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.: FFR30006

Title: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study to Evaluate the Efficacy and Safety of Once-Daily, Intranasal Administration of GW685698X Aqueous Nasal Spray 100mcg* for 4 Weeks in Adult and Adolescent Subjects (12 years of age and older) with Vasomotor Rhinitis (VMR)

Rationale: This study was conducted to evaluate the efficacy and safety of fluticasone furoate 100mcg* once daily (QD) nasal spray in subjects with VMR whose symptoms were triggered predominantly by weather/temperature changes.

Phase: III

Study Period: 11 July 2005 – 16 January 2006

Study Design: 4-week, randomised, double-blind, placebo-controlled, parallel-group, multicentre study

Centres: Forty-six centres in six countries randomized subjects in this study: USA (32 sites), Germany (4 sites), Czech Republic (3 sites), Canada (3 sites), Norway (2 sites) and Romania (2 sites).

Indication: Vasomotor Rhinitis (VMR)

Treatment: Subjects meeting specified symptom criteria were randomized to 4 weeks treatment with fluticasone furoate nasal spray 110mcg once daily (QD) or vehicle placebo nasal spray QD.
*NOTE: GW685698X aqueous nasal spray 110mcg (actual); Drug content of Fluticasone Furoate Nasal Spray (FFNS) 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 is to compare the efficacy and safety of FFNS 110mcg once daily (QD) aqueous nasal spray with vehicle placebo nasal spray in adult and adolescent subjects (≥ 12 years of age) with vasomotor rhinitis (VMR).

Primary Outcome/Efficacy Variable:
The primary efficacy variable was mean change from baseline over the entire treatment period in daily, reflective total nasal symptom scores (rTNSS). The total nasal symptom score (TNSS) was the sum of three individual symptom scores for rhinorrhea, nasal congestion and postnasal drip, where each symptom was scored on a scale of 0 to 3. The rTNSS was a rating of the severity of symptoms over the previous 12 hours and was performed in the morning (AM rTNSS) and evening (PM rTNSS). The daily rTNSS was the average of the AM rTNSS and PM rTNSS assessments.

Secondary Outcome/Efficacy Variable(s):
- Mean change from baseline over the entire treatment period in AM, pre-dose, instantaneous total nasal symptom scores (iTNSS)
- Overall Evaluation of Response to Therapy (evaluated on a 7-point categorical scale)

Statistical Methods: The primary analysis method was the comparison of treatment groups (FFNS 110mcg vs. placebo) using analysis of covariance (ANCOVA) with adjustments for baseline rTNSS, country, age, and gender. The least squares mean changes for each treatment group were summarized and compared. The 95% confidence interval (CI) and p-value for the treatment mean difference (fluticasone furoate and placebo) were reported. The secondary efficacy measures concerning nasal symptoms were analyzed similarly to the primary analysis. The response to therapy data was summarized and analyzed using a logistic regression model.
Approximately 350 subjects were required for this study, with 175 subjects in each of the two treatment groups: FFNS 110mcg and placebo nasal spray. The standard deviation for the mean change from baseline over the entire treatment period in daily rTNSS was assumed to be 1.7, based on previous VMR and perennial nonallergic rhinitis (PNAR) studies with other intranasal corticosteroids (fluticasone proprionate nasal spray) and antihistamines (azelastine hydrochloride). Using a two-sample t-test with a two-sided significance level of 0.05, the chosen sample size provided 90% power to detect a difference of 0.6 between active treatment and placebo in the mean change from baseline over the entire treatment period in daily rTNSS.

Study Population: Male and female subjects were eligible for treatment as outpatients if they were ≥12 years of age and had a diagnosis of VMR.

	Placebo	Fluticasone Furoate (FF) 110mcg
Number of Subjects:		
Planned, N	175	175

Randomised, N	173	179
Completed, n (%)	160	167
Total Number Subjects Withdrawn, N (%)	13 (8)	12 (7)
Withdrawn due to Adverse Events n (%)	3 (2)	3(2)
Withdrawn due to Lack of Efficacy n (%)	1 (<1)	0
Withdrawn for other reasons n (%)	9 (6)	9 (5)
Demographics	Placebo	FF 110mcg
N (ITT)	173	179
Females: Males	122:51	125:54
White, n (%)	163 (94)	169 (94)
Mean Age, years (SD)	45.0 (14.66)	46.6 (16.77)
12-<18 years	9 (5)	13 (7)
18-<65 years	149 (86)	140 (78)
65-<75 years	14 (8)	16 (9)
≥75 years	1 (<1)	10 (6)
Primary Efficacy Results:		
Daily rTNSS (ITT)	Placebo N=172	FF 110mcg N=176
LS Mean Change (SE)	-1.71 (0.16)	-2.05 (0.15)
LS Mean Difference	-0.335	
p-value	0.0504	
95% CI	-0.67, 0.00	
Secondary Outcome Variable(s):		
AM pre-dose iTNSS	Placebo N=170	FF 110mcg N=176
LS Mean Change (SE)	-1.48 (0.16)	-1.87 (0.16)
LS Mean Difference	-0.393	
95% CI	(-0.74, -0.05)	
Overall Response to Therapy, n (%)	Placebo N=168	FF 110mcg N=176
Significantly Improved	26 (15)	33 (19)
Moderately Improved	37 (22)	40 (23)
Mildly Improved	45 (27)	47 (27)
No Change	52 (31)	50 (28)
Mildly Worse	1 (<1)	3 (2)
Moderately Worse	4 (2)	1 (<1)
Significantly Worse	3 (2)	2 (1)
Safety Results: All adverse events (AEs) occurring between Visit 1 (Screening) and Visit 6/Early Withdrawal were collected. On-therapy AEs were defined as those occurring between randomization and Visit 6/Early Withdrawal. In addition, as follow-up contact was made to all subjects 3 to 5 days after study completion (Visit 6) to assess post-treatment AEs. On-therapy SAEs were defined as those occurring between randomization and the follow-up contact.		
	Placebo N=173	FF 110mcg N=179
Most Frequent Adverse Events – On-Therapy	n (%)	n (%)
Subjects with any AE(s), n (%)	65 (38)	61 (34)
Headache	23 (13)	12 (7)
Nasopharyngitis	8 (5)	8 (4)
Epistaxis	4 (2)	4 (2)
Pharyngolaryngeal pain	1 (<1)	5 (3)
Diarrhoea	0	5 (3)
Back pain	2 (1)	3 (2)
Sinus headache	3 (2)	2 (1)
Upper respiratory tract infection	4 (2)	1 (<1)
Dysmenorrhoea	3 (2)	1 (<1)
Neck pain	3 (2)	0

Pain in extremity	3 (2)	0
Serious Adverse Events - On-Therapy n (%) [n considered by the investigator to be related to study medication]		
	Placebo N=173	FF 110mcg N=179
Subjects with non-fatal SAEs, n (%)	0	0
Subjects with fatal SAEs, n (%)	0	0

Conclusion:

- Once-daily FFNS 110mcg nasal spray failed to demonstrate efficacy when compared with placebo in adults and adolescents ≥12 years of age with VMR as specifically defined for this study as those subjects who have symptoms triggered predominantly by weather/temperature changes.
- Data from this study demonstrated the safety of FFNS110mcg in adults and adolescents ≥12 years of age with VMR, as specifically defined for this study as those subjects who have symptoms triggered predominantly by weather/temperature changes, over a 4-week treatment period. FFNS110mcg was well-tolerated in this study based upon AE reporting, nasal examinations, vital signs, laboratory values, or ECG following treatment with FFNS 110mcg in comparison with placebo nasal spray.

Publications: No publication

Date updated: 6-Mar-2008