Intranasal Fluticasone Propionate
A Reappraisal of its Pharmacology and Clinical Efficacy in the Treatment of Rhinitis

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Summary
The intranasal corticosteroid fluticasone propionate is an effective agent for the treatment of rhinitis, demonstrating potent local anti-inflammatory activity and little, if any, systemic activity. Intranasal fluticasone propionate has shown clinical efficacy similar to that of other intranasal corticosteroids, including beclomethasone (administered at up to a 2-fold higher dosage than fluticasone), budesonide, flunisolide and triamcinolone acetonide, and provides greater relief from nasal symptoms (including nasal blockage) than antihistamine agents and
intranasal sodium cromoglycate. Its efficacy in the treatment of seasonal allergic rhinitis and perennial allergic and nonallergic rhinitis has been demonstrated in large well-controlled studies in which the drug maintained adequate control of symptoms when administered in a once daily dose of 200μg. In addition, fluticasone propionate has shown similar efficacy to that of beclomethasone in the treatment of nasal polyps; however, its use in the postoperative setting requires further investigation.

Intranasal fluticasone propionate is well tolerated in the majority of patients, the incidence of adverse events being similar to that seen with placebo. Pharmacoeconomic analyses indicate that intranasal fluticasone propionate is significantly more cost-effective than the antihistamines terfenadine and loratadine. Overall quality of life was improved to a similar extent by fluticasone propionate and beclomethasone.

In conclusion, recent clinical experience has confirmed that intranasal fluticasone propionate is a convenient, effective and well tolerated alternative to other intranasal corticosteroids and antihistamines for the treatment of rhinitis when administered once daily.

Fluticasone propionate has a 3- and 1.5-fold higher affinity for the glucocorticoid receptor than budesonide and the active metabolite of beclomethasone, respectively. The anti-inflammatory activity of intranasal fluticasone propionate has been demonstrated in nasal allergen provocation tests in patients with allergic rhinitis and also in skin vasoconstriction assays, in which the potency of fluticasone propionate was at least twice that of beclomethasone and was similar to or up to 3-fold greater than that of budesonide. Fluticasone propionate reduced both the early and late responses to allergen challenge, as evidenced by reductions in the levels of inflammatory cells and mediators in nasal lavage fluid. In addition, the nasal inspiratory peak flow from 0 to 24 hours after allergen challenge was significantly improved with fluticasone propionate compared with placebo. Fluticasone propionate was more effective in improving total nasal airflow than the antihistamines terfenadine, astemizole and loratadine.

Treatment with intranasal fluticasone propionate reduced the number of eosinophils and basophils in nasal lavage fluid in patients with rhinitis, but had no effect on the levels of neutrophils, goblet cells or epithelial cells.

With regard to the hypothalamic-pituitary-adrenal (HPA) axis, well designed clinical trials have shown fluticasone to have no effect on plasma or urinary cortisol levels in patients with rhinitis.

Little is known about the pharmacokinetic properties of intranasal fluticasone propionate, as plasma concentrations are generally below the limit of detection after administration by this route (<50 ng/L). The amount of fluticasone propionate present in the systemic circulation after intranasal administration has been estimated to be <2% of the dose. As oral bioavailability is negligible (<1%), it is likely that the small systemic exposure observed after intranasal administration results from absorption of the drug through the nasal mucosa.

Studies in healthy male volunteers using intravenous and oral formulations of fluticasone propionate reported the drug to have a rapid plasma clearance rate (1.11 L/min), similar to that of hepatic blood flow. The mean volume of distribution at steady-state was 318L. Low plasma concentrations of fluticasone propionate following oral administration may be attributed to the fact that the drug is poorly absorbed and is subject to extensive hepatic metabolism. Most oral flutica-