CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-114/S006

STATISTICAL REVIEW(S)

STATISTICAL REVIEW AND EVALUATION
CLINICAL STUDIES

Date:

AUG 13 2000

NDA#:	20-114/SE5-006
Applicant:	Wallace Laboratories
Name of Drug:	Astelin (azelastine hydrochloride)
Indication:	Vasomotor rhinitis in adults and children 12 years of age and older
Documents Reviewed:	3/24/99 Volumes 1.1; 8-12, electronic data; 1/14/2000
Statistical Reviewer:	Stephen E. Wilson, Dr.P.H. (Biostatistics)
Medical Input:	Charles Lee, M.D.

The sponsor has submitted the results of two multicenter, double-blind, placebo controlled, parallel group clinical trials (Studies 335 and 336) in support of the claim that Astelin Nasal Spray, 137 mcg, is safe an effective for "the treatment of symptoms of vasomotor rhinitis in adults and children 12 years of age and older." The primary efficacy variable for these studies was an average change from baseline of Total Vasomotor Rhinitis Symptom Scores [the TVRSS (including nasal congestion, sneezing, rhinorrhea and postnasal drip, scaled from 0 – 3, ranging from "none" to "severe")] recorded during the three-week treatment periods of the trials. A total of 426 subjects were randomized in the two studies (223 patients in Study 335, and 303 in Study 336).

Study Results

The reported statistical comparisons, based on the results of both studies, demonstrate that (under the conditions of each trial) the test treatment (Astelin Nasal Spray, 137 mcg) was significantly more effective than placebo. As reported by the sponsor, it appears that both studies included well-balanced treatment populations at baseline and had relatively few dropouts, protocol violations or non-compliant patients. The intent-to-treat populations used in the primary analyses included 97.8% and 96.9% of the randomized patients in Studies 335 and 336, respectively. Analyses of the primary endpoints (TVRSS) and individual symptom scores were based on ANCOVA (with baseline as a covariate), including terms for treatment and center.

The primary efficacy results from the two studies, demonstrating the sponsor's claimed efficacy, were remarkably similar (see Table 1, below). Both the three-week average (overall) and endpoint ANCOVA analyses demonstrated strong, statistically significant results. Scores were similar at baseline and the recorded improvements were almost exactly the same in the two studies (e.g., mean improvement in the Azelastine treatment groups of the two studies was 1.54, while the placebo groups were within about 3% of each other.) The results for individual symptom scores and the weekly scores for TVRSS and symptoms contributed to the strong evidence that the drug worked in the circumstances of the trials designed and conducted by the sponsor.

Table 1. Results of primary efficacy analyses based on change from baseline in TVRSS

Analysis	Study	Treatment Group	N	Improvement			
				Baseline	Mean	SEM	P-Value
Overall	335	Azelastine	111	6.51	1.54	0.14	0.002
		Placebo	107	6.64	0.84	0.17	
	336	Azelastine	97	6.52	1.54	0.18	0.005
		Placebo	99	6.65	0.88	0.18	
Endpoint	335	Azelastine	111	6.51	1.86	0.21	0.49
		Placebo	107	6.64	1.26	0.22	
	336	Azelastine	97	6.52	1.86	0.23	0.004
		Placebo	99	6.65	1.01		

Conclusion

This reviewer was able use the data supplied by the sponsor to verify the results of these studies and concurs with the Medical Reviewer, Dr. Charles Lee, (ref. Medical Officer Review dated 8/25/2000) that these results provide statistical evidence that azelastine was effective in relieving the symptoms included in the TVRSS.

/S/

Stephen E. Wilson, Dr.P.H.
Team Leader

This review contains 2 pages of text.

cc:
Archival NDA 20-114/SE5-006
HFD-570
HFD-570/Chowdhury/Lee/Borders
HFD-715/Div. File
HFD-715/Wilson/Nevius

APPEARS THIS WAY
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