Temporal Trends in Compliance With the Alosetron Risk Management Program

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BACKGROUND

Under a Risk Management Program (RMP) intended to assure safe use, alosetron was reintroduced in November 2002 for treatment of female patients with severe diarrhea-predominant irritable bowel syndrome (IBS) who have not responded to conventional therapy, where IBS is defined as at least six of the following symptoms or conditions for 12 weeks in the past 24 weeks: (1) ≥2 bowel movements daily; (2) abdominal pain or cramping; (3) abdominal bloating; (4) onset of symptoms is related to meals; (5) bowel movements are often straining or painful; (6) bowel movements are usually formed but some are not; (7) bowel movements may be changed in number or frequency; and (8) the patient’s symptoms have been sufficiently severe to impact the quality of life. Alosetron is contraindicated in patients with a history of ischemic or inflammatory bowel disease, previous inflammatory bowel disease (e.g., Crohn’s disease, ulcerative colitis), or unexplained rectal bleeding. Alosetron has been associated with a higher risk of ischemic colitis, which can be fatal. Alosetron is also contraindicated in patients with a current history of myocardial infarction, unstable angina, or cerebrovascular accident (CVA). Alosetron is contraindicated in women who are pregnant or breastfeeding. Alosetron is only approved for the treatment of severe diarrhea-predominant IBS in women. Comorbidity medical conditions have been ruled out. These patients have one or more of the following severity criteria:

1. Frequent and severe abdominal pain/discomfort
2. Frequent bowel urgency or fecal incontinence
3. Disability or restriction of daily activities due to IBS
4. Physicians are recommended to begin treatment at the lowest dosage (0.5 mg twice daily) for 1 month to determine the occurrence of constipation, a known adverse event associated with alosetron. Based on patient response, the dosage of alosetron can be increased to 1 mg twice daily.

RMP requirements include the following:

• Physicians
  – Enroll in the prescribing program
  – Assess patient regarding risks and benefits of treatment
  – Sign physician-patient agreement (PPA) form
  – Affix a blue program sticker to all prescriptions
• Patients
  – Read the PPA
  – PharMerica
  – Dispense a medication guide
  – Verify the presence of the blue sticker for new prescriptions of alosetron.

A key component of the RMP is a cohort study that has been conducted by RTI Health Solutions in which all users of alosetron have the opportunity to participate through a continuous enrollment process. RTI Health Solutions randomly selects patients for inclusion through questionnaires. The primary objectives of the study are:

• To measure how well physicians and patients are following the RMP requirements for prescribing and using alosetron
• To measure how well patients complied with the information provided to them
• To monitor temporal trends in compliance with this alosetron RMP

Data are collected on a customized schedule based on the patients’ enrollment and follow-up are shown in Figure 1. Figure 2. Data collection includes enrollment (sent to patient), week 10, and (week 5, 1 year) Patient enrollment and follow-up are shown in Figure 1. Patients are invited to complete and return a pre-enrollment card. After patients are invited to complete a baseline questionnaire, response to follow-up remained high over the follow-up period (> 95% each year) Figure 3. Table 1. Percentage of Correct Patient Responses to Baseline Knowledge Questionnaire. Column 1: Calendar Year Percentage Correct Baseline 2003 2004 2005 2006 2007 2008 2009 0 10 20 30 40 50 60 70 80 90 100

No. Patients on Study (%)

• Study patients may not necessarily represent all users of alosetron. However, we identified no data to suggest that they do not. Comparisons of participants with national/prescription data show similar distribution of age, sex, geographic region, and specialty of prescribers. Enrollment through cards via prescriptions was high (~ 50% throughout the study). Thus, it appears that participants may have been high in regards to patients who experienced side effects who were more likely to possess greater familiarity and comfort with the clinical decisions and treatment processes and with the RMP requirements for prescribing and using alosetron.

METHODS

• Patients are invited to complete a baseline questionnaire, located in every medication package for alosetron or obtained from a prescribing physician. Patient enrollment and follow-up are shown in Figure 1. Figure 2. Patients were invited to complete the questionnaire by phone between 2003–2009. Data are collected on a customized schedule based on the patients’ enrollment start date.

RESULTS

• As of December 31, 2009, 6,066 patients enrolled in the cohort study by completing a baseline form. Overall, 33% were white and 92% female. The distribution of age at enrollment was 32% < 45 years, 48% 45–64 years, and 20% ≥ 65 years. There has been high variation in demographic characteristics over time.

DISCUSSION

• Temporal trends in reported responses at baseline are very useful for understanding the characteristics of patients and compliance with the requirements for minimizing risk.

• Since inception of the alosetron RMP, most participants in the study have consistently met eligibility criteria over time. Figure 4. PROportion of Correct Patient Responses to Baseline Knowledge Questionnaire. Column 1: Calendar Year Percentage Correct Baseline 2003 2004 2005 2006 2007 2008 2009 0 10 20 30 40 50 60 70 80 90 100

• Among those completing a baseline questionnaire, response to follow-up remained high over the follow-up period (> 95% each year) Figure 5. Table 2. Percentage of Correct Patient Responses to Baseline Knowledge Questionnaire. Column 1: Calendar Year 2003 2004 2005 2006 2007 2008 2009 0 10 20 30 40 50 60 70 80 90 100

• Frequent bowel urgency or fecal incontinence
• IBS history, symptoms, impact on quality of life, and treatment before
• Current dosage of alosetron and frequency of use

• Overall, 33% were white and 92% female. The distribution of age at enrollment was 32% < 45 years, 48% 45–64 years, and 20% ≥ 65 years. There has been high variation in demographic characteristics over time.

LIMITATIONS

• Study patients may not necessarily represent all users of alosetron. However, we identified no data to suggest that they do not. Comparisons of participants with national/prescription data show similar distribution of age, sex, geographic region, and specialty of prescribers. Enrollment through cards via prescriptions was high (~ 50% throughout the study). Thus, it appears that participants may have been high in regards to patients who experienced side effects who were more likely to possess greater familiarity and comfort with the clinical decisions and treatment processes and with the RMP requirements for prescribing and using alosetron.

• By design, this study uses a passive recruitment process. Thus, the sample population is unknown until the patients initiate contact with the program.

STRENGTHS

• The program provides real-time monitoring of RMP compliance through the experience of the patients.

• The program has now been evaluated for over 7 years and suggests consistent effectiveness and compliance with the RMP over time.

CONCLUSIONS

The study demonstrated high compliance and little variation in compliance with the RMP among participants in the cohort study over the 7 years since inception.

REFERENCES


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Provenance: 9th International Conference on Pharmacoeconomics & Therapeutic Risk Management
August 19, 2010
Brighton, England, UK