

Popularity of Personal Health Records Growing

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As physicians struggle to decide whether and when to incorporate electronic health records into their practices, personal health records are gaining popularity.

Personal health records (PHRs) allow patients to store and access their medical information electronically. Various versions are available through physicians,

health systems, insurers, and employers, and are offered on a stand-alone, subscription basis. But with so many models, no two records are likely to be the same and each may present different challenges for the physician-patient relationship.

"We're really in a kind of Wild West situation with the PHR," said Dr. Peter Basch, an internist and medical director for eHealth at MedStar Health, a seven-hospital system in Washington and Baltimore.

Currently, two types of records are dom-

inant—those that are linked to a physician's or health system's electronic health record, and free-standing records, Dr. Basch said.

With connected PHRs, patients can usually access subsets of their medical data and communicate with their physicians' offices on selected matters such as scheduling appointments. With a free-standing PHR, patients generally have greater control of the data that are entered and over who can access the data. The market is more mature now in terms of connected

PHRs, especially those that are linked to large medical groups and large health systems, Dr. Basch said.

In an effort to tame some of the variability in the market, Health Level Seven Inc. (HL7), a national organization that sets health information technology standards, has released a proposed personal health record standard. In August, HL7 unveiled its Personal Health Record System Functional Model, and sought public comments.

The HL7 general model can be cus-

Amitiza®
(lubiprostone) Capsules

Initial U.S. Approval: 2006

BRIEF SUMMARY OF PRESCRIBING INFORMATION- Please see package insert for complete prescribing information.

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

The recommended dosage for Amitiza is 24 mcg taken twice daily orally with food. Physicians and patients should periodically assess the need for continued therapy.

3 DOSAGE FORMS AND STRENGTHS

Amitiza is available as an oval, orange, soft gelatin capsule with "SPI" printed on one side. Each capsule contains 24 mcg of lubiprostone.

4 CONTRAINDICATIONS

Amitiza is contraindicated in patients with known 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 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.

Adverse reactions in dose-finding, efficacy, and long-term clinical studies:

The data described below reflect exposure to Amitiza in 1175 patients (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 (any dosage) 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 and in patients receiving Amitiza 24 mcg twice daily are shown.

Table 1: Percent of Patients with Adverse Reactions in Clinical Studies of Amitiza

System/Adverse Reaction ¹	Placebo	Amitiza	Amitiza	Amitiza
	N = 316 %	24 mcg Once Daily N = 29 %	24 mcg Twice Daily N = 1113 %	Any Dosage ² N = 1175 %
Gastrointestinal disorders				
Nausea	3	17	29	29
Diarrhea	<1	7	12	12
Abdominal pain	3	3	8	8
Abdominal distension	2	–	6	6
Flatulence	2	3	6	5
Vomiting	–	–	3	3
Loose stools	–	–	3	3
Abdominal discomfort ³	–	3	2	2
Dyspepsia	<1	–	2	2
Dry mouth	<1	–	1	1
Stomach discomfort	<1	–	1	1
Nervous system disorders				
Headache	5	3	11	11
Dizziness	<1	3	3	3
General disorders and site administration conditions				
Edema	<1	–	3	3
Fatigue	<1	–	2	2
Chest discomfort/pain	–	3	2	2
Respiratory, thoracic, and mediastinal disorders				
Dyspnea	–	3	2	2

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

² Includes patients dosed at 24 mcg once daily, 24 mcg twice daily, and 24 mcg three times daily.

³ This term combines "abdominal tenderness," "abdominal rigidity," "gastrointestinal discomfort," and "abdominal discomfort."

Nausea: Approximately 29% of patients who received Amitiza (any dosage) experienced an adverse reaction of nausea; 3% of patients had severe nausea while 8% 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 (any dosage) experienced an adverse reaction of diarrhea; 3% 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 list of adverse reactions includes those that occurred in less than 1% of patients receiving Amitiza (any dosage) in dose-finding, efficacy, and long-term clinical studies and that were considered by the investigator to be probably or definitely related to treatment with study drug. Moreover, the list includes only those events that occurred in at least two patients and more frequently in patients receiving Amitiza than those receiving placebo.

Gastrointestinal disorders: fecal incontinence, defecation urgency, frequent bowel movements, intestinal functional disorder, constipation, eructation
Musculoskeletal and connective tissue disorders: muscle cramp, joint swelling, myalgia

Nervous system disorders: dysgeusia, syncope, tremor

Respiratory, thoracic, and mediastinal disorders: pharyngolaryngeal pain, cough

Skin and subcutaneous tissue disorders: hyperhidrosis, cold sweat

General disorders and administration site conditions: influenza, pain

Metabolism and nutrition disorders: decreased appetite

Psychiatric disorders: anxiety

tomized so that it can be used with each of the various PHR models available in the marketplace. A vote is expected later this year on whether the PHR functional model will become an approved standard.

Another possible way to accelerate the development of the personal health record market is through the Certification Commission for Healthcare Information Technology (CCHIT), a body that already certifies ambulatory and inpatient electronic health record systems.

The CCHIT is looking at the area of personal health records, according to its chairman, Dr. Mark Leavitt. However, any certification of PHR products would be at

least a year away, since the CCHIT has not developed certification criteria in that area. Although the PHR industry is still in its early stages, it is not necessary to wait for the industry to fully mature before developing certification criteria. In fact, setting standards early can be helpful, Dr. Leavitt said.

The PHR marketplace may get a boost from the CCHIT long before a PHR certification process gets started, he added. Through its electronic health record certification process, the CCHIT is requiring that records have the capability to send patient summary information, which would be helpful in populating a patient's PHR.

Many factors are driving the growth of

PHRs. Employer groups, frustrated with escalating health costs, represent one faction pushing for PHR development. While the evidence is not yet in, the theory is that PHRs would allow patients to be better consumers, potentially saving employers money, Dr. Basch said.

Health insurers also are getting into the act. For example, Aetna recently announced that starting in January 2008, federal enrollees in any of the company's medical plans will have access to a password-protected online PHR. The record would include claims information on physician office visits, labs, diagnoses, treatment, and prescriptions. Even Medicare is testing

the PHR field. In June, Medicare launched a pilot program to allow certain beneficiaries to access a PHR through participating Medicare Advantage and Part D drug plans.

There also are some patients who care deeply about having PHRs because they are managing chronic conditions for themselves or family members, Dr. Basch said.

Even if most consumers are not clamoring for PHRs, when surveyed, they do favor the concept. In a November 2006 survey commissioned by the Markle Foundation, nearly two-thirds of the 1,003 adults polled said they would like to access their medical information electronically, and 72% of those under age 40 said they would like to access their health information online.

But consumers who were surveyed also had significant concerns about the privacy and security of their records. For example, 80% said they were very concerned about identity theft, and 77% said they were very concerned about their medical information being used for marketing purposes.

Concerns about security and privacy are shared by physicians. With a free-standing PHR, physicians could receive requests from patients to populate their data, but they might be reluctant to send such sensitive data in an unsecured way or in a way that could compromise the security of their own electronic systems, Dr. Basch said.

An even more complicated question for physicians is what to do with information they receive from a PHR that may be entered or edited by the patient. If patients are restricting PHR content from their physicians, it could limit the utility of the record, said Dr. Michael Barr, vice president for practice advocacy and improvement at the American College of Physicians.

While the ACP has been supportive of the development of PHRs, the different PHR models have different implications for the physician-patient relationship and for office workflow, he said. ■

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of Amitiza. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Voluntary reports of adverse reactions occurring with the use of Amitiza include the following: syncope, malaise, increased heart rate, muscle cramps or muscle spasms, rash, and asthenia.

7 DRUG INTERACTIONS

Based upon the results of *in vitro* human microsome studies, there is low likelihood of drug-drug interactions. *In vitro* studies using human liver microsomes indicate that cytochrome P450 isoenzymes are not involved in the metabolism of lubiprostone. Further *in vitro* studies indicate microsomal carbonyl reductase may be involved in the extensive biotransformation of lubiprostone to the metabolite M3 (See *Pharmacokinetics, Metabolism* [12.3]). Additionally, *in vitro* studies in human liver microsomes demonstrate that lubiprostone does not inhibit cytochrome P450 isoforms 3A4, 2D6, 1A2, 2A6, 2B6, 2C9, 2C19, or 2E1, and *in vitro* studies of primary cultures of human hepatocytes show no induction of cytochrome P450 isoforms 1A2, 2B6, 2C9, and 3A4 by lubiprostone. No additional drug-drug interaction studies have been performed. Based on the available information, no protein binding-mediated drug interactions of clinical significance are anticipated.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic effects: Pregnancy Category C. [See *Warnings and Precautions* (5.1).]

Teratology studies with lubiprostone have been conducted in rats at oral doses up to 2000 mcg/kg/day (approximately 332 times the recommended human dose, based on body surface area), and in rabbits at oral doses of up to 100 mcg/kg/day (approximately 33 times the recommended human dose, based on body surface area). Lubiprostone was not teratogenic in rats or rabbits. In guinea pigs, lubiprostone caused fetal loss at repeated doses of 10 and 25 mcg/kg/day (approximately 2 and 6 times the recommended human dose, respectively, based on body surface area) administered on days 40 to 53 of gestation.

There are no adequate and well-controlled studies in pregnant women. However, during clinical testing of Amitiza at 24 mcg twice daily, four women became pregnant. Per protocol, Amitiza was discontinued upon pregnancy detection. Three of the four women delivered healthy babies. The fourth woman was monitored for 1 month following discontinuation of study drug, at which time the pregnancy was progressing as expected; the patient was subsequently lost to follow-up.

Amitiza should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. If a woman is or becomes pregnant while taking the drug, the patient should be apprised of the potential hazard to the fetus.

8.3 Nursing Mothers

It is not known whether lubiprostone is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from lubiprostone, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been studied.

8.5 Geriatric Use

The efficacy of Amitiza in the elderly (≥ 65 years of age) subpopulation was consistent with the efficacy in the overall study population. Of the total number of constipated patients treated in the dose-finding, efficacy, and long-term studies of Amitiza, 15.5% were ≥ 65 years of age, and 4.2% were ≥ 75 years of age. Elderly patients taking Amitiza (any dosage) experienced a lower incidence rate of associated nausea compared to the overall study population taking Amitiza (18% vs. 29%, respectively).

8.6 Renal Impairment

Amitiza has not been studied in patients who have renal impairment.

8.7 Hepatic Impairment

Amitiza has not been studied in patients who have hepatic impairment.

10 OVERDOSAGE

There have been two confirmed reports of overdosage with Amitiza. The first report involved a 3-year-old child who accidentally ingested 7 or 8 capsules of 24 mcg of Amitiza and fully recovered. The second report was a study patient who self-administered a total of 96 mcg of Amitiza per day for 8 days. The patient experienced no adverse reactions during this time. Additionally, in a Phase 1 cardiac repolarization study, 38 of 51

patients given a single oral dose of 144 mcg of Amitiza (6 times the recommended dose) experienced an adverse event that was at least possibly related to the study drug. Adverse reactions that occurred in at least 1% of these patients included the following: nausea (45%), diarrhea (35%), vomiting (27%), dizziness (14%), headache (12%), abdominal pain (8%), flushing/hot flash (8%), retching (8%), dyspnea (4%), pallor (4%), stomach discomfort (4%), anorexia (2%), asthenia (2%), chest discomfort (2%), dry mouth (2%), hyperhidrosis (2%), and syncope (2%).

16 HOW SUPPLIED/STORAGE AND HANDLING

Amitiza is available as an oval, orange, soft gelatin capsule with "SPI" printed on one side. Each capsule contains 24 mcg of lubiprostone. Amitiza is available as follows:

- Bottles of 100 (NDC 64764-240-10)
- Bottles of 60 (NDC 64764-240-60)

Store at 25°C (77°F); excursions permitted to 15°–30°C (59°–86°F). PROTECT FROM EXTREME TEMPERATURES.

17 PATIENT COUNSELING INFORMATION

17.1 Dosing Instructions

Patients should take a single 24 mcg capsule of Amitiza twice daily with food or a meal. The capsule should be taken once in the morning and once in the evening daily as prescribed. Physicians and patients should periodically assess the need for continued treatment with Amitiza.

17.2 Nausea and Diarrhea

Patients should take Amitiza with food or a meal to reduce symptoms of nausea. Patients on treatment who experience severe nausea or diarrhea should inform their physician.

Marketed by:

Sucampo Pharmaceuticals, Inc., Bethesda, MD 20814
and

Takeda Pharmaceuticals America, Inc., Deerfield, IL 60015

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