

# COPD After Heart Attack Poses Double Whammy

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CHICAGO — Chronic obstructive pulmonary disease is a lethal comorbidity for myocardial infarction patients, and its deadly punch has grown over time, according to a community-based review of more than 3,000 patients.

In addition, chronic obstructive pulmonary disease (COPD) has become increasingly common in patients with a my-

ocardial infarction, affecting 16% of patients who had an MI during 2000-2005, compared with 8% in 1979-1985, Dr. Francesca Bursi and her associates reported in a poster at the annual meeting of the American College of Cardiology.

The deadly impact of coexisting COPD was so strong it negated an overall temporal trend toward fewer patients dying post MI. The risk of post-MI death in patients with COPD, compared with those without COPD, rose from a 21% increased risk in

1979-1985 to a 2.6-fold increased risk during 2000-2005, said Dr. Bursi, a cardiologist at the Mayo Clinic in Rochester, Minn.

Although the Mayo Clinic researchers had no explanation for the increased impact of COPD on post-MI mortality, they said their findings underscored the need to enhance therapy and follow-up for patients who face this double whammy.

They reviewed data collected on 3,259 residents of Olmsted County, Minn., who had an MI during 1979-2005 and were

monitored through the clinic's county-based community surveillance program. During an average follow-up of 4.8 years, 1,436 (44%) of these MI patients died.

For the group overall, the confluence of MI and COPD boosted the risk of death by a statistically significant 38%, compared with patients without COPD, in an analysis that adjusted for several differences including age, gender, smoking, hypertension, medications used, and revascularization treatment. ■

## amitiza®

(lubiprostone) capsules

Initial U.S. Approval: 2006

**BRIEF SUMMARY OF PRESCRIBING INFORMATION – Please see package insert for full prescribing information.**

### 1 INDICATIONS AND USAGE

#### 1.1 Chronic Idiopathic Constipation

Amitiza® is indicated for the treatment of chronic idiopathic constipation in adults.

#### 1.2 Irritable Bowel Syndrome with Constipation

Amitiza is indicated for the treatment of irritable bowel syndrome with constipation (IBS-C) in women ≥ 18 years old.

### 2 DOSAGE AND ADMINISTRATION

Amitiza should be taken twice daily orally with food and water. Physicians and patients should periodically assess the need for continued therapy.

#### 2.1 Chronic Idiopathic Constipation

24 mcg twice daily orally with food and water.

#### 2.2 Irritable Bowel Syndrome with Constipation

8 mcg twice daily orally with food and water.

### 3 DOSAGE FORMS AND STRENGTHS

Amitiza is available as an oval, gelatin capsule containing 8 mcg or 24 mcg of lubiprostone.

• 8-mcg capsules are pink and are printed with "SPI" on one side

• 24-mcg capsules are orange and are printed with "SPI" on one side

### 4 CONTRAINDICATIONS

Amitiza is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Pregnancy

The safety of Amitiza in pregnancy has not been evaluated in humans. In guinea pigs, lubiprostone has been shown to have the potential to cause fetal loss. Amitiza should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Women who could become pregnant should have a negative pregnancy test prior to beginning therapy with Amitiza and should be capable of complying with effective contraceptive measures. See *Use in Specific Populations* (8.1).

#### 5.2 Nausea

Patients taking Amitiza may experience nausea. If this occurs, concomitant administration of food with Amitiza may reduce symptoms of nausea. See *Adverse Reactions* (6.1).

#### 5.3 Diarrhea

Amitiza should not be prescribed to patients that have severe diarrhea. Patients should be aware of the possible occurrence of diarrhea during treatment. Patients should be instructed to inform their physician if severe diarrhea occurs. See *Adverse Reactions* (6.1).

#### 5.4 Dyspnea

In clinical trials conducted to study Amitiza in treatment of chronic idiopathic constipation and IBS-C there were reports of dyspnea. This was reported at 2.5% of the treated chronic idiopathic constipation population and at 0.4% in the treated IBS-C population. Although not classified as serious adverse events, some patients discontinued treatment on study because of this event. There have been postmarketing reports of dyspnea when using Amitiza 24 mcg. Most have not been characterized as serious adverse events, but some patients have discontinued therapy because of dyspnea. These events have usually been described as a sensation of chest tightness and difficulty taking in a breath, and generally have an acute onset within 30–60 minutes after taking the first dose. They generally resolve within a few hours after taking the dose, but recurrence has been frequently reported with subsequent doses.

#### 5.5 Bowel Obstruction

In patients with symptoms suggestive of mechanical gastrointestinal obstruction, the treating physician should perform a thorough evaluation to confirm the absence of such an obstruction prior to initiating therapy with Amitiza.

### 6 ADVERSE REACTIONS

#### 6.1 Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

#### Chronic Idiopathic Constipation

*Adverse reactions in dose-finding, efficacy, and long-term clinical studies:* The data described below reflect exposure to Amitiza in 1175 patients with chronic idiopathic constipation (29 at 24 mcg once daily, 1113 at 24 mcg twice daily, and 33 at 24 mcg three times daily) over 3- or 4-week, 6-month, and 12-month treatment periods; and from 316 patients receiving placebo over short-term

exposure (≤ 4 weeks). The total population (N = 1491) had a mean age of 49.7 (range 19–86) years; was 87.1% female; 84.8% Caucasian, 8.5% African American, 5.0% Hispanic, 0.9% Asian; and 15.5% elderly (≥ 65 years of age). Table 1 presents data for the adverse reactions that occurred in at least 1% of patients who received Amitiza 24 mcg twice daily and that occurred more frequently with study drug than placebo. In addition, corresponding adverse reaction incidence rates in patients receiving Amitiza 24 mcg once daily is shown.

**Table 1: Percent of Patients with Adverse Reactions (Chronic Idiopathic Constipation)**

System/Adverse Reaction <sup>1</sup>	Placebo	Amitiza	Amitiza
	N = 316 %	24 mcg Once Daily N = 29 %	24 mcg Twice Daily N = 1113 %
<b>Gastrointestinal disorders</b>			
Nausea	3	17	29
Diarrhea	< 1	7	12
Abdominal pain	3	3	8
Abdominal distension	2	-	6
Flatulence	2	3	6
Vomiting	-	-	3
Loose stools	-	-	3
Abdominal discomfort <sup>2</sup>	< 1	3	2
Dyspepsia	< 1	-	2
Dry mouth	< 1	-	1
Stomach discomfort	< 1	-	1
<b>Nervous system disorders</b>			
Headache	5	3	11
Dizziness	< 1	3	3
<b>General disorders and site administration conditions</b>			
Edema	< 1	-	3
Fatigue	< 1	-	2
Chest discomfort/pain	-	3	2
<b>Respiratory, thoracic, and mediastinal disorders</b>			
Dyspnea	-	3	2

<sup>1</sup>Includes only those events associated with treatment (possibly, probably, or definitely related, as assessed by the investigator).

<sup>2</sup>This term combines "abdominal tenderness," "abdominal rigidity," "gastrointestinal discomfort," and "abdominal discomfort."

*Nausea:* Approximately 29% of patients who received Amitiza 24 mcg twice daily experienced an adverse reaction of nausea; 4% of patients had severe nausea while 9% of patients discontinued treatment due to nausea. The rate of nausea associated with Amitiza (any dosage) was substantially lower among male (7%) and elderly patients (18%). Further analysis of the safety data revealed that long-term exposure to Amitiza does not appear to place patients at an elevated risk for experiencing nausea. The incidence of nausea increased in a dose-dependent manner with the lowest overall incidence for nausea reported at the 24 mcg once daily dosage (17%). In open-labeled, long-term studies, patients were allowed to adjust the dosage of Amitiza down to 24 mcg once daily from 24 mcg twice daily if experiencing nausea. Nausea decreased when Amitiza was administered with food. No patients in the clinical studies were hospitalized due to nausea.

*Diarrhea:* Approximately 12% of patients who received Amitiza 24 mcg twice daily experienced an adverse reaction of diarrhea; 2% of patients had severe diarrhea while 2% of patients discontinued treatment due to diarrhea.

*Electrolytes:* No serious adverse reactions of electrolyte imbalance were reported in clinical studies, and no clinically significant changes were seen in serum electrolyte levels in patients receiving Amitiza.

*Less common adverse reactions:* The following adverse reactions (assessed by investigator as probably or definitely related to treatment) occurred in less than 1% of patients receiving Amitiza 24 mcg twice daily in clinical studies, occurred in at least two patients, and occurred more frequently in patients receiving study drug than those receiving placebo: fecal incontinence, muscle cramp, defecation urgency, frequent bowel movements, hyperhidrosis, pharyngolaryngeal pain, intestinal functional disorder, anxiety, cold sweat, constipation, cough, dysgeusia, eructation, influenza, joint swelling, myalgia, pain, syncope, tremor, decreased appetite.

#### Irritable Bowel Syndrome with Constipation

*Adverse reactions in dose-finding, efficacy, and long-term clinical studies:* The data described below reflect exposure to Amitiza 8 mcg twice daily in 1011 patients with IBS-C for up to 12 months and from 435 patients receiving placebo twice daily for up to 16 weeks. The total population (N = 1267) had a mean age of 46.5 (range 18–85) years; was 91.6% female; 77.5% Caucasian, 12.9% African American, 8.6% Hispanic, 0.4% Asian; and 8.0% elderly (≥ 65 years of age). Table 2 presents data for the adverse reactions that occurred in at least 1% of patients who received Amitiza 8 mcg twice daily and that occurred more frequently with study drug than placebo.