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Cutivate™ Cream

fluticasone propionate

To the Medical and Pharmaceutical Professions

Presentation
Fluticasone Propionate (micronised) HSE 0.05% w/w. (See List of Excipients).

Indications
Adults:
For the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses such as: eczema including atopic 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; or prickly heat.

Children:
For children and infants aged three months and over who are unresponsive to lower potency corticosteroids Cutivate Cream is indicated for the relief of the inflammatory and pruritic manifestations of atopic dermatitis under the supervision of a specialist. Expert opinion should be sought prior to the use of Cutivate Cream in other corticosteroid responsive dermatoses in children.

Dosage and Administration
Eczema/Dermatitis
For adults, children and infants aged three months and over, apply a thin film of Cutivate Cream to the affected skin areas once daily.

Other indications
Apply a thin film of Cutivate Cream to the affected skin areas twice daily.

Duration of use:
Daily treatment should be continued until adequate control of the condition is achieved. Frequency of application should thereafter be reduced to the lowest effective dose.

When Cutivate is used in the treatment of children, if there is no improvement within 7 – 14 days, treatment should be withdrawn and the child re-evaluated. Once the condition has been controlled (usually within 7-14 days), frequency of application should be reduced to the lowest effective dose for the shortest possible time. Continuous daily treatment for longer than 4 weeks is not recommended.

For topical administration.

Contra-indications
Rosacea.
Acne vulgaris.
Perioral dermatitis.
Primary cutaneous viral infections (eg., herpes simplex, chickenpox).
Hypersensitivity to any of the ingredients.
Perianal and genital pruritus.
The use of Cutivate 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.

Precautions and Warnings
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 to ensure the amount applied is the minimum that provides therapeutic benefit. Long-term continuous use should be avoided in children. The safety and efficacy of fluticasone propionate when used continuously for longer than 4 weeks has not been established.
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 and referral to a dermatologist is required before using Cutivate Cream to treat psoriasis in children.
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.

Fluticasone propionate 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.

Pregnancy and Lactation
Pregnancy: 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.

Lactation: 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.
Administration of fluticasone propionate during pregnancy and lactation should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus or baby.

Adverse Reactions
Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥1/10,000 and <1/1000) and 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 Precautions and Warnings).

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
Common: Pruritus.
Uncommon: Local burning.
Very rare: Thinning, striae, hypertrichosis, hypopigmentation, allergic contact dermatitis, exacerbation of dermatoses, pustular psoriasis.
Local burning and pruritus have been reported.

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.

Overdosage
Acute overdosage is very unlikely to occur, however, in the case of chronic overdosage or misuse the features of hypercortisolism may appear and in this situation topical steroids should be discontinued gradually. However, because of the risk of acute adrenal suppression this should be done under medical supervision.

Pharmacodynamic Properties
Mode of action:
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.

Pharmacokinetic Properties
Pharmacokinetic data for the rat and dog indicate rapid elimination and extensive metabolic clearance. 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. 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. The major route of metabolism is hydrolysis to a carboxylic acid, which has very weak glucocorticoid or anti-inflammatory activity. 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 hours.
In man metabolic clearance is extensive, and elimination is consequently rapid. Thus drug entering the systemic circulation via the skin will be rapidly inactivated. Oral bioavailability approaches zero, due to poor absorption and extensive first pass metabolism. Therefore systemic exposure of fluticasone propionate from any ingestion of Cutivate will be low.

Pharmaceutical Precautions and Recommendations
Do not store above 30°C. Do not Freeze

List of Excipients
Liquid paraffin
Cetostearyl Alcohol
Isopropyl myristate
Cetomacrogol 1000
Propylene Glycol
Imidurea
Sodium phosphate
Citric acid (monohydrate)
Purified water

Shelf Life
Shelf life is indicated on the outer pack.

Further Information:
Pre-clinical safety
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 congential abnormalities, such as cleft palate or lip.
Studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, fertility and general reproductive performance revealed no special hazard for humans, other than that anticipated for a potent steroid.

Manufactured by:
Glaxo Operations UK Limited*
Barnard Castle
UK
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GlaxoSmithKline

THIS IS A MEDICAMENT

Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab Health Ministers
Union of Arab Pharmacists