

Lubiprostone Approved for Irritable Bowel Syndrome With Constipation in Adult Women

The US Food and Drug Administration (FDA) recently approved lubiprostone (Amitiza, Sucampo/Takeda) for the treatment of irritable bowel syndrome with constipation (IBS-C) in women over 18 years of age. FDA approval was based on two studies involving 1,154 patients diagnosed with IBS-C, of whom more than 90% were women. Patients enrolled in the studies were experiencing mild abdominal discomfort or pain associated with at least two of the following symptoms: fewer than 3 spontaneous bowel movements per week that did not result from the use of laxatives; hard stools; and moderate or severe straining with bowel movements. In the studies, more patients who received lubiprostone reported moderate or significant symptom relief over a 12-week treatment period compared to patients who received placebo. Long-term treatment with the drug was evaluated in a study in which all patients were administered lubiprostone for 9–13 months. Common side effects included nausea, diarrhea, and abdominal pain, whereas less frequent side effects included urinary tract infections, dry mouth, syncope, peripheral edema, dyspnea, and heart palpitations, according to the FDA. Lubiprostone was previously approved for the treatment of chronic idiopathic constipation at the dosage of 24 µg twice daily, which is higher than the doses of 8 µg twice-daily recommended for IBS-C in adult women. According to the FDA, the drug was not approved for IBS-C in men because its efficacy was not conclusively demonstrated in the studies. IBS-C has been shown to be twice as prevalent in women than in men.

Fluvastatin and Hepatitis C Replication

Led by Ted Bader, MD, of the Veteran's Administration Medical Center and University of Oklahoma Health Sciences Center in Oklahoma City, Oklahoma, researchers sought to evaluate the safety and antiviral effects of fluvastatin in patients with chronic hepatitis C virus (HCV), as earlier in vitro experiments with fluvastatin revealed antiviral effects against HCV. This prospective study, which was recently published online in the *American Journal of Gastroenterology*, examined 31 veterans with chronic HCV who were administered oral doses of fluvastatin (20–320

mg daily) for 2–12 weeks with weekly monitoring of HCV RNA levels and liver examinations. Reductions in the viral load ($P < .01$) versus that of a control group were considered suppressive.

The authors found that among patients receiving 80 mg or less of fluvastatin daily, 11 of 22 (50%) patients responded with reductions in their HCV RNA levels. The first decrease occurred within 4 weeks (9/11, 82%), and the greatest weekly change in HCV RNA levels was a reduction of $1.75 \log_{10}$. When HCV RNA levels decreased in responders, they remained relatively constant for 2–5 weeks (7/9, 78%) or they rebounded immediately on the following examination to a nonsignificant change from baseline ($n=2$). Continued lowering of HCV RNA levels was evident in 2 of 19 (22%) patients at the conclusion of the study. There was no evidence of worsening in the liver examinations. The authors concluded that the use of fluvastatin as in vivo monotherapy revealed clinical suppressive effects of HCV that were modest, variable, and often short-lived and that these findings provided proof-of-concept for pilot trials combining fluvastatin with standard therapy. In fact, the researchers have already initiated a phase II randomized controlled trial that combines fluvastatin with the standard HCV treatment of pegylated interferon and ribavirin.

Long-term Efficacy of Laparoscopic Antireflux Surgery

According to the May issue of *Archives of Surgery*, Denise W. Gee, MD, of Massachusetts General Hospital and Harvard Medical School in Boston, Massachusetts, and colleagues investigated long-term effects and quality-of-life issues in patients undergoing laparoscopic antireflux surgery. The Gastroesophageal Reflux Disease–Health-related Quality-of-Life Scale (GERD-HRQL), a validated survey instrument, was mailed to 405 consecutive patients who underwent primary or revision laparoscopic funduplications (LFs) from 1997 to 2006 in a tertiary care referral center. The study also assessed reoperation rate, patient satisfaction, and medication use of the patients.

The authors reported a response rate of 54% to their questionnaire. Participants averaged age 52 years and 60% of the patients were women. Median follow-up consisted of 60 months (range, 4–75 months). In patients who underwent primary LF, the mean (SD) GERD-

HRQL score was 5.71 (7.99) (range, 0–45, with 0 representing the absence of symptoms). Seventy-one percent of patients who underwent primary antireflux surgery were satisfied with their long-term results, compared to only 35% of patients who underwent revision antireflux surgery. Forty-three percent of patients took antireflux medications following surgery; half of these patients did not have any recurrence of GERD, as documented by diagnostic testing. Only 3 patients (1.2%) required reoperation. Among patients who underwent revision LF, higher GERD-HRQL scores (mean [SD], 14.25 [10.33]) were reported, as well as lower satisfaction (35%) and greater probability of requiring antireflux medication (78%). Patients who had body mass indexes (BMIs) between 25 and 35 had lower GERD-HRQL scores than patients who were thin (BMI <25) or morbidly obese (BMI ≥35). The authors concluded that, unlike the current medical literature, patients undergoing primary LF performed by an experienced surgical team have near-normal GERD-HRQL scores at long-term follow-up and low reoperation rates and are satisfied with their decision to undergo surgery. The authors also noted that results following revision LF are not as positive, which emphasizes the importance of appropriate patient selection and surgical technique with the use of primary LF.

Omega-3 Free Fatty-Acid Supplementation in Crohn's Disease

Researchers, led by Brian G. Feagan, MD, of the University of Western Ontario in Ontario, Canada, evaluated the use of oral, high-dose omega-3 free fatty-acid supplements for maintenance therapy in patients with Crohn's disease in remission. The researchers conducted two randomized, double-blind, placebo-controlled studies (Epanova Program in Crohn's Study 1 [EPIC-1] and EPIC-2) at 98 centers in Canada, Europe, Israel, and the United States between January 2003 and February 2007. The investigators evaluated data from 363 patients with quiescent Crohn's disease in EPIC-1 and 375 patients in EPIC-2. Patients who had a Crohn's Disease Activity Index (CDAI) score of less than 150 points were randomly assigned to either 4 g daily of omega-3 free fatty acids or placebo for up to 58 weeks. During the trials, the patients were not allowed to use any other treatments for their Crohn's disease. The main outcome measure was clinical relapse, which was classified as a CDAI score of 150 points or greater and an increase of more than 70 points from baseline, or the initiation

of treatment for active Crohn's disease. The results of the EPIC studies were published in an April issue of the *Journal of the American Medical Association*.

According to the authors, in EPIC-1, 188 patients received omega-3 free fatty-acid supplements compared to 186 patients who received placebo. In EPIC-2, 189 patients received the supplements compared to 190 patients who received placebo. The researchers did not find any significant difference in the relapse rates between the two treatment groups in EPIC-1 or EPIC-2. The 1-year relapse rates in EPIC-1 were 31.6% in the omega-3 free fatty-acid arm and 35.7% in the placebo arm (hazard ratio, 0.82; 95% confidence interval [CI], 0.51–1.19; $P=.30$). In EPIC-2, the 1-year relapse rates were 47.8% in the omega-3 free fatty-acid arm and 48.8% in the placebo arm (hazard ratio, 0.90; 95% CI, 0.67–1.21; $P=.48$). The authors concluded that treatment with omega-3 free fatty acids in these trials was not efficacious for preventing relapse in Crohn's disease patients and did not recommend their use, despite the fact that they are currently widely used.

In Brief

In a retrospective study of patients with pancreatic-fluid collection and/or fistulae, 16% of the patients also had a disconnected pancreatic tail. Endoscopic and surgical drainage techniques were typically successful initially, but both suffered from a high rate of recurrence in the setting of disconnected pancreatic tail syndrome. The majority of patients required long-term follow-up due to complications and/or ongoing symptoms. (*Gastrointest Endosc.* 2008;67:673-679.)

Researchers conducting a double-blind, placebo-controlled trial found that amitriptyline significantly improved overall quality of life in adolescents with irritable bowel syndrome and recommended its use as a therapeutic option for adolescents with this disorder. (*J Pediatr.* 2008;152:685-689.)

A prospective study demonstrated that *Helicobacter pylori* eradication does not reduce histologic gastric intestinal metaplasia scores but does change the cellular phenotype of gastric intestinal metaplasia. The study authors noted that this change of phenotype may be an important factor in the reduction of cancer incidence after the eradication of *H. pylori*. (*Clin Gastroenterol Hepatol.* 2008;6:409-417.)