of these adverse reactions was generally comparable to placebo and comparator groups.

Prolonged and intensive treatment with potent corticosteroid preparations may cause local atrophic changes in the skin such as thinning, striae, hypertrichosis and hypopigmentation.

Exacerbation of the signs and symptoms of the dermatoses and allergic contact dermatitis have been reported with corticosteroid use.

Treatment of psoriasis with a corticosteroid (or its withdrawal) may provoke the pustular form of the disease.

Common: Pruritus.

Uncommon: Local burning.

Overdose

Acute overdosage is very unlikely to occur, however, in the case of chronic overdosage or misuse the features of hypercortisolism may appear.

In this situation topical steroids should be discontinued gradually under medical supervision because of the risk of adrenal insufficiency.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

Fluticasone propionate is a glucocorticoid with high topical anti-inflammatory potency but low HPA-axis suppressive activity after dermal administration. It therefore has a therapeutic index which is greater than most of the commonly available steroids.

It shows high systemic glucocorticoid potency after subcutaneous administration but very weak oral activity, probably due to metabolic inactivation. In vitro studies show a strong affinity for, and agonist activity at, human glucocorticoid receptors.

Fluticasone propionate has no unexpected hormonal effects, and no overt, marked effects upon the central and peripheral nervous systems, the gastrointestinal system, or the cardiovascular or respiratory systems.

Pharmacokinetics

Absorption

Bioavailability is very low after topical or oral administration, due to limited absorption through the skin or from the gastrointestinal tract, and because of extensive first pass metabolism.

Oral bioavailability approaches zero, due to poor absorption and extensive first pass metabolism. Therefore systemic exposure of fluticasone propionate from any ingestion of fluticasone propionate cream will be low.

Distribution

Distribution studies have shown that only minute traces of orally administered compound reach the systemic circulation, and that any systemically available fluticasone propionate is rapidly eliminated in the bile and excreted in the faeces.

Fluticasone propionate does not persist in any tissue, and does not bind to melanin.

Metabolism

Pharmacokinetic data for the rat and dog indicate rapid elimination and extensive metabolic clearance. In man too, metabolic clearance is extensive, and elimination is consequently rapid. Thus drug entering the systemic circulation via the skin will be rapidly inactivated. The major route of metabolism is hydrolysis to a carboxylic acid, which has very weak glucocorticoid or anti-inflammatory activity.

Elimination

In all test animal species the route of excretion was independent of the route of administration of fluticasone propionate. Excretion is predominantly faecal and is essentially complete within 48 h.

Pre-clinical Safety Data

Reproductive studies suggest that administration of corticosteroids to pregnant animals can result in abnormalities of foetal development including cleft palate/lip. However, in humans, there is no convincing evidence that systemic corticosteroids cause an increased incidence of congenital abnormalities, such as cleft palate or lip.

In a fertility and general reproductive performance study in rats, fluticasone propionate administered subcutaneously to females at up to 50 micrograms/kg per day and to males up to 100 micrograms/kg per day (later reduced to 50 micrograms/kg per day) had no effect upon mating performance or fertility.

Fluticasone propionate was not shown to be mutagenic in a range of in vitro bacterial and mammalian cell assays. Long-term studies to investigate the carcinogenic potential of fluticasone propionate when given topically and orally did not show any evidence of carcinogenicity.

PHARMACEUTICAL PARTICULARS

List of Excipients

Liquid paraffin
Cetostearyl Alcohol
Isopropyl myristate
Cetomacrogol 1000
Propylene Glycol
Imidurea
Sodium phosphate
Citric acid monohydrate
Purified water.

Incompatibilities

None.

Shelf Life

The expiry date is indicated on the packaging.

Special Precautions for Storage

Store below 30oC.
Do not freeze.

Nature and Contents of Container

As registered locally.
Not all presentations are available in every country.
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