Cutivate
Version GDSv14/IPIv04
indicated for adults, children and infants aged 3 months and over for the relief of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. These include the following:

- Atopic dermatitis (including infantile atopic dermatitis)
- Nummular dermatitis (discoid eczema)
- Prurigo nodularis
- Psoriasis (excluding widespread plaque psoriasis)
- Lichen simplex chronicus (neurodermatitis) and lichen planus
- Seborrhoeic dermatitis
- Irritant or allergic contact dermatitis
- Discoid lupus erythematosus
- An adjunct to systemic steroid therapy in generalized erythroderma
- Pruritus without inflammation
- Pruritus caused by occlusive dressing
- Perianal and genital pruritus
- Dermatomas in infants under 3 months of age, including dermatitis and nappy rash.

**Warnings and Precautions**

**CUTIVATE** Cream should be used with caution in patients with a history of local hypersensitivity to corticosteroids or to any of the excipients in the preparation. Local hypersensitivity reactions (see Adverse Reactions) may resemble symptoms of the condition under treatment.

- Manifestations of hypercortisolism (Cushing’s Syndrome) and reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, leading to a glucocorticosteroid insufficiency, can occur in some individuals as a result of increased systemic absorption of topical steroids. If either of the above are observed, withdraw the drug gradually by reducing the frequency of application, or by substituting a less potent corticosteroid. Abrupt withdrawal of treatment may result in glucocorticosteroid insufficiency (see Adverse Reactions).
- Risk factors for increased systemic effects are:
  - Potency and formulation of topical steroid
  - Duration of exposure
  - Application to a large surface area
  - Use on occluded areas of skin e.g. on intertriginous areas or under occlusive dressings (in infants the nappy may act as an occlusive dressing)
  - Increasing hydration of the stratum corneum
  - Use on thin skin areas such as the face
  - Use on broken skin or other conditions where the skin barrier may be impaired
  - In comparison with adults, children and infants may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic adverse effects. This is because children have an immature skin barrier and a greater surface area to body weight ratio compared with adults.
- Visual disturbance has been reported by patients using systemic and/or topical corticosteroids. If a patient has blurring vision or other visual disturbances, consider evaluation of possible causes which may include cataract, glaucoma or central serous chorioretinopathy.

**Children**

- In infants and children under 12 years of age, long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal suppression is more likely to occur.
- **Use in Psoriasis**
  - Topical steroids should be used with caution in psoriasis as rebound relapses, development of tolerance, risk of generalized patchy psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin have been reported in some cases. If used in psoriasis, careful patient supervision is important.

**Application to the Face**

- Prolonged application to the face is undesirable as this area is more susceptible to atrophic changes.
- **Application to the Eyelids**
  - If applied to the eyes, care is needed to ensure that the preparation does not enter the eye as cataract and glaucoma might result from repeated exposure.

**Concomitant Infection**

- 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 administration of appropriate antimicrobial therapy.

**Infection Risk with Occlusion**

- Bacterial infection is encouraged by the warm, moist conditions within skin folds or caused by occlusive dressings. When using occlusive dressings, the skin should be cleansed before a fresh dressing is applied.

**Chronic leg ulcers**

- Topical corticosteroids are sometimes used to treat the dermatitis around chronic recurrent atopic dermatitis once an acute episode has been treated effectively.

**Dosage and Administration**

- Children are more likely to develop local and systemic side effects of topical corticosteroids because of immature skin barrier and a greater surface area to body weight ratio compared with adults.

**Application to a large surface area**

- Potency and formulation of topical corticosteroids and, in general, require shorter courses and less potent agents than adults.

**Care should be taken when using CUTIVATE Cream to ensure the amount applied is the minimum that provides therapeutic benefit.**

**Elderly**

- Clinical studies have not identified differences in responses between the elderly and younger patients. The greater frequency of decreased hepatic or renal function in the elderly may delay elimination if systemic absorption occurs. Therefore the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.

**Renal/Hepatic Impairment**

- In case of systemic absorption (when application is over a large surface area for a prolonged period), metabolism and elimination may be delayed therefore increasing the risk of systemic toxicity. Therefore the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.

**Contraindications**

- The following conditions should not be treated with CUTIVATE Cream:
  - Untreated cutaneous infections
  - Rosacea
  - Acne vulgaris
  - Perioral dermatitis
  - Perianal and genital pruritus
  - Pruritus without inflammation

- Dermatomas in infants under 3 months of age, including dermatitis and nappy rash.

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Administration of CUTILATE Cream during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant. If used during lactation, CUTILATE Cream should not be applied to the breasts to avoid accidental ingestion by the infant.

Effects on Ability to Drive and Use Machines
There have been no studies to investigate the effect of CUTILATE on driving performance or the ability to operate machinery. A detrimental effect on such activities would not be anticipated from the adverse reaction profile of topical CUTILATE Cream.

Adverse Reactions

Post-Marketing Data
Adverse drug reactions (ADRs) are listed below by MedDRA system organ class and by frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/10000) and very rare (<1/100000), including isolated reports.

Infections and infestations

Very rare: Opportunistic infection

Immune System Disorders

Very rare: Hypersensitivity

Endocrine disorders

Very rare: Hypothalamic-pituitary-adrenal (HPA) axis suppression: Increased weight/obesity, Delayed weight gain/growth retardation in children, Cushingoid features (e.g. moon face, central obesity), Decreased endogenous cortisol levels, Hyperglycaemia/glucosuria, Hypertension, Osteoporosis, Cataract, Glaucoma

Skin and Subcutaneous Tissue Disorders

Common: Pruritus
Uncommon: Local skin burning
Very rare: Skin thinning, atrophy, striae, telangiectasias, pigmentation changes, hypertrichosis, allergic contact dermatitis, exacerbation of underlying symptoms, pustular pustulosis, erythema, rash, urticaria.

Overdose

Symptoms and Signs
Topically applied fluticasone propionate may be absorbed in sufficient amounts to produce systemic effects. Acute overdosage is very unlikely to occur, however, in the case of chronic overdosage or misuse the features of hypercorticism may appear (see Adverse Reactions).

Treatment
In the event of overdose, CUTILATE Cream should be withdrawn gradually by reducing the frequency of application, or by substituting a less potent corticosteroid because of the risk of glucocorticosteroid insufficiency.

Further management should be as clinically indicated or as recommended by the national poisons center, where available.

Pharmacological Properties

Pharmacodynamics

ATC Code
DOTAC (Corticosteroid, potent (Group III)).

Mechanism of Action
Topical corticosteroids have anti-inflammatory, antipruritic, and vasoconstrictive properties. They act as anti-inflammatory agents via multiple mechanisms to inhibit late phase allergic reactions, including decreasing the density of mast cells, decreasing chemotaxis and activation of eosinophils, decreasing cytokine production by lymphocytes, monocytes, mast cells and eosinophils, and inhibiting the metabolism of arachidonic acid.

Fluticasone propionate is a glucocorticoid with high topical anti-inflammatory potency but low HPA-axi 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.

Pharmacodynamic Effects
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 CUTILATE 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 predominantely faecal and is essentially complete within 48 hours.

Pre-Clinical Safety Data
Carcinogenesis/Mutagenesis

Carcinogenesis
Long-term topical and oral studies in animals to investigate the carcinogenic potential of fluticasone propionate did not show any evidence of carcinogenicity.

Genotoxicity
Fluticasone propionate was not shown to be mutagenic in a range of in vitro bacterial and mammalian cell assays.

Fertility
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.

Pregnancy
Subcutaneous administration of fluticasone propionate to mice (150 micrograms/kg/day), rats (100 micrograms/kg/day) or rabbits (300 micrograms/kg/day) during pregnancy produced foetal abnormalities including cleft palate. Oral administration did not produce foetal abnormalities, consistent with the low bioavailability of fluticasone propionate by the oral route.

Pharmaceutical Particulars

List of Excipients
- Liquid paraffin
- Cetostearyl alcohol
- Isopropyl myristate
- Cetomacrogol 1000
- Propylene glycol
- Imidurea
- Sodium phosphate
- Citric acid monohydrate
- Purified water.

Incompatibilities
No incompatibilities have been identified.

Shelf-Life
The expiry date is indicated on the packaging.

Special Precautions for Storage
Store below 30°C.

Do not freeze.

Nature and Contents of Container
As registered locally.

Not all presentations are available in every country.

Instructions for Use/Handling
There are no special requirements for use or handling of this product.

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