The study listed may include approved and nonapproved 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 registry, healthcare professionals should consult prescribing information for the product approved in their country.

Title of Study:	Randomized, Placebo-Controlled, Cross-Over Study to Evaluate the Effect of the Coadministration of Desloratadine (5 Milligram) Plus Pseudoephedrine (240 Milligram) on Nasal Congestion Compared to Desloratadine 5 Milligram Alone, and Placebo, in Subjects With Seasonal Allergic Rhinitis Who Have Been Exposed to Pollen in the Vienna Challenge Chamber (VCC) (Protocol No. P02560)
Studied Period:	Fall 2003 — **Clinical Phase:** 2

Objective(s)

Primary Objective(s): The primary objective of this study was to evaluate the effect of pseudoephedrine (PSE) 240 mg on nasal congestion when taken in combination with desloratadine (DL) 5 mg in subjects with seasonal allergic rhinitis (SAR) who were exposed to pollen in the Vienna Challenge Chamber (VCC). This objective was accomplished by comparing the effect on nasal congestion over the 7.5-hour observation period of DL 5 mg taken alone to that of DL 5 mg and PSE 240 mg taken in combination.

Secondary Objective(s): The key secondary objective was to evaluate the effect of pseudoephedrine (PSE) 240 mg alone on nasal congestion over the 7.5-hour observation period compared with placebo. Another secondary objective was to evaluate the safety profile of postdose adverse events and vital signs compared with predose evaluations. Postdose blood pressure and pulse were collected hourly and at the final time point.

Methodology: This was a randomized, placebo-controlled, four-way crossover, single-center, double-blind study of DL, PSE, placebo, and the concurrent use of DL and PSE, in subjects with SAR conducted in conformance with Good Clinical Practices.

Number of Subjects: 73 subjects were treated; 68 of them completed all four phases

Diagnosis and Criteria for Inclusion: Subjects were between 18 and 65 years of age, of any race, with at least a 2-year history of grass SAR. In addition, subjects were to meet the following key criteria:

Key Inclusion Criteria:

- A positive skin test for the grass pollen allergen used in the chamber at screening or within the prior 12 months;
- A negative urine pregnancy test (female subjects of childbearing potential) at screening and at monthly intervals;
- The following minimum scores at some point during each of the 120-minute screening period challenge sessions:
  - Nasal Congestion Score of at least 2 (moderate);
  - Total Nasal Symptoms Score of at least 6;
  - Total Non-nasal Symptoms Score of at least 2.
- Freedom from any clinically significant disease, other than SAR, that would interfere with the study evaluations.

Key Exclusion Criteria:

- An upper or lower respiratory tract infection within 4 weeks before screening;
- Dependence on nasal, oral, or ocular decongestants, nasal topical antihistamines, or nasal steroids, in the opinion of the investigator;
- A known potential for hypersensitivity, allergy, or idiosyncratic reaction to the study drug or excipients.

Duration of Treatment: After a screening phase of 1-28 days, subjects received one dose of treatment at each of four treatment visits. There was at least a 10-day washout period between each treatment visit.

Test Product, Dose, Mode of Administration: Desloratadine 5 mg plus pseudoephedrine 240 mg.

Reference Therapy, Dose, Mode of Administration: DL 5 mg tablet alone with PSE placebo capsule, PSE 240 mg capsule alone with DL placebo tablet, and placebo (DL 5 mg tablet placebo tablet plus PSE 240 mg placebo capsule. Treatments were administered orally.

Criteria for Evaluation

Primary Efficacy Comparisons: The primary efficacy parameter was the subjectively evaluated nasal decongestant effect, expressed as an average change from baseline over the 7.5 hour evaluation period. The primary comparison for this variable is DL 5 mg plus PSE 240 mg taken in combination versus DL 5 mg alone.

Secondary Efficacy Comparisons: The key secondary endpoint is:

- Average change from baseline in nasal congestion between PSE 240 mg and placebo over the 7.5-hour evaluation period and at each time point.

Other secondary comparisons include:

- Average change from baseline in total and individual symptom scores over the study period and at each time point.
- Onset of action: defined as the first time point at which a consistent, statistically significant ($p \leq 0.05$) reduction in total symptom score is achieved (active vs placebo) relative to predose baseline symptom scores.
- Average change from baseline in peak nasal inspiratory flow (PNIF) over the study period and at each time point.
- Average change from baseline in nasal airway airflow as measured by rhinomanometry over the study period and at each time point.
- Average change from baseline in nasal secretion weights over the study period and at each time point.

All pairwise treatment comparisons were performed for all efficacy endpoints.

Statistical Methods: The primary efficacy variable was nasal congestion. The nasal decongestant effect was expressed as an average change from baseline over the 7.5-hour evaluation period. The primary comparison for this variable was DL 5 mg plus PSE 240 mg taken in combination vs DL 5 mg alone. Pairwise comparisons were made using linear contrasts of the treatment means obtained from an analysis of variance (ANOVA) model that extracts sources of variance due to treatment, subject, and phase. An ANOVA model using treatment, phase, subject, and treatment-by-phase interaction was performed to evaluate any carryover effects. The same ANOVA models were also used for the primary variable at each time point. Summary statistics for the primary variable were to be provided for the subgroups sex and race. Analysis of the primary efficacy variable was also performed for the subjects who completed all four phases of treatment.

All of the secondary analyses used the same ANOVA model as for the primary efficacy endpoint. All pairwise treatment comparisons were performed primarily to estimate treatment differences.

SUMMARY - CONCLUSIONS:

RESULTS:

Efficacy: The results for average change from baseline in nasal congestion, for all 73 treated subjects, showed decreases of 27.3% for DL 5 mg + PSE 240 mg, 9.5% for DL 5 mg, 22.6% for PSE 240 mg, and 4.9% for placebo. The combination of DL plus PSE and PSE alone was significantly ($P<0.001$) more effective in relieving nasal congestion than DL 5 mg alone or placebo. These results were similar to those for the 68 subjects who completed all four phases of treatment.

For secondary efficacy parameters that are considered objective assessments of nasal congestion (ie, PNIF and rhinomanometry), the combination of DL 5 mg and PSE and PSE alone were more effective than DL alone or placebo.

Assessment of subjective symptoms other than nasal congestion also supported the results of the nasal congestion assessment.

For the secondary efficacy parameter that is considered an objective assessment of rhinorrhea, ie, weights of nasal secretions, all three active treatments were significantly superior to placebo in reducing the weights from baseline but were not significantly different from each other.

Safety: Over the course of the study, 10 subjects reported adverse events: 4 (6%) after DL 5 mg + PSE 240 mg, 4 (6%) after DL 5 mg, 3 (4%) after PSE 240 mg, and 4 (6%) after placebo. The most common adverse

event for all treatments was headache, which occurred in 3 (4%) subjects after DL 5 mg + PSE 240 mg, 1 (1%) after DL 5 mg, 3 (4%) after PSE 240 mg, and 1 (1%) after placebo. Most adverse events, although severe, occurred many days after treatment, and most were considered unlikely related to treatment according to the investigator. No notable differences among treatments were apparent. There were no serious adverse events during the study. The only treatment discontinuation for an adverse event occurred after placebo treatment. No treatment differences were apparent in change from baseline in vital signs.

CONCLUSIONS:

- Combination treatment with DL 5 mg and PSE 240 mg was significantly more effective than DL 5 mg alone or placebo, and numerically more effective than PSE 240 mg alone, in relieving nasal congestion. The combination of DL and PSE was also more effective than its components and placebo in relieving most other symptoms of SAR in the Vienna Pollen Chamber.

- The objective assessments of nasal airflow (PNIF and rhinomanometry) supported the subjective symptom assessment of nasal congestion.

- The objective assessment of nasal secretion weights supported the subjective assessment of the symptom of rhinorrhea.

- All treatments were safe and well tolerated.

Date of the Report: 16 APR 2005