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.: FFR102123
Title: A randomised double-blind placebo controlled parallel group multicentre long term study to evaluate the safety of once-daily, intranasal administration of GW685698X aqueous nasal spray 100mcg* for 52 weeks in adult and adolescent subjects with perennial allergic rhinitis.
Rationale: The primary objective of this study was to assess the safety and tolerability of 12 months treatment with fluticasone furoate nasal spray 110mcg once daily (QD) in subjects ≥12 years of age with PAR.
Phase: III
Study Period: 14Sep2004 - 09Dec2005
Study Design: This was a 52-week, double-blind, randomised, parallel group, placebo-controlled trial. Following a 7- to 14-day screening period, eligible subjects were randomised to 52 weeks' treatment with fluticasone furoate nasal spray 110mcg QD or vehicle placebo nasal spray in a 3:1 ratio. A follow-up visit was performed 7 days after the last visit.
Centres: Seventy-five (75) centres in thirteen countries (Australia, Chile, Estonia, Germany, Italy, Latvia, Lithuania, Netherlands, New Zealand, Romania, Russia, Spain, and Sweden).
Indication: Perennial allergic rhinitis
Treatment: Subjects were randomised to 52 weeks' treatment with fluticasone furoate nasal spray 110mcg QD or vehicle placebo nasal spray in a 3:1 ratio. *NOTE: GW685698X 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 of this study was to assess the safety and tolerability of 12 months treatment with fluticasone furoate nasal spray 110mcg once daily (QD) in subjects ≥12 years of age with PAR.
Primary Outcome/Efficacy Variable: This is a general long-term safety study. Safety assessments were as follows: adverse events reporting, routine laboratory tests (haematology and chemistry, including complete blood count with differential and liver function tests) and urinalysis , digital centrally-read 12-lead Electrocardiograms (ECG) vital signs (systolic and diastolic blood pressure, heart [pulse] rate,) nasal examinations, 24-hour urinary cortisol assessments, ocular examinations with slit-lamp, funduscopic and tonometry assessments. In addition, plasma concentration of fluticasone furoate was measured to examine population pharmacokinetics in this subject population.
Secondary Outcome/Efficacy Variable(s): As this was primarily a safety study no primary efficacy endpoint was defined. Efficacy was assessed throughout the study period as a measure of treatment compliance upon analysis.
Statistical Methods: The purpose of this study was to provide a long-term safety database for assessing the safety and tolerability of 12 months' treatment with fluticasone furoate nasal spray 110mcg in adult and adolescent subjects with PAR. No statistical hypotheses were tested and no inferential analysis was performed. Summary statistics were provided for all safety and efficacy data. The sample size was calculated based on the ICH guidelines which recommend that a minimum of 300 subjects treated with active drug for 6 months and 100 subjects treated for 12 months are required for a new chemical entity. To achieve this, a total of 700 subjects (525 for fluticasone furoate nasal spray 110mcg and 175 for placebo nasal spray) were planned to be randomised. The proposed sample size allowed for more than 350 subjects to be treated with the active drug for 6 months, assuming a drop out rate of 25-30% over the first six months of the treatment period, and also allowed for approximately 100 placebo-treated subjects to complete the 12-month study for the purposes of treatment comparison on safety parameters, assuming a drop out rate of 40% over the 12-month treatment period. Safety data were summarized based on the ITT Population, defined as all randomized subjects who have received at least one dose of study drug. Urinary cortisol (UC) data were also analyzed for the UC Population, which excluded subjects whose urine samples were considered to have confounding factors that could affect the interpretation of the results. The Pharmacokinetic (PK) Population included all subjects who provided plasma samples for measurement of fluticasone furoate concentration.
Study Population: Male and female subjects >11 years of age with a diagnosis of PAR

	Placebo	Fluticasone furoate (FF) 110mcg
Number of subjects planned, N	175	525
Randomized,[0] N	201	605
Completed, n (%)	144 (72%)	448 (74%)
Total Number Subjects Withdrawn, n (%)	57 (28%)	157 (26%)
Withdrawn due to Adverse Events, n (%)	7 (3%)	38 (6%)
Withdrawn due to Lack of Efficacy, n (%)	5 (2%)	6 (<1%)
Lost to follow-up	4 (2%)	9 (1%)
Withdrawn due to protocol violation	20 (10%)	49 (8%)
Subject decided to withdraw	15 (7%)	48 (8%)
Withdrawn for other reasons, n (%)	6 (3%)	7(1%)
[0]Excludes 4 subjects who were randomized but did not receive any study treatment.		

Primary Efficacy Results:
This was a safety study. See Safety Results below.

Secondary Outcome Variable(s):
There are no secondary outcome variables.

Safety Results
All AEs related to study participation were collected from Visit 1 through Visit 16/Early Withdrawal. On-therapy AEs were defined as events with an onset date the same as or after the treatment start date but prior to or the same as the treatment stop date + 1. A follow up visit 5 to 7 days after the last dose conducted at Visit 16 to assess for adverse events. The 10 most common AEs in each treatment group are shown in the table.

Most Frequent AEs On-therapy	Placebo (N=201) n (%)	FF 110mcg (N=605) n (%)
Subjects with at least one AE	142 (71)	464 (77)
Headache	69 (34)	186 (31)
Nasopharyngitis	51 (25)	157 (26)
Epistaxis	17 (8)	123 (20)
Pharyngolaryngeal pain	18 (9)	53 (9)
Back pain	12 (6)	39 (6)
Upper respiratory tract infection	16 (8)	37 (6)
Influenza	13 (6)	32 (5)
Cough	7 (3)	29 (5)
Abdominal pain upper	11 (5)	23 (4)
Toothache	5 (2)	29 (5)
Dysmenorrhoea	8 (4)	22 (4)
Pyrexia	9 (4)	21 (3)
Ear pain	8 (4)	10 (2)

Serious Adverse Events - On-Therapy
n (%) [n considered by the investigator to be related to study medication]

	Number (%) of Subjects	
	Placebo (N=201)	FF 110mcg (N=605)
Subjects with Serious Adverse Event, n (%) [n] Includes both non-fatal and fatal	4 (2%) [0]	20 (3%) [0]
Appendicitis	1 (<1%) [0]	1 (<1%) [0]
Acute tonsillitis	0	1 (<1%) [0]
Herpes zoster	0	1 (<1%) [0]
Infectious mononucleosis	1 (<1%) [0]	0
Pharyngeal abscess	0	1 (<1%) [0]
Pelvic infection	0	1 (<1%) [0]

Pneumonia	1 (<1%) [0]	0
Tonsillitis	0	1 (<1%) [0]
Tracheitis obstructive	0	1 (<1%) [0]
Cervical vertebral fracture	0	1 (<1%) [0]
Concussion	0	1 (<1%) [0]
Contusion	0	1 (<1%) [0]
Facial bones fracture	0	1 (<1%) [0]
Fall	0	1 (<1%) [0]
Foot fracture	0	1 (<1%) [0]
Wound	0	1 (<1%) [0]
Breast cancer	0	1 (<1%) [0]
Malignant melanoma	0	1 (<1%) [0]
Uterine leiomyoma	0	1 (<1%) [0]
Haemorrhoids	0	1 (<1%) [0]
Inguinal hernia	0	1 (<1%) [0]
Biliary colic	0	1 (<1%) [0]
Cholecystitis	0	1 (<1%) [0]
Ovarian cyst	1 (<1%) [0]	0
Uterine haemorrhage	0	1 (<1%) [0]
Uterine polyp	0	1 (<1%) [0]
Necrosis	0	1 (<1%) [0]
Syncope vasovagal	0	1 (<1%) [0]
Nephrotic syndrome	0	1 (<1%) [0]
Interstitial lung disease	1 (<1%) [0]	0
Subjects with fatal SAEs, n (%) [n]	0	0

Conclusion: See publications below.

Publications: Rosenblut A, Bardin PG, Muller B, M. Faris MA, Wu W, Caldwell MF, Fokkens WJ. Long-term safety of fluticasone furoate nasal spray in adults and adolescents with perennial allergic rhinitis. Allergy 2007;62:1071-1077.

Rosenblut A, Bardin P, Fokkens W, Faris M, Wu W, Caldwell M, Rinia B. Long-term safety of fluticasone furoate* nasal spray (FFNS) 110 mcg once-daily in adults and adolescents with perennial allergic rhinitis (*USAN approved name) Allergy 2007;62(Suppl. 83): 227 (abstract).

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