The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: FFR101747
Title: A Randomised, Double-Blind, Placebo-Controlled, Two-Week Crossover, Knemometric Assessment of the Effect of Fluticasone Furoate Nasal Spray 100mcg* Once Daily on Short-Term Growth in Children Aged 6 to 11 Years with Seasonal and/or Perennial Allergic Rhinitis
Rationale: Intranasal corticosteroids are considered an effective treatment for the symptoms of allergic rhinitis, both in children and in adults. For this reason, they are recommended as a first-line treatment in expert guidelines, specifically when congestion is a major component of the patient's presentation. From a general perspective, intranasally-administered corticosteroids have generally demonstrated a low incidence of systemic adverse effects; however one concern in children has been their effects on growth. Since the effect on growth has varied with the particular corticosteroid studied and by route, the possibility of an effect must be explored as new agents become available. Fluticasone furoate (FF), the investigational drug for this study, is a novel corticosteroid with potent glucocorticoid activity. As the maximal dose to be prescribed, fluticasone furoate 110mcg once daily was evaluated in a paediatric population aged 6 to 11 years with SAR and/or PAR in order to assess any effect on short-term lower leg growth using knemometry.
Phase: III
Study Period: 11 April 2005 – 16 November 2005
Study Design: Following a two-week, single-blind, Placebo run-in period, each child was randomly allocated in a 1:1 ratio to a double-blind treatment sequence of either fluticasone furoate nasal spray 110mcg QD followed by Placebo nasal spray QD, or Placebo nasal spray QD followed by fluticasone furoate nasal spray 110mcg QD. Each double-blind treatment in the sequence was administered for two weeks. The two double-blind treatment periods were separated by a two-week, washout period, during which single-blind, Placebo nasal spray was administered. A follow-up phone call was made three to seven days after completing the last treatment to assess for adverse events. The study consisted of five visits and five treatment periods: Run-in (Screening), Treatment Period 1, Washout, Treatment Period 2 and Follow-Up. Each treatment period lasted approximately two weeks.
Centres: One centre in Denmark
Indication: Allergic Rhinitis
Treatment: Fluticasone Furoate nasal spray 110mcg once daily (QD) *NOTE: Fluticasone furoate aqueous nasal spray 110mcg (actual); Drug content of Fluticasone Furoate Nasal Spray was approximated at 25mcg/spray in all Phase 3 clinical trial documentation pending confirmation from final batch and stability testing. Final testing and analyses determined one spray to contain 27.5mcg of fluticasone furoate, equating to 110mcg for the recommended adult dose of two sprays administered to each nostril.
Objectives: The primary objective was to determine the effect on lower-leg growth rate of treatment with fluticasone furoate (FF) nasal spray 110mcg QD versus Placebo nasal spray QD in children aged 6 to 11 years with seasonal allergic rhinitis (SAR) and/or perennial allergic rhinitis (PAR).
Primary Safety Variable: Mean growth rate (mm/wk) in lower-leg length, as determined by knemometry, over a two-week treatment period with fluticasone furoate nasal spray 110mcg QD versus a two-week treatment period with Placebo nasal spray QD.
Secondary Safety Variable(s): The frequency and type of clinical adverse events (AEs) experienced during treatment; nasal examinations; vital signs (systolic and diastolic blood pressure, heart rate [pulse]).
Statistical Methods: The primary objective of this study was to demonstrate that fluticasone furoate 110mcg QD was non-inferior compared with Placebo on lower-leg growth rate, measured by knemometry. The primary analysis method was the comparison of the treatment groups (fluticasone furoate vs. Placebo) using analysis of covariance (ANCOVA), adjusting for baseline lower-leg growth rate measured by knemometry, age, and gender. Treatment and period were included as fixed effects in the model and subject was included as a random effect. The primary analysis was conducted on the Growth Population that excluded from the intent to treat (ITT) population subjects who did not have sufficient or reliable lower-leg growth data in order to provide an estimate for both two-week treatment periods (fluticasone furoate and Placebo) or subjects who received any protocol-prohibited medications that may have affected short term growth (e.g. systemic or inhaled corticosteroid medications that could have confounding effects on the interpretation of the growth rate). An ITT analysis of the primary safety endpoint was also performed. Data from previous GSK studies and the literature for other knemometry studies gave estimates of mean lower-leg growth rate for Placebo-treated subjects of 0.40mm/wk to 0.50mm/wk, and an estimate of the standard deviation of 0.30mm/week. Fluticasone furoate 110mcg QD was considered to be non-inferior to Placebo with respect to lower-leg

growth rate if the lower limit of the 2-sided 95% confidence interval for the treatment difference (fluticasone furoate minus Placebo) was greater than or equal to -0.20mm/wk (approximately 40-50% of the Placebo growth rate). Assuming normally distributed data and a true treatment difference (fluticasone furoate minus Placebo) of 0.0mm/wk, 50 completed subjects (25 subjects per sequence) provided at least 90% power. In anticipation of a drop-out rate of 10% after randomisation, approximately 56 subjects were required to be randomised to achieve completion of at least 50 subjects.				
Study Population:				
	TOTAL			
Number of Subjects:				
Planned, N	56			
Randomised,	58 (100)			
Completed, n (%)	57 (98)			
Total Number Subjects Withdrawn, N (%)	1 (2)			
Withdrawn due to Adverse Events n (%)	0			
Withdrawn due to Lack of Efficacy n (%)	0			
Withdrawn for other reasons n (%)	1 (2)			
Demographics	ITT Population		Growth Population	
N (ITT)	58		53	
Females: Males	19:39		18:35	
Mean Age, years (SD)	9.1 (1.37)		9.0 (1.39)	
White, n (%)	56 (97)		51 (96)	
Primary Efficacy Results: there were no efficacy assessments in this study.				
Primary Safety Results: Lower-leg Growth Rate (Growth Population)				
	Placebo (N=53)		Fluticasone furoate (FF) 110mcg QD (N=53)	
	Raw	Change in Rate	Raw	Change in Rate
Baseline				
n	26		27	
Mean (SE)	0.38 (0.066)		0.40 (0.042)	
Mean Treatment Period 1 (SE)	0.45 (0.046)	0.07 (0.085)	0.44 (0.059)	0.04 (0.085)
Mean Treatment Period 2 (SE)	0.40 (0.050)	0.00 (0.065)	0.39 (0.078)	0.01 (0.113)
LS Mean (SE)	0.42 (0.04)		0.40 (0.04)	
LS Mean Difference	-0.016			
p-value against Placebo	0.780			
95% Confidence Interval	-0.13, 0.10			

Safety Results: All AEs occurring during study participation were collected from the Screening visit through to the follow-up phone call, three to seven days after the end of treatment.		
	Placebo (N=57)	FF 110mcg QD (N=58)
All AEs and Drug-Related AEs Reported in >=2 Subjects in any Treatment Group during the Treatment Period (ITT Population)	n (%)	n (%)
Subjects with any AE(s), n (%)	10 (18)	10 (17)
Nasopharyngitis (cold syndrome)	4 (7)	1 (2)
Epistaxis	0	3 (5)
Headache	3 (5)	1 (2)
Cough	1 (2)	2 (3)
Vomiting	3 (5)	0
Diarrhoea	2 (4)	0
Serious Adverse Events No fatal or non-fatal SAEs were reported during the study		
Conclusion: See publications below.		

Publications:

Gradman J, Caldwell MF, Wolthers OD. A 2-week, crossover study to investigate the effect of fluticasone furoate nasal spray on short-term growth in children with allergic rhinitis. Clin Ther. 2007; 29(8):1738-1747.

Gradman J, Caldwell M, Wolthers O. Knemometric assessment of short-term lower-leg growth in children with allergic rhinitis (AR) treated with fluticasone furoate* (FF) nasal spray *USAN approved name. J Allergy Clin Immunol. 2007;119(1):S304 (abstract).

Gradman J, Caldwell M, Wolthers O. Comparison of short term lower leg growth in children treated with fluticasone furoate* nasal spray and vehicle placebo spray (* USAN approved name). Allergy 2007;62(Suppl. 83): 226 (abstract).

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