Fluticasone propionate is a medium potency corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of cutaneous conditions characterized by inflammatory processes involving the skin, such as corticosteroid-responsive dermatoses in adults.

**DOSAGE AND ADMINISTRATION**

Fluticasone Propionate Ointment, 0.005% should be used in the treatment site. Fluticasone Propionate Ointment, 0.005% should not be used on the face, underarms, or groin areas unless directed by a physician.

Fluticasone Propionate Ointment, 0.005% contains fluticasone propionate 0.005 mg in a base of liquid paraffin, microcrystalline wax, propylene glycol, and sorbitan sesquioleate.

**CLINICAL PHARMACOLOGY**

Like other topical corticosteroids, fluticasone propionate is anti-inflammatory, antipruritic, and vasoconstrictor properties. The mechanism of the anti-inflammatory activity of the topical steroids, in general, is unclear. However, corticosteroids are thought to act by the induction of phosphatase inhibitors, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of pro-inflammatory mediators such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

Fluticasone propionate is lipophilic and has a strong affinity for the glucocorticoid receptor. It has weak affinity for the progesterone receptor, and virtually no affinity for the mineralocorticoid, estrogen, or androgen receptors. The therapeutic potency of glucocorticoids is related to the half-life of the glucocorticoid-receptor complex. The half-life of the fluticasone propionate-glucocorticoid receptor complex is approximately 10 hours.

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**PRECAUTIONS – Pediatric Use**

Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing’s syndrome than mature patients because of the continuing process of growth and development, and the younger patient’s relatively greater total body water, which may result in higher systemic availability of corticosteroids. In addition, absorption of topical products may be increased by the use of occlusive dressings or by the large surface area of young children.

Carcinogenesis, Mutagenesis, Impairment of Fertility – Two 18-month studies were performed in mice to evaluate the carcinogenic potential of fluticasone propionate when given topically (as 0.05% ointment) and orally. No evidence of carcinogenicity was found in either study.

ADVERSE REACTIONS

Topically applied fluticasone propionate ointment may be absorbed in sufficient amounts to produce systemic effects (see ADVERSE REACTIONS). Following an intravenous dose of 1 mg in healthy volunteers, fluticasone propionate showed polyexponential kinetics and had an average terminal half-life of 10 hours.

Fluticasone propionate has a molecular weight of 500.6. It is a white to off-white powder and is insoluble in water.

**Pharmacokinetics**

Absorption – The activity of Fluticasone Propionate Ointment, 0.005% is due to the parent drug, fluticasone propionate. The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Occlusive dressings enhance penetration. Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. In a study of 6 healthy volunteers applying 25 g of fluticasone propionate ointment 0.005% twice daily to the trunk and legs for up to 5 days under occlusion, plasma levels of fluticasone ranged from 0.08 to 0.22 ng/mL.

In an animal study using radio labelled 0.05% fluticasone propionate cream and ointment preparations, rats received topical a dose of 1 g/kg for a 24-hour period. Total recovery of radioactivity was approximately 80% at the end of 7 days. The majority of the dose (73%) was recovered from the surface of the application site. Less than 1% of the dose was absorbed in the skin at the application site. Approximately 5% of the dose was absorbed systemically through the skin. Absorption of the skin continued for the duration of the study (7 days), indicating a long retention time at the application site.

Distribution – Following intravenous administration of 1 mg of fluticasone propionate in healthy volunteers, the initial phase disposition for fluticasone propionate was rapid and consistent with its high lipid solubility and tissue binding. The apparent volume of distribution averaged 4.2-L/kg (range, 2.3-18.7-L/kg). The mean protein binding of fluticasone propionate bound to human plasma proteins averaged 91%. Fluticasone propionate is weakly and reversibly bound to erythrocytes.

Elimination – Metabolism – No metabolites of fluticasone propionate were detected in an in vitro study of radiolabeled fluticasone propionate incubated in a human skin homogenate. The total blood clearance of systemically absorbed fluticasone propionate averaged 1093 mL/min (range, 618-1702 mL/min) after a 1 mg intravenous dose, with renal clearance accounting for less than 0.02% of the total. Fluticasone propionate is metabolized in the liver by cytochrome P450 3A4-mediated hydrolysis of the 5-fluoromethoxy carboxylic acid grouping. This transformation occurs in 1 metabolic step to produce the inactive 17-β-carboxylic acid metabolite, the only known metabolite detected in man. This metabolite has approximately 2000 times less affinity than the parent drug for the glucocorticoid receptor of human lung cytosol. Fluticasone propionate is weakly and reversibly bound to erythrocytes.