Topical Fluticasone Propionate
A Review of its Pharmacological Properties and Therapeutic Use in the Treatment of Dermatological Disorders

Caroline M. Spencer and Lynda R. Wiseman
Adis International Limited, Auckland, New Zealand

Synopsis
Fluticasone propionate is a fluoromethyl androstane 17β-carboxylic acid that is classified for dermatological use as a moderate potency corticosteroid. It is available in 0.05% cream and 0.005% ointment formulations for the treatment of patients with inflammatory dermatoses responsive to corticosteroids.

Although it demonstrates greater activity than other corticosteroids of similar potency in vasoconstrictor assays in humans, fluticasone propionate demonstrates low potential to cause significant systemic effects such as suppression of the hypothalamopituitary-adrenal (HPA) axis. This is because it has a high affinity for the glucocorticoid receptor and high lipophilicity, and the small amount of
drug that is absorbed is rapidly metabolised to the inactive carboxylic acid derivative in the liver (i.e. it has low systemic bioavailability).

In clinical trials, the efficacy of fluticasone propionate cream at 4 weeks did not differ significantly from that of hydrocortisone butyrate 0.1% cream in patients with moderate to severe atopic dermatitis and betamethasone valerate 0.1% cream in patients with moderate to severe psoriasis. Likewise, after 4 weeks, the ointment form of fluticasone propionate had similar efficacy to betamethasone dipropionate 0.05% in patients with psoriasis or atopic dermatitis, although the latter agent may have a faster onset of activity in patients with atopic dermatitis. Fluticasone propionate ointment was generally more effective than hydrocortisone butyrate ointment in patients with psoriasis.

A sustained response was usually observed after about 1 week's application of fluticasone propionate, and although once and twice daily administration had similar efficacy, a twice daily regimen may have a slightly faster onset of effect.

In trials which included both adults and children, the only adverse events reported were local cutaneous reactions (most frequently, pruritus).

Thus, fluticasone propionate, with its low potential for systemic toxicity and possible advantage of once daily administration, is a useful addition to the topical corticosteroids available for the treatment of psoriasis and atopic dermatitis.

Pharmacological Profile

Vasoconstriction assays in humans showed that fluticasone propionate is more active than beclomethasone dipropionate, betamethasone valerate, triamcinolone acetonide and fluocinolone acetonide. However, it caused little if any significant hypothalamic-pituitary-adrenal (HPA) axis suppression in studies conducted in patients and healthy volunteers.

Fluticasone propionate binds to the glucocorticoid receptor faster than several other corticosteroids and the fluticasone propionate-receptor complex dissociates more slowly. As a result, this complex (which is responsible for the therapeutic activity of corticosteroids) has a longer half-life than other corticosteroid-receptor complexes. Indeed, fluticasone propionate had a greater in vitro relative receptor affinity than 32 other corticosteroids. Importantly, fluticasone propionate is highly selective for the glucocorticoid receptor and has little or no activity at other steroid receptors.

Fluticasone propionate 0.05% cream produced only 3% skin thinning compared with placebo in a study which used pulsed A-scan ultrasound to assess changes. This effect was independent of the duration of treatment (2, 4, 6 or 8 weeks) in 40 healthy volunteers and was reversed within 2 to 4 weeks of treatment discontinuation.

The commercially available formulation of fluticasone propionate cream was preferred over commercially available preparations of betamethasone valerate, hydrocortisone valerate, fluocinonide, triamcinolone acetonide and mometasone creams in terms of appearance, cosmetic acceptability and physicochemical properties in a blinded laboratory analysis.

The pharmacokinetic profile of fluticasone propionate cream or ointment in healthy volunteers or patients has not been published.

In rats, radiolabelled fluticasone propionate cream or ointment had a long retention time at the application site. After administration of a single 1 g/kg dose (removed from the skin after 24 hours), percutaneous absorption was low with only about 5% of the dose being absorbed through the skin over a 7-day period.