



## Therapeutic Class Review<sup>SM</sup>

### lubiprostone (Amitiza<sup>TM</sup>)

July 2006

#### New Product for Review:

Lubiprostone (Amitiza<sup>TM</sup>) [Sucampo]

#### Dossier Provided by Manufacturer: No

**Dossier Evaluation:** not applicable

1- dossier w/missing components

2- all components present, except pharmacoeconomic model

3- all components present (comprehensive)

#### Executive Summary

- Constipation:
  - Affects more than 30 million Americans.
  - Results in more than 2.5 million visits to physicians annually.
  - Is more likely to affect females than males.
  - Is more likely to occur in older patients; exponential increase after age 65.
  - Accounts for \$708 million in OTC laxative sales in 2004.
- Chronic constipation is believed to be a disorder of colonic motility.
- Idiopathic constipation refers to the fact that there is no known cause for the constipation (not due to other diseases or drugs).
- A standard definition for constipation is problematic because bowel habits vary greatly among individuals.
- There are many effective OTC medications available for treating constipation.
- In addition to its labeling for treatment of chronic idiopathic constipation, lubiprostone (Amitiza) is also being studied in constipation predominant irritable bowel syndrome (IBS).
- Although clinical trials with these medications have been for short durations (from 2 to 12 weeks), chronic use of these medications is likely.

#### Evidence

- Two trials provide possibly useful evidence for the efficacy of lubiprostone (Amitiza) in the treatment of chronic idiopathic constipation:
  - Spontaneous bowel movements (SBMs) at the end of week 1 was followed as the primary endpoint.

- The number of responders was reported at the end of each week of the trial ( $\geq 4$  SBMs/week).
- The NNT for responders was 5 over 4 weeks.
- There are no long-term trials that establish the efficacy of lubiprostone (Amitiza) beyond 4 weeks.
- There are no head-to-head trials with that provide evidence for efficacy of lubiprostone (Amitiza) relative to any other product used to treat constipation.
- Available harms information is not reliable for purposes of long-term safety of lubiprostone (Amitiza).
- Nausea was the most common harm reported during controlled trials, occurring in 31.4% (placebo 5.5%) of patients.
- The NNH for all gastrointestinal adverse events was 3 over 4 weeks.
- The NNH for discontinuations due to adverse events was 10 over 4 weeks.
- Use of lubiprostone (Amitiza) in pregnant women may lead to pregnancy loss (chemical structure is similar to prostaglandin E<sub>1</sub>).

## Decision

Lubiprostone (Amitiza) is non-preferred/non-formulary because:

- There are several effective, lower cost preferred options available to our members for treating chronic constipation.
- There is no evidence that lubiprostone (Amitiza) is more effective, safer, or better tolerated than preferred alternatives.

## Products

Drug Products	FDA approval <sup>a</sup>	FDA approved indications	Usual Dose/Route	Potential Off-label Uses <sup>b</sup>
lubiprostone (Amitiza™) <sup>1</sup>	01/2006	1. Chronic idiopathic constipation in adults	24 mcg p.o. BID (with food)	<ul style="list-style-type: none"> <li>▪ IBS with constipation</li> <li>▪ Constipation 2° to other causes (eg. narcotics)</li> </ul>
lactulose syrup <sup>c</sup> (Chronulac®) - - generics	06/1979	1. Constipation 2. Hepatic encephalopathy	20 to 30 Gm (30 to 45 ml) p.o. TID to QID	<ul style="list-style-type: none"> <li>▪ Post-op pain after hemorrhoidectomy</li> <li>▪ Lactose intolerance</li> </ul>
polyethylene glycol 3350 (Miralax™) <sup>2</sup> - - generics	02/1999	3. Occasional constipation (2 weeks or less or as directed by physician)	17 Gm p.o. QD (in 8 oz. of fluid)	<ul style="list-style-type: none"> <li>▪ Dysfunctional voiding</li> <li>▪ Fecal impaction</li> </ul>
tegaserod (Zelnorm®) <sup>3</sup>	07/2002	1. Irritable bowel syndrome (IBS) with constipation 2. Chronic idiopathic constipation	6 mg p.o. BID (before meals)	<ul style="list-style-type: none"> <li>▪ Constipation 2° to other causes (eg. narcotics)</li> </ul>

<sup>a</sup> Date applies to approval date for the original brand name medication where there are now generics available.

<sup>b</sup> As listed in © 1974 - 2006 Thomson MICROMEDEX database or as referenced.

## References

1. Amitiza™ (lubiprostone) Prescribing Information. Sucampo Pharmaceuticals, Inc: Bethesda, MD, February 2006.
2. Miralax™ (polyethylene glycol 3350) Prescribing Information. Braintree Laboratories, Inc: Braintree, MA, November 2001.

3. Zelnorm<sup>®</sup> (tegaserod) Prescribing Information. Novartis Pharmaceuticals Corporation: East Hanover, NJ, August 2004.
4. Center for Drug Evaluation and Research. Approval package for application number NDA 21-908; Medical Review. Available at: [http://www.fda.gov/cder/foi/nda/2006/021908s000\\_Etreva\\_MEDR.pdf](http://www.fda.gov/cder/foi/nda/2006/021908s000_Etreva_MEDR.pdf). Accessed on 6/1/2006.
5. Center for Drug Evaluation and Research. Approval package for application number NDA 21-908; Statistical Review. Available at: [http://www.fda.gov/cder/foi/nda/2006/021908s000\\_Etreva\\_STATR.pdf](http://www.fda.gov/cder/foi/nda/2006/021908s000_Etreva_STATR.pdf). Accessed on 6/1/2006.
6. Johanson JF, Gargano MA, Patchen ML, et al. Efficacy and safety of a novel compound, RU-0211, for the treatment of constipation (Abstract M1511). *Gastroenterology*. 2002;122(4):A-315.
7. Johanson JF, Gargano MA, Holland PC, et al: Phase III, randomized withdrawal study of RU-0211, a novel chloride channel activator for the treatment of constipation (abstract 749). *Gastroenterology* 2004; 126(4 Suppl 2):A-100.
8. Frizelle F, Barclay M. Constipation in adults [search date October 2005]. *Clin Evid*. 2006;15:1-12.
9. American Gastroenterological Association Clinical Practice and Practice Economics Committee. AGA technical review on constipation. *Gastroenterology*. 2000;199(6):1766-78.
10. The Bowel Guidelines : Constipation Panel. Practice guidelines for the management of constipation in adults. Available at: <http://www.rehabnurse.org/profresources/BowelGuideforWEB.pdf>. Accessed on 6/1/2006.