# A Patient Follow-Up Survey Program for LOTRONEX® (alosetron HCl): Assessing Compliance with the Risk Management Program

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## Abstract

**Background**: In November 2002, Lotronex® (alosetron HCl) was reintroduced to the U.S. market for women with severe diarrhea-predominant IBS who have failed to respond to conventional therapy, whose IBS symptoms are chronic, and for whom other explanatory gastrointestinal medical conditions have been ruled out. In support of the reintroduction, GlaxoSmithKline (GSK) implemented a risk management program (RMP). As part of the evaluation of the RMP, GSK sponsored a patient follow-up study, conducted by RTI Health Solutions, in which all users of Lotronex have the opportunity to participate.

**Objective**: The primary objective of this epidemiological study is to measure how well physicians and patients are following the RMP requirements for prescribing and using Lotronex and how well patients comprehend the information provided to them.

**Methods**: Patients voluntarily enroll in the study via pre-enrollment forms provided by their physicians or in the medication packaging. Following consent and formal enrollment, data are collected by mail at baseline, and by mail or telephone after five and ten weeks, and quarterly thereafter. Questions focus on patient clinical eligibility and compliance with education, prescribing, and dispensing requirements. Questions measuring patient comprehension of the educational materials were rigorously tested through cognitive interviewing and added to the baseline questionnaire.

**Results**: Between December 9, 2002 and March 31, 2004, 4,196 patients enrolled in the study. Fifty-three percent (53%) of pre-enrollment forms came from patients who received them from their physician. Once enrolled, 67% continued to respond to the follow-up questionnaires with an average follow-up time of approximately 6 months. The response rate for each follow-up assessment was over 95%. Further, 89% of patients at baseline met the full clinical eligibility criteria for treatment with Lotronex. At baseline, over 90% of patients reported signing a physician-patient agreement (PPA), having discussions with their physician about using Lotronex, and having read the medication guide.

**Conclusion**: Results indicate a high rate of compliance with respect to appropriate patient prescribing, patients signing the PPA, and reading and understanding the patient materials. This suggests that patients are engaged in active dialogue about their symptoms and the use of Lotronex.

## Introduction

- Lotronex was initially approved in the U.S. market in February 2000 for women with diarrhea-predominant IBS.
- Due to concerns about safety, Lotronex was voluntarily withdrawn on November 1, 2000 by GSK in consultation with the U.S. Food and Drug Administration (FDA).
- In June 2002, the FDA approved the Supplemental New Drug Application for Lotronex under restricted conditions of use. The restrictions included a Risk Management Program (RMP); the Prescribing Program for Lotronex, which is a component of the RMP; and a revised indication that reflected the intent to reserve Lotronex for patients in whom the medical benefits outweigh the risks, namely, women with severe diarrhea-predominant IBS. These changes were reflective of the serious gastrointestinal adverse events, some fatal, that have been reported with the use of Lotronex.
- GSK has undertaken evalution of the RMP through a variety of mechanisms, including the Patient Follow-up Survey Program.

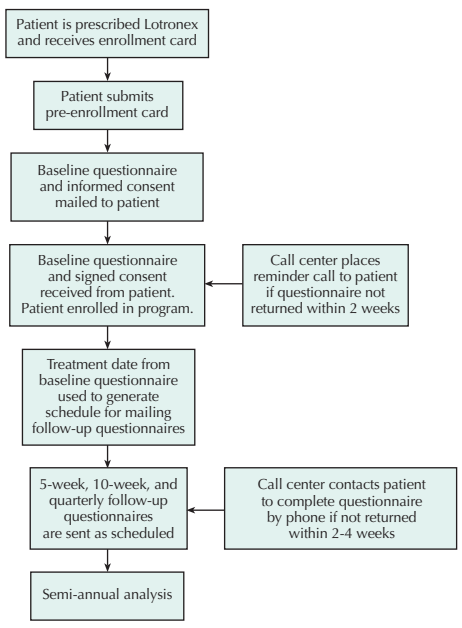
### Primary Objectives of Patient Follow-up Survey Program

- Assess the extent to which the patient satisfies the guidelines for treatment with Lotronex.
- Measure how well physicians and patients are following the RMP requirements for prescribing and using Lotronex.
- Measure patient comprehension of information provided via patient materials and physician discussion.

## Methods

Patients are invited to complete a pre-enrollment card, located in every medication package for Lotronex or obtained from a prescribing physician.

The following graphic illustrates the flow of data collection through the patient follow-up survey program.




## Methods (continued)

- All questions were rigorously tested through cognitive interviewing.
- Although adverse events are not solicited, reports of adverse events are volunteered by patients. In these cases, information is anonymized and provided to GSK according to standard operating procedures.

### Baseline Data Collected

Baseline data collected include

- IBS history
- Symptoms, impact on quality of life, and treatment prior to Lotronex
- Current dosage and frequency of use of Lotronex
- Patient interaction with prescribing physician
- Comprehension of educational materials

### Follow-Up Assessments

5 weeks, 10 weeks, and quarterly, including

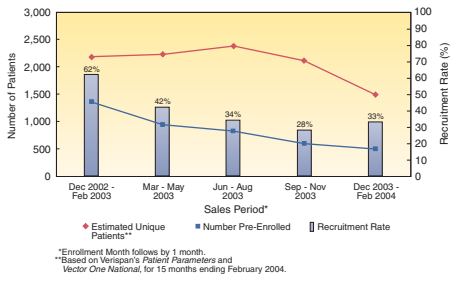
- Current dosage and frequency of Lotronex
- Continued interaction with the prescribing physician.

## Results

### Response Rates

- As of March 31, 2004,
  - 4,618 pre-enrollment cards from a total of 4,196 unique patients were received (422 duplicate cards were received).
  - 3,660 completed baseline assessments were received.
- Estimated 40% of all patients with a prescription for Lotronex pre-enrolled in the survey program and 35% completed a baseline questionnaire.
- Of pre-enrollment cards received, 53% were issued by the prescribing physician's office.

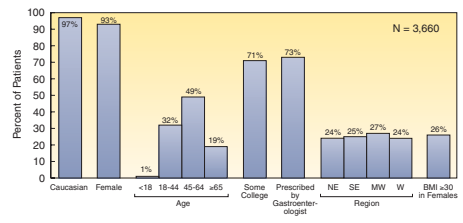
**Patterns of Sales and Pre-Enrollment**




### Descriptive Statistics

Descriptive statistics of participating patients at baseline are detailed in the following graph.

**Selected Patient Characteristics at Baseline (N = 3,660)**



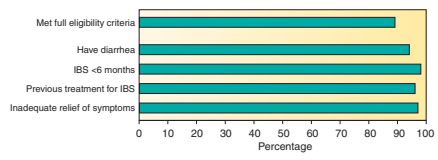

- 53% of patients had used Lotronex prior to its reintroduction in November 2002.

### Eligibility

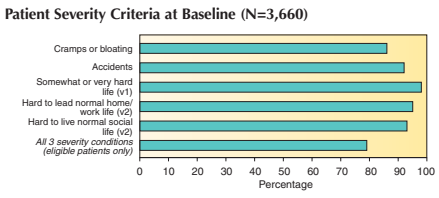
- 90% of women and 80% of men met all eligibility criteria for receiving Lotronex.
- At baseline, 94% of patients reported diarrhea as their main bowel problem.
- 1% of patients (N=31) reported constipation as their main problem. Of these, 65% (N=20) have discontinued use of Lotronex.
- 5% of patients (N=162) reported "other" as their main bowel problem.
- 98% of the enrolled patients met at least one of the three eligibility criteria, with 76% fulfilling all three severity criteria (see graph below).

The following graph shows compliance with patient eligibility criteria at baseline.

**Patient Eligibility Criteria at Baseline (N=3,660)**




**Patient Severity Criteria at Baseline (N=3,660)**

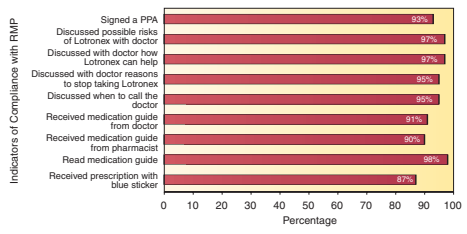



- There were no meaningful differences between eligibility and severity of males and females.

## Results (continued)

### Compliance

The following graph illustrates compliance with various aspects of the RMP at baseline.




- 268 patients reported adverse events, which included reports of lack of efficacy. No new signals have emerged from the study.

### Retention Rates

- Once patients are enrolled in the survey, retention rates are exceptionally high (see table below).
- There were no meaningful differences between patients continuing in the study and those lost to follow-up.

**Retention Rates**

| Patient Population | Response Rate |
|---|---|
| Baseline respondents* | 89% |
| Week 5 follow-up respondents | 97% |
| Week 10 follow-up respondents | 98% |
| Quarter 1 follow-up respondents | 98% |
| Quarter 2 follow-up respondents | 97% |
| Quarter 3 follow-up respondents | 98% |

*Among those patients who submitted a pre-enrollment form.

### Limitations

- Study patients may not necessarily represent all users of Lotronex. Comparisons with national prescription data show similar distributions of age, sex, geographic region, and specialty of prescribers for study patients and national prescriptions.
- By design, this program uses a passive recruitment process. In the Lotronex survey program, the sample population is unknown until the patients initiate contact with the program.
- All survey data are self-reported by patients and not confirmed by their physicians.

### Strengths

- The program provides real-time monitoring of RMP compliance.
- Once enrolled, the retention rate across multiple follow-up assessments remains greater than 95%.
- There were no meaningful differences between patients continuing in the study and those lost to follow-up.
- There are few benchmarks of this type of program for comparing response rates; however, the patient survey program for Accutane® and generic isotretinoin recently reported participation rates between 16% and 26% (Brinker, 2004).

### Discussion

Compliance with all aspects of the Lotronex RMP process that were monitored through this study was extremely high.

Data indicate that 98% of patients meet at least one of the three eligibility criteria for severity, and that 80% of the eligible female patients in the survey suffer from all three severity symptoms. These data suggest that compliance with the severity criteria is high and perhaps this is an indication of conservative physician prescribing patterns for Lotronex and/or an indication of the types of patients who choose to use Lotronex and/or participate in the survey.

The results of the patient survey suggest that patients are actively engaging with their physicians about the RMP. Over 90% of patients report

- Having a discussion with their physicians about risks and benefits
- Receiving and reading the medication guide
- Signing the PPA form.

These data, coupled with the high education level of participating patients, indirectly suggest that these users of Lotronex are knowledgeable about the risks and benefits of Lotronex.

## Acknowledgments

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## References

Brinker, A. (2004). *Isotretinoin Pregnancy Prevention Program Evaluation: Prescription Compliance Survey and Patient Surveys*. Presented to the Joint Dermatologic and Ophthalmic Drugs and Drug Safety and Risk Management Advisory Committee of the U.S. Food and Drug Administration (FDA), February 26. Available: http://www.fda.gov/ohrms/dockets/ac/04/slides/4017S1_07_Brinker.ppt (accessed August 2004).

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