Optimal Treatment of Chronic Constipation in Managed Care: Review and Roundtable Discussion

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Anthony J. Lembo, MD
Faculty

James C. Eoff III, PharmD, is Executive Associate Dean and Professor of Clinical Pharmacy at the University of Tennessee (UT) College of Pharmacy in Memphis, Tennessee. He is responsible for recruitment, admissions, and student affairs in the College. Dr. Eoff received both his bachelor and doctorate degrees in pharmacy from the UT College of Pharmacy. He served on the faculty full time from 1970 to 1978, at which time he purchased Balmoral Pharmacy in Memphis. He rejoined the College in 1984 and served as interim Dean of the College in 1989. He also holds the position of Director of the UT College of Pharmacy's Minority Center of Excellence and is the principal investigator of a $2,800,000 grant for the Center's funding.

Dr. Eoff was appointed to the Tennessee Board of Pharmacy in 1978 and served as President of the Board of Pharmacy in 1982. He has served as President of the UT College of Pharmacy Alumni Association on 2 occasions, and he was the recipient of the Outstanding Alumni Award of the College of Pharmacy in 1987. He was awarded the UT National Alumni Association’s Outstanding Teacher Award for 4 years and received the Distinguished Community Service Award in 1990. Dr. Eoff has taught numerous courses over his career including orientation to pharmacy, nonprescription drugs, drug abuse, clinical pharmacy, and therapeutics. He also taught a review course for the pharmacy licensure examination for more than 30 years and is Co-Editor of the American Pharmacists Association’s Complete Pharmacy Review.

Dr. Eoff is active in many professional organizations including the American Pharmaceutical Association, the National Community Pharmacists Association, the American Society of Health-System Pharmacists, the American Association of Colleges of Pharmacy, and the Tennessee Pharmacist’s Association, who honored him as their 1989 recipient of the A. H. Robbins “Bowl of Hygeia” Award for outstanding community service. Dr. Eoff served as President of the Tennessee Society of Independent Pharmacists from 1989-1990 and as President of the Tennessee Pharmacist’s Association from 1996-1997.

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**Target Audience and Activity Purpose**

Pharmacy and medical directors as well as managed care pharmacists and physicians interested in the diagnosis and treatment of chronic constipation.

**Learning Objectives**

Upon completion of this educational activity, the participant should be able to:

1. Describe management strategies for the various etiologies of constipation, including drug-related causes.
2. Evaluate the clinical impact and cost-effectiveness of traditional and newer treatment options for chronic constipation.
3. Recommend appropriate treatments based on efficacy, safety, and the potential for drug interactions while accounting for comorbid conditions.
4. Summarize the impact of constipation on health-related quality of life.

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**Continuing Education Credit**

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Dr. Eoff has no conflicts to disclose.

Dr. Lembo discloses participation on the speakers’ bureaus of Prometheus; Salix Pharmaceuticals, Inc.; and Takeda Pharmaceuticals North America, Inc., and as a consultant for Prometheus; Salix Pharmaceuticals, Inc.; Takeda Pharmaceuticals North America, Inc.; Ironwood Pharmaceutical; and Wyeth Pharmaceuticals.

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Disclosure of Off-Label Use

This educational activity contains discussion of unapproved (investigational) use of linaclotide and prucalopride for constipation as well as alvimopan and intravenous methylnaltrexone for opioid-induced constipation. Please refer to the official prescribing information for each product for description of approved indications, contraindications, and warnings.

Method of Participation

There are no fees to participate in and receive credit for this activity. Credit is awarded to participants scoring 70% or better on the online posttest and completing the course evaluation. Two opportunities to pass the posttest are allowed. A CE statement can be printed upon successful completion.
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ABSTRACT

BACKGROUND: Prevalence studies estimate that chronic constipation affects 12%-19% of Americans. This prevalence rate exceeds that of many highly publicized chronic conditions, including diabetes and asthma. Identifying the etiology of each patient’s constipation is essential for determining treatment and management plans. The etiology of chronic constipation falls into 2 broad categories: primary or idiopathic constipation caused by physical and functional problems, and secondary constipation resulting from a variety of organic conditions as well as the use of certain medications. Patients may have more than one cause of their constipation. Treatment options may be based not only on the cause but may be dictated by a patient’s health care coverage and the inclusion criteria of different health care plans.

OBJECTIVES: To (a) present key information on the causes, diagnosis, and treatment recommendations for patients with chronic constipation; (b) describe how chronic constipation impacts quality of life; and (c) describe how all providers can work to improve the quality of care and health outcomes for patients with chronic constipation.

SUMMARY: Chronic constipation is a prevalent condition that disproportionately affects women and the elderly. Most agents are available over-the-counter, although their efficacy has not been extensively tested. Few pre-scription agents are currently available, and they are more costly; therefore, patients must be symptomatic for at least 6 months prior to diagnosis.5 While these criteria stand as guidelines for diagnosis, it is acknowledged that bowel habits differ across individuals; one person may feel distraught and uncomfortable having only 2 bowel movements a week, while another may find this frequency to be normal. Even though this factor is often stressed, the scale of the economic costs associated with constipation is becoming evident. In the United States, the number of constipation-related physician visits reached 5.7 million in 2006; of these, 2.7 million visits had constipation (both direct and indirect) as the primary diagnosis.8 Because patients who suffer from constipation may be embarrassed and reluctant to discuss their symptoms with their providers, their underlying conditions may go undiagnosed, resulting in a missed opportunity for intervention.9

Impact of Chronic Constipation

Health Care and Health Care Costs

The scale of the economic costs associated with constipation is commonly discussed conditions (Figure 1).1 Constipation may be perceived as being less prevalent and burdensome than other conditions, such as asthma and diabetes. In spite of this impression, estimated prevalence rates of constipation exceed many of the more commonly discussed conditions (Figure 1).2 While health care providers use the frequency of bowel movements (i.e., <3 bowel movements per week) to define constipation, patients report that they consider straining (81%) and hard stools (72%), among other symptoms, to define constipation.3 Constipation is classified as chronic if it occurred for 12 weeks during the previous year, although these weeks need not be consecutive. A consensus definition of chronic constipation, known as the Rome III Criteria (Table 1)4 requires a patient to have experienced at least 2 of the following symptoms of constipation over the past 3 months: <3 bowel movements per week, straining, lumpy/hard stools, sensation of anorectal obstruction, sensation of incomplete defecation, or manual maneuvers required to defecate. In addition, the Rome III Criteria note that a patient should not meet the suggested criteria for irritable bowel syndrome (IBS) and that loose stools are rarely present without the use of laxatives. Although symptoms of constipation are assessed over the prior 3 months, patients must be symptomatic for at least 6 months prior to diagnosis.3 While these criteria stand as guidelines for diagnosis, it should be acknowledged that bowel habits differ across individuals; one person may feel distraught and uncomfortable having only 2 bowel movements a week, while another may find this frequency to be normal. Even though this factor is often stressed, the number of bowel movements should not be used as the sole indicator of chronic constipation.

In terms of demographics, women are twice as likely to report constipation than men (18.3% vs. 9.2%) and are much more likely to receive care for constipation (35.6% vs. 19.5%), although the gap between women and men decreases with age.3,6 Constipation is more common in older adults, with a prevalence rate approximating 30%-40% in those over the age of 65 years.7 Compared with whites, the prevalence of constipation is 30% higher among nonwhite populations.7
Prevalence of Constipation Compared With Other Common Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Prevalence</th>
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<tbody>
<tr>
<td>Coronary Heart Disease</td>
<td>6%</td>
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<tr>
<td>Diabetes</td>
<td>8%</td>
</tr>
<tr>
<td>Asthma</td>
<td>11%</td>
</tr>
<tr>
<td>Migraines</td>
<td>15%</td>
</tr>
<tr>
<td>Constipation</td>
<td>12%-19%b</td>
</tr>
<tr>
<td>Hypertension</td>
<td>23%</td>
</tr>
</tbody>
</table>

*Derived from Higgins and Johanson (2004) and Pleis and Lethbridge-Cejky (2007). Average reported prevalence rate of constipation is estimated between 12% and 19% (total range from 2% to 27%).

Health-Related Quality of Life

Along with absenteeism and daily life restrictions, chronic constipation has a significant negative impact on individuals' health-related quality of life (QOL). In a recent study of 2,870 subjects from 7 countries, constipation was associated with impairment in health-related QOL. The impairment seen in chronic constipation is similar to that observed in patients with longstanding illnesses such as gastroesophageal reflux disease, diabetes, heart disease, or depression. The study also noted that women with constipation report more health-related QOL impairment than constipated men. Patients with chronic constipation secondary to pelvic floor dysfunction (i.e., pelvic dyssynergia) have an even greater impairment in health-related QOL (and psychological distress) than patients with chronic constipation due to slow-transit constipation (STC).

Etiopathogenesis and Other Risk Factors

The first step in managing patients with chronic constipation is to determine whether the symptoms of constipation are due to primary constipation (i.e., idiopathic, functional) or secondary constipation (i.e., due to an organic disease, such as hypothyroidism or colorectal cancer).

Primary (Idiopathic, Functional) Constipation

Primary constipation can be divided into 3 pathophysiological groups.

1. Normal-transit constipation is the most common subtype of primary constipation. Despite stool passing through the colon at a normal rate, patients perceive difficulty in evacuating their bowels. This group frequently overlaps with patients experiencing irritable bowel syndrome with constipation (IBS-C). The primary distinction between chronic constipation and IBS-C is the prominence of abdominal pain or discomfort in IBS.

2. Slow-transit constipation occurs most commonly in women and is characterized by infrequent bowel movements, limited urgency, or straining to defecate. Most patients with STC have impaired phasic colonic motor activity from a decrease in high-amplitude propagated contractions, abnormal rectosigmoid contractile activity, and reduced release of neurotransmitters or altered contractile response.

**TABLE 1** Rome III Definition of Functional Constipation

- Two or more of the following for the last 3 months:
  - Straining during at least 25% of defecations
  - Hard or lumpy stools in at least 25% of defecations
  - Sensation of incomplete evacuation in at least 25% of defecations
  - Sense of anorectal obstruction in at least 25% of defecations
  - Manual maneuvers to facilitate in at least 25% of defecations
  - Less than 3 bowel movements per week
- Loose stools are rarely present without the use of laxatives.
- Criteria for irritable bowel syndrome are not fulfilled.

*Derived from Choung et al. (2003).*
3. Pelvic floor dysfunction (i.e., pelvic floor dyssynergia) is characterized by dysfunction of the pelvic floor or anal sphincter, with patients having poor ability to coordinate these muscles during defecation. Patients with pelvic floor dysfunction frequently report straining at stools and feelings of incomplete evacuation. At times, patients with pelvic floor dysfunction will require perineal or vaginal pressure during defecation to allow stools to pass. There is considerable overlap of patients with pelvic floor dysfunction and STC.17 Because pelvic floor dysfunction can cause slow colon transit, patients with STC should be evaluated for pelvic floor dysfunction.

Secondary Constipation
A variety of medical conditions and medications may lead to chronic constipation. The following list contains some of the more common causes of secondary constipation.

- **Medications:** Many medications may cause or contribute to constipation (Table 2).9,18 Reducing the dosage of the constipation-causing medication, finding an alternative agent, or stopping use of the constipation-causing medication may assist in relieving symptoms. Studies have shown that analgesics are significantly associated with constipation.19,20 Narcotic use is a common cause of chronic constipation and can significantly reduce QOL. When starting narcotics, concurrent laxative use should be considered in an attempt to prevent constipation.21,22
- **Endocrine or metabolic disorders:** Hypothyroidism, hypercalcaemia, hyperparathyroidism, and diabetes
- **Neurologic conditions:** Hirschsprung’s disease, autonomic neuropathy, multiple sclerosis, and Parkinson’s disease
- **Structural abnormalities:** Anorectal disorders, colonic structures, colonic mass lesions with obstruction, and idiopathic megarectum
- **Psychogenic conditions:** Anxiety, depression, somatization, and eating disorders; also, antidepressants and psychotropic agents
- **Gastrointestinal tract conditions:** Colon cancer, anal fissure, mucosal prolapse, Crohn’s disease, and stricture pseudo-obstruction
- **Lifestyle:** Inadequate dietary fiber or fluid intake, inactivity, and ignoring the urge to defecate

Complications of Chronic Constipation
Chronic constipation may lead to additional health problems. The following complications are sometimes associated with chronic constipation.23

- Hemorrhoids, which can be caused by straining and pushing. Hemorrhoids may be internal or external and cause rectal bleeding.
- Fecal impaction refers to the accumulation of dry, hardened feces in the rectum or colon, thus causing an obstruction. This complication is the most common reason for hospitalization due to chronic constipation.

### Table 2: Medications Commonly Associated With Secondary Constipation

<table>
<thead>
<tr>
<th>Medications Commonly Associated With Secondary Constipation</th>
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</thead>
<tbody>
<tr>
<td>- Anticholinergics</td>
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<tr>
<td>- Antidepressants</td>
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<tr>
<td>- Antihistamines</td>
</tr>
<tr>
<td>- Anti-convulsants</td>
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<tr>
<td>- Calcium-channel blockers</td>
</tr>
<tr>
<td>- Clonidine (Catapres)</td>
</tr>
<tr>
<td>- Diuretics</td>
</tr>
<tr>
<td>- Iron</td>
</tr>
<tr>
<td>- Levodopa (Larodopa)</td>
</tr>
<tr>
<td>- Narcotics</td>
</tr>
<tr>
<td>- Nonsteroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>- Opioids</td>
</tr>
<tr>
<td>- Psychotropics</td>
</tr>
<tr>
<td>- Sympathomimetics</td>
</tr>
</tbody>
</table>

*Derived from Locke et al.9 and Prather and Ortiz-Comacho.20*

- **Diagnosis**

A thorough medical history and physical examination, particularly a detailed rectal examination, is essential to evaluate and diagnose a patient with symptoms of chronic constipation. During the history, clinicians should request information about current medications (including OTC and herbal agents in addition to prescription agents); health conditions; duration of constipation; and description of stool movements, frequency, and formation. During the rectal examination, providers should first look for perianal excoriation, skin tags/hemorrhoids, anocutaneous reflex, anal fissure, and prolapse during straining. Next, a digital rectal examination should be performed to assess for masses in the rectum and a rectocele (an outpouching typically in the anterior rectal wall). Significant tenderness in the anal canal may be suggestive of an anal fissure. Finally, an assessment of the
anal sphincter resting tone and its augmentation during squeeze and relaxation in simulated defecation should be assessed.

Along with a thorough history and physical examination, basic laboratory testing—including complete blood count as well as serum glucose, thyroid-stimulating hormone, calcium, and creatinine levels—is recommended, although there are limited data to support these recommendations. The role of endoscopy in the evaluation of constipation is controversial. In a retrospective study of 563 patients with constipation undergoing colonic surveillance for colon cancer, researchers found a similar colon cancer detection rate in asymptomatic historical controls.26

Colonoscopy is recommended for almost all patients ≥50 years of age as part of routine colorectal screening.27 The American Society of Gastroenterology Endoscopy guidelines do not recommend routine colonoscopy for patients with chronic constipation in the absence of alarm features or warning signs.28 These warning signs include unintentional weight loss; family history of cancer, IBS, or celiac disease; rectal bleeding; and iron deficiency anemia.

Diagnostic testing to evaluate colonic transit and pelvic floor functioning can be useful, especially in patients with refractory constipation. Procedures include the following 5 tests:

1. Colonic transit: The simplest method to measure colonic transit involves the ingestion of a single capsule containing radio-opaque markers (i.e., Sitz marker), followed by a subsequent plain x-ray of the abdomen 5 days after ingestion of the markers. This test is most helpful in distinguishing normal-transit and slow-transit constipation. Radio nuclide scintigraphy is another way to measure colonic transit; however, this test is not widely available and is more expensive and time intensive than the radio-opaque marker test.

2. Balloon expulsion: In this procedure, a latex balloon is inserted into the rectum and filled with air or water. The patient is then asked to expel the balloon. Failure to expel the balloon within 60 seconds is suggestive of pelvic floor dysfunction.

3. Anorectal manometry: This test is conducted by inserting a pressure-sensitive catheter with a balloon at its tip through the anal canal. This test provides an assessment of rectal sensation, anorectal reflexes, rectal compliance, and anal sphincter pressures during squeeze and bear-down maneuvers.

4. Dynamic pelvic magnetic resonance imaging (MRI): This test provides an assessment of the functional anatomy during defecation and therefore may identify pelvic floor dysynergia as well as anatomical defects that entrap the rectum and obstruct defecation.

5. Defecography: Similar to dynamic MRI, defecography evaluates the functioning of the anorectum (e.g., anorectal angle and pelvic floor descent) as well as anatomical abnormalities (e.g., internal rectal prolapse or a rectocele).

### Management Strategies

Most patients with chronic constipation should first attempt lifestyle modifications: increasing dietary fiber intake to 15-20 g per day, drinking plenty of fluid, and maintaining a regular exercise program. Despite limited data supporting their use in clinical practice, these lifestyle changes promote general health and may improve bowel symptoms in some patients.22-25 Another behavioral modification to consider includes ensuring that patients spend an adequate amount of time on the toilet for bowel movements, preferably at a regularly scheduled time (typically in the morning to coincide with the body's natural gastrocolic response).

For patients who continue to experience symptoms of chronic constipation, additional treatment may be necessary. Current OTC and prescription options include bulking agents; stool softeners; osmotic and stimulant laxatives; and lubiprostone, a chloride channel activator. The American College of Gastroenterology (ACG) Task Force on Chronic Constipation's systematic review of the literature prior to 2005 concluded that there is little evidence to support the use of many of these agents in patients with chronic constipation with the exception of the osmotic laxative lactulose and polyethylene glycol (PEG), which were found to be effective at improving stool frequency and stool consistency in patients with chronic constipation.23 Recommendations by the ACG Task Force as well as the level of evidence for treatment options in chronic constipation are shown in Table 3.24-40 These recommendations do not include lubiprostone which was not approved by the U.S. Food and Drug Administration (FDA) until January 2006.

Anorectal biofeedback provides patients with feedback on their pelvic floor mechanics, particularly relaxation of the anorectal sphincter in association with defecation. Patients with pelvic floor dysfunction should be treated with anorectal biofeedback because they are more likely to respond to this technique (i.e., pelvic floor retraining) than to laxatives.24,41,42

### Pharmacological Treatments

A majority (96%) of patients who seek consultation for constipation have already attempted self-medication with OTC products including bulking agents, stimulants, saline laxatives, and stool softeners. Despite their frequent use, a survey conducted several years ago found that nearly one-half of patients with chronic constipation were not completely satisfied with the efficacy of these treatments. The following text reviews some of the commonly used treatment options for chronic constipation.

#### Bulk Laxatives (OTC)

Bulk laxatives, also known as fiber supplements, soften the stool and increase bulk to facilitate defecation. They are generally considered to be first-line treatment for most patients with chronic constipation. The primary, commercially available, bulk-forming agents are psyllium, methylcellulose, and calcium polycarbophil, which may have a 2- or 3-day onset of action. People who begin using bulk agents and report no relief should first increase the frequency and dosage to the maximum recommendations before...
# Treatment Agents: Dosage, Cost, and Comments

<table>
<thead>
<tr>
<th>Type</th>
<th>Generic Name</th>
<th>Dosage</th>
<th>Monthly Cost</th>
<th>ACG Grade</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bulking laxatives</strong></td>
<td></td>
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</tr>
<tr>
<td>Psyllium</td>
<td>Titrated up to 30 g per day in divided doses</td>
<td>$1.71-$10.26</td>
<td>B</td>
<td>Taken from the ground seed husk of the ispaghula plant; needs to be taken with plenty of water to avoid intestinal obstruction; undergoes bacterial degradation that may contribute to side effects of bloating and flatus; allergic reactions, such as anaphylaxis and asthma, have been reported but are rare.</td>
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<tr>
<td>Methylcellulose</td>
<td>Titrated up to 6 g per day in divided doses</td>
<td>$8.62-$27.49</td>
<td>B</td>
<td>Semisynthetic cellulose fiber relatively resistant to colonic bacterial degradation; tends to cause less bloating and flatus than psyllium.</td>
<td></td>
</tr>
<tr>
<td>Polycarbophil</td>
<td>Titrated up to 4 g per day in divided doses</td>
<td>$7.92-$31.69</td>
<td>B</td>
<td>Synthetic polymer of acrylic acid that is resistant to bacterial degradation.</td>
<td></td>
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<tr>
<td><strong>Osmotic laxatives</strong></td>
<td></td>
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<tr>
<td>Magnesium hydroxide</td>
<td>30-60 mL daily</td>
<td>$11.41-$22.82</td>
<td>B</td>
<td>Small percentage is actively absorbed in the small intestine; remainder draws water into the intestines along an osmotic gradient.</td>
<td></td>
</tr>
<tr>
<td>Polyethylene glycol</td>
<td>17 g per day</td>
<td>$25.26</td>
<td>A</td>
<td>Organic polymer that is poorly absorbed and not metabolized by colonic bacteria.</td>
<td></td>
</tr>
<tr>
<td>Lactulose</td>
<td>15-30 mL qd-bid</td>
<td>$18.72-$37.44</td>
<td>A</td>
<td>Synthetic disaccharide consisting of galactose and fructose linked by a bond resistant to lactase and therefore not absorbed by the small intestine; undergoes bacterial fermentation in the colon resulting in formation of short-chain fatty acids; bacteria in the colon can metabolize up to 80 g of lactulose each day; gas and bloating are common side effects.</td>
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<tr>
<td><strong>Stimulant laxatives</strong></td>
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<tr>
<td>Anthraquinones</td>
<td>Sennosides</td>
<td>8.6-30 mg qd-bid</td>
<td>$8.11-$48.69</td>
<td>B</td>
<td>Anthraquinones are converted by colonic bacteria to their active form, which increase electrolyte transport into the bowel and stimulate intestinal motility; may cause melanosi coli, a benign condition that is usually reversible within 12 months, no definitive association between anthraquinones and colon cancer or myenteric nerve damage has been established.</td>
</tr>
<tr>
<td>Diphenylmethane derivatives</td>
<td>Bisacodyl</td>
<td>10-15 mg po daily; 10-mg rectal suppository daily</td>
<td>$4.74-$7.10</td>
<td>B</td>
<td>Hydrolyzed by endogenous esterases; stimulates secretion and motility of small intestine and colon.</td>
</tr>
<tr>
<td><strong>Stool softeners</strong></td>
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<tr>
<td>Docusate sodium</td>
<td>50-100 mg qd-bid</td>
<td>$2.93-$5.87</td>
<td>B</td>
<td>Ionic detergents that soften the stool by allowing water to interact more effectively with solid stool; may have modest effects on fluid absorption and secretion; efficacy in constipation is not well established.</td>
<td></td>
</tr>
<tr>
<td>Docusate calcium</td>
<td>240 mg daily</td>
<td>$6.29</td>
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<tr>
<td><strong>Emollients</strong></td>
<td></td>
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</tr>
<tr>
<td>Mineral oil</td>
<td>5-45 mL po qhs</td>
<td>$9.83-$29.50</td>
<td>B</td>
<td>Alters stool by being emulsified into the stool mass and providing lubrication for passage of the stool; long-term use can cause malabsorption of fat-soluble vitamins, anal seepage, and lipoid pneumonia in patients predisposed to aspiration of liquids.</td>
<td></td>
</tr>
<tr>
<td><strong>Chloride channel activator</strong></td>
<td>Lubiprostone</td>
<td>8 mcg bid (IBS-C); 24 mcg bid (chronic constipation)</td>
<td>$219.98-$228.56</td>
<td>Not graded</td>
<td>Activates ClC-2s in the intestine, causing fluid secretion and possible secondary effects on motility; nausea is common; administer with food and water; approved for use in adults with chronic constipation and in women &gt;18 years of age with IBS-C.</td>
</tr>
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*From: Lembo A. Chronic constipation. AGA Web site. Available at: www.gastro.org/user-assets/Documents/08_Publications/06_GIHep_Annual_Review/Articles/Lembo.pdf.*

*Prices are estimated for a 30-day supply. Ranges are rough averages for minimum to maximum recommended doses. The costs were derived from the average of the prices in August 2008 for 2-3 products for each agent at www.drugstore.com including 60 units of either 8 mcg or 24 mcg capsules of lubiprostone.

*Grade “A” is supported by Level I evidence (randomized controlled trials [RCT] with appropriate methodology); Grade “B” is supported by Level II evidence (RCT with inappropriate methodology); Grade “C” is supported by Level III evidence (nonrandomized trials with contemporaneous controls) or level IV evidence (nonrandomized trials with historical controls). Graded Recommendations available at: www.gi.org/patients/ibsrelief/pdf/gs20037147p.pdf.*


ACG = American College of Gastroenterology; bid = twice daily; CIC-2 = type-2 chloride channel; IBS-C = irritable bowel syndrome with constipation; PEG = polyethylene glycol; qd = every day, qhs = every night, po = by mouth.
switching to other agents. Some patients report a worsening in bloating, flatulence, and abdominal pain with fiber supplements; therefore, the dose should be gradually increased over several weeks. Fiber supplements are generally safe, but they can interfere with absorption of some medicines (e.g., warfarin, digoxin, nitrofurantoin, salicylates) as well as calcium and iron. Psyllium can cause bowel obstruction if taken without sufficient water. Bulk laxatives are most effective in patients with normal-transit constipation. In one study, up to 80% of patients in that subgroup reported complete relief of constipation symptoms in response to fiber (15-30 g per day) compared with 20%-30% of patients with a defecatory disorder or STC.44

Stimulant Laxatives (OTC)
Stimulants cause rhythmic muscle contractions in the intestines by acting on the nerve plexus of intestinal smooth muscle as well as decrease absorption of water and electrolytes from the large intestine. Their onset of action is generally between 6 to 12 hours. Due to the limited data currently available on stimulant laxatives for chronic constipation, the ACG Task Force concluded that there is insufficient evidence to make a recommendation regarding the effectiveness of stimulant laxatives in patients with chronic constipation.25 Currently available primary stimulants are senna and bisacodyl. Stimulants are generally taken at bedtime and may cause diarrhea, cramping, and abdominal pain. In addition, senna products may discolor the urine, and chronic use may cause melanosis coli, a brown-black pigmentation of the colonic mucosa. This condition does not lead to colon cancer and is reversible over time after discontinuation of use. Electrolyte imbalance can occur in patients who experience significant diarrhea.

Stool Softeners (OTC)
Stool softeners are surface-acting agents that moisten the stool through a detergent action. Available agents are docusate sodium and docusate calcium, and they are commonly used in hospitalized patients, especially after childbirth or surgery. However, the ACG Task Force found insufficient data to support their widespread use.25 Data suggest that stool softeners may be inferior to psyllium in patients with chronic constipation. In a 2-week, multicenter, double-blind study, use of psyllium (5.1 g twice daily) was found to be superior to docusate sodium (100 mg twice daily) for increasing stool frequency.45

Emollients (OTC)
Emollients promote stool movement through the intestines by softening and coating the stool. Mineral oil is the most common example. Chronic use of emollients may decrease absorption of fat-soluble vitamins (A, D, E, K) as well as some drugs. Unfortunately, no placebo-controlled trials of emollients in adult patients have been conducted; however, in pediatric patients with chronic constipation, mineral oil was found to be superior to stimulant laxatives46 but inferior to osmotic laxatives.47 It should be noted that children and elderly patients may accidently aspirate this agent, which could produce lipoid pneumonia.

Osmotic Laxatives (OTC and Prescription)
Osmotic agents draw water into the colon and facilitate passage of stool. Agents include magnesium-based therapies, such as magnesium hydroxide (milk of magnesia) and citrate of magnesia; poorly absorbed sugars, including sorbitol and prescription lactulose; and the chemically inert polymer PEG and PEG 3350. The best-studied osmotic laxatives are PEG and lactulose (prescription only), and there are well-designed, randomized, placebo-controlled trials supporting their effectiveness in treating chronic constipation.48,49 While both have been found to be effective, an open-label trial found PEG to be superior to lactulose for increasing stool frequency and reducing straining.48 A 6-month placebo-controlled study of PEG 3350 found sustained and safe positive effects in patients with chronic constipation. Fifty-two percent in treatment versus 11% using placebo were successfully treated based on efficacy measures. While adverse events, such as diarrhea, flatulence, and nausea, occurred more frequently with PEG, the difference in occurrence was not statistically significant.49 No randomized placebo-controlled trials have been conducted with magnesium products in patients with chronic constipation; therefore, the ACG Task Force found insufficient evidence to make a recommendation about their effectiveness in chronic constipation.24 Primary adverse effects are flatulence, bloating, abdominal cramping, nausea, and diarrhea with higher doses. Electrolyte imbalances have been reported with extended use, especially in young children and people with renal insufficiency.

Chloride Channel Activators (Prescription)
Lubiprostone is the first chloride channel activator to be approved by the FDA. As a novel bicyclic fatty acid, it works by activating type-2 chloride channels on the surface of intestinal epithelial cells to enhance intestinal fluid secretion and integrity of the epithelial tight junctions. Lubiprostone is the only medication approved by the FDA for long-term treatment of chronic idiopathic constipation in adult men and women. It is the only agent for chronic constipation that is FDA approved for patients >65. The recommended dose for chronic constipation is 24 mcg twice daily. In April 2008, the FDA approved its use in women >18 years of age with IBS-C at a dosage of 8 mcg twice daily.50

In a randomized, double-blind, placebo-controlled trial, lubiprostone 24 mcg twice daily resulted in a greater mean number of spontaneous bowel movements (SBMs) than placebo (5.7 vs. 3.5; P<0.001 at week 1). Within 24 hours of starting the medication, 57% of those given lubiprostone reported an SBM compared with 37% of those given placebo (P=0.002). Stool consistency, straining, and constipation severity also significantly improved. The most common adverse effects of lubiprostone were nausea (32%) and headaches (12%) compared with 3% and 6%,

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respective, with placebo.\textsuperscript{51} It is recommended that patients take lubiprostone with food to reduce the potential for nausea.\textsuperscript{49} In addition, women who are capable of becoming pregnant should have a negative pregnancy test before starting the medication and should use effective contraception while taking lubiprostone.\textsuperscript{52} There are insufficient data regarding the safety of lubiprostone in pregnancy; therefore, the manufacturer does not recommend its use during pregnancy.\textsuperscript{40}

\section*{Peripheral Opioid Antagonists for Opioid-Induced Constipation}

Two peripherally active opioid antagonists were recently approved by the FDA. A meta-analysis demonstrated that methylnaltrexone and alvimopan were better than placebo in reversing opioid-induced increased gastrointestinal transit time and constipation. The incidence of adverse events with opioid antagonists was similar to placebo, and adverse events were generally mild to moderate in severity. The authors concluded that while methylnaltrexone and alvimopan show promise, further data are required to fully assess their place in therapy.\textsuperscript{53}

\subsection*{Methylnaltrexone Bromide}

In late April 2008, the FDA approved a new medication for treating opioid-induced chronic constipation in terminally ill patients with advanced conditions such as incurable cancer, end-stage heart and lung diseases, and AIDS.\textsuperscript{54} Methylnaltrexone bromide is a derivative of naltrexone that does not cross the blood-brain barrier. It acts as a selective antagonist at peripheral opioid receptors without blocking the central effects, as analgesia does. Opioids interfere with normal bowel function by relaxing intestinal smooth muscle cells, which prevents the intestine from contracting normally.\textsuperscript{21} Methylnaltrexone bromide blocks opioid receptors on the intestinal muscle cells, thus allowing the bowels to function normally. The drug is not recommended for patients with known or suspected intestinal obstructions.

\subsection*{Alvimopan}

Alvimopan is a peripherally acting mu-opioid receptor antagonist developed to block the adverse side effects of opioid analgesics on the gastrointestinal tract. Like methylnaltrexone bromide, it acts without blocking the central effects, as analgesia does. Along with treating opioid-induced constipation, the FDA approved alvimopan in May 2008 for use with post-operative ileus "to accelerate the time to upper and lower gastrointestinal recovery following partial large or small bowel resection surgery with primary anastomosis."\textsuperscript{55}

\section*{Tegaserod: Removed From the Market}

Tegaserod, a serotonin 5-HT\textsubscript{4} receptor partial agonist, was approved by the FDA in July 2002 for women with IBS-C and for men and women <65 years of age with idiopathic constipation. While found to be very effective, its safety profile came under fire when the FDA reviewed data from 29 clinical trials and more than 18,000 patients and found a small increased risk in cardiovascular adverse events (including angina, heart attacks, and stroke) when compared with controls taking placebo.\textsuperscript{56} In March 2007, marketing for tegaserod was discontinued. However, the manufacturer initiated a restricted access program in collaboration with the FDA in July 2007. After 8 months, this access program was reassessed, and the product was voluntarily withdrawn from the market in April 2008.\textsuperscript{57}

\section*{Future Therapy Options}

\subsection*{Linaclotide}

Linaclotide is a first-in-class compound that is being tested for treatment of IBS-C, chronic constipation, and other gastrointestinal disorders. Linaclotide is an agonist of guanylate cyclase type-c, which is a receptor found on the lining of the intestine. In a phase 2b study, linaclotide was found to increase SBMs and complete spontaneous bowel movements (CSBMs), with a significant, dose-related improvement in bowel habits. There was no evidence of rebound constipation, and the most common adverse event was dose-dependent diarrhea.\textsuperscript{58}

\subsection*{Prucalopride}

5HT-4 receptor agonists target serotonin-4 receptors, which are involved in initiating peristalsis in the intestines. Prucalopride is a highly selective complete 5-HT\textsubscript{4} agonist that has been shown to increase bowel movements and appears to be effective in the treatment of chronic constipation. In a 12-week randomized, placebo-controlled trial of prucalopride 2 mg and 4 mg daily, bowel changes and adverse events were studied. The percentage of participants in the treatment groups having 3 or more CSBMs per week, averaged over the study period, was significantly higher in the 2 treatment groups versus placebo (2 mg: 47.3%; 4 mg: 46.6%; placebo: 25.8%). The most frequently reported adverse events included headache and abdominal pain, and no significant cardiovascular effects occurred. These recent findings hold promise that prucalopride may be a safe, effective treatment for chronic constipation.\textsuperscript{59}

\section*{Cost of Treatment}

Of the total costs for managing and treating constipation, a large portion is spent by patients on OTC agents. Although few prescription medications exist for constipation, acquisition costs for these agents are high, and these costs must be considered when managed care plans assess formularies and coverage. In addition, diagnostic testing and surgeries contribute to the direct costs reported for constipation. Managed care plans often weigh the secondary and tertiary costs related to a condition to help guide decisions on the appropriateness and level of coverage for more expensive interventions.
Pharmacoeconomics

Laxatives

Because a majority of chronic constipation patients first attempt to self-medicate the condition and because first-line treatments for symptom relief are traditional OTC products, it is not surprising that expenditures for these treatments are high. An estimated $800 million was spent on laxatives, stool softeners, and other symptom-relieving products. Because these are OTC treatments, the cost burden is primarily (if not totally) shouldered by the patients themselves. Unfortunately, very few studies have directly compared treatment options for chronic constipation. While prescription drugs may appear to be more effective, often lower-cost (nonprescription) medications may be substituted successfully.

With a captive audience, nursing homes are good sites to test these hypotheses. For example, one nursing home lowered its cost for constipation prevention and management by switching from lactulose to regular use of sorbitol. In this population, the efficacy of sorbitol was equivalent to prior use of lactulose, and the need for additional laxatives and rescue products was reduced. Overall, the nursing home reported a 27%-55% reduction in costs compared with other management strategies reported in the literature. An even less expensive alternative has been the increasing use of oat bran in the diets of nursing home residents with constipation. A small study examined the use of dietary fiber compared with a control group. A dietary fiber supplement in the form of an oat bran cake allowed 59% of the treatment group to discontinue laxative use. While these switches may not work for all patients, these results stress that, in terms of cost savings, treatment can commence with simpler therapies (e.g., laxatives, fiber) and then proceed to more aggressive agents if symptoms do not resolve.

Lubiprostone

Some health plans require patients to fail with more conservative OTC therapies before authorizing coverage of lubiprostone. Lubiprostone may be placed on the highest copayment level (nonpreferred or nonformulary) of multtier medication benefits because many OTC products may be effective options when compared with this more expensive prescription medication. Still, as part of a step therapy program, lubiprostone's demonstrated effectiveness makes it an important option for many patients who are not successfully treated by OTC agents.

Methylnaltrexone Bromide

Methylnaltrexone bromide reduces the incidence of opioid-induced constipation when nearing the end of life. While this medication is obviously targeted to a subcategory of patients, its subcutaneous injection administration and projected costs make this an interesting case for managed care to weigh the cost-benefits and cost-effectiveness when making formulary inclusion decisions.

Although methylnaltrexone bromide may actually be administered either subcutaneously or intravenously, it is currently only FDA approved for subcutaneous use. Ongoing clinical trials regarding the intravenous use of methylnaltrexone can be found at www.clinicaltrials.gov (1 completed, 1 in progress, 1 recruiting). Past studies have already concluded that repeated intravenous administration of methylnaltrexone appears to be safe and effective, and intravenous doses of 0.32 mg per kg are well tolerated.

Technology and Diagnostic Testing Costs

Questions have been raised concerning which diagnostic tests are the most appropriate to order and when they should be ordered. In addition, some have questioned the effectiveness of these tests in determining when surgery is warranted. Evidence to support routine laboratory testing is lacking. Similarly, there is a paucity of data to support the use of radiography and endoscopy in patients with constipation but no warning signs as part of a routine workup. While certain diagnostic tools, such as colonic transit, anorectal manometry, and balloon expulsion tests, are useful in determining the abnormalities and possible etiology of constipation symptoms, no single test can adequately define the pathophysiology. Therefore, it is not always clear which tests have the most utility or are the most cost-effective.

Conclusions

1. Chronic constipation is a prevalent condition that disproportionately affects women and the elderly.
2. Chronic constipation can be categorized as primary (idiopathic, functional) constipation or as secondary constipation resulting from comorbidities or other factors, including medications. Diagnostic testing and tools are useful in determining the etiology and classifying the subtype of constipation as well as guiding recommended therapy.
3. Treatment begins with empiric recommendations including an increase in fiber, exercise, and water intake and may include OTC agents, such as osmotic and stimulant laxatives. Even though evidence for the efficacy of many of these medications is lacking, some patients find that these lifestyle changes and therapies provide significant relief of symptoms.
4. There are a limited number of FDA-approved medications to treat chronic constipation. Because of the expense of these agents, they are typically only prescribed when traditional OTC treatments fail.
Roundtable Discussion with James C. Eoff III, PharmD, and Anthony J. Lembo, MD

Educating the Patient on Prevention and Management

When educating patients about prevention and treatment of constipation, what should a provider stress?

Lembo: Lifestyle factors are what we should emphasize. First, stress eating a healthy diet, such as limiting processed foods and increasing dietary fiber, typically to 20 g per day. In addition, patients should also be educated to exercise regularly and to keep well hydrated by drinking at least 8-ounce glasses of water a day.

Is there a distinction between dietary versus commercial fibers? Are commercial fibers more effective?

Lembo: There’s no evidence that commercial fibers are more effective than dietary fibers for chronic constipation. Psyllium is the best studied of the commercial fibers, while bran is the best studied of the dietary fibers. Both have strong evidence of their effectiveness, especially in patients with mild to moderate constipation.\(^{34,45,63}\) Commercial fibers are more convenient for people, and it is easier to control the amount of fiber intake. Instead of making adjustments because of the variability of your diet from day-to-day, you know exactly what you’re getting when you take a commercial fiber. It is important to stress that the patient should drink plenty of water when eating or taking a commercial fiber, particularly psyllium.

How effective are OTC products?

Eoff: Many OTC products are quite effective if the right product is used and used correctly. You will know whether most OTC products are effective in the treatment of chronic constipation within 6 weeks, but you need to ensure that patients use the proper dose for the product. With fiber agents, taking the recommended dose for several weeks is very important. While you will see initial effects within several days, this allows patients to determine whether there is true relief and whether they are getting rid of any additional symptoms besides focusing solely on the number of bowel movements. Are they still experiencing a lot of straining, hard stools, or abdominal pain? If those symptoms are continuing, then they may need to try other medicines. One key question and concern is whether patients are taking the full dose of the medicine. For example, while taking an agent like psyllium, some people will use a teaspoon of the fiber product rather than a tablespoon. They might then say, “Well, this is not working.” Yet, it’s because they are not using the maximum dose or are not dosing multiple times daily as recommended.

Also, it would be important to work with the patient to identify what types of symptoms they are still experiencing. We know a lot of people who still have other symptoms, even though they are being treated for constipation and have increased the number of bowel movements per week. How can we address those symptoms? Do patients continue to strain excessively, feel like they have not evacuated completely, or have very hard, dry stools? We would then look at alternative agents and determine whether they really need additional fiber. What type of fiber are they taking? Do they need to shift to some osmotic agents (either saline or a PEG product), or should a stimulant with a stool softener be considered?

Many agents are available, and each has its own mechanism of action. Approximately one-half of patients using treatments are still not getting relief from symptoms.\(^4\) This suggests that they may need to consult either their primary care provider or a pharmacist to determine whether they are using the right product and whether alternative agents might be more effective in alleviating their symptoms. Most algorithms suggest the use of OTC agents first before you jump to a prescription agent, which can be more expensive.\(^{24,25,65}\) The Johanson et al. survey of patients noted that while 96% had used and 72% were currently using constipation relief therapy, 47% were not completely satisfied with their treatment. This lack of satisfaction was primarily due to lack of efficacy (82%).\(^9\)

Lembo: This questionnaire asked patients whether they had “complete” satisfaction with their treatment. Complete relief is a high hurdle to overcome, especially with currently available treatments. Because patients with significant but not “complete” relief were not assessed by this study, it likely overestimates the magnitude of dissatisfaction with currently available treatments.

Eoff: Will anybody ever be completely satisfied? Complete satisfaction would result from not needing to use any agents.

Lembo: Right. Still, it is important information and tells us what goal we should strive for.

With continued use of laxatives, OTC agents, and prescriptions, are there any interactions with other drugs of which people should be aware?

Lembo: Most of these agents are pretty well tolerated. We worry about giving magnesium, such as milk of magnesia or magnesium citrate, to people with renal insufficiency or administering phosphorus-based compounds.

Eoff: Although it was thought that psyllium may decrease absorption of digoxin, warfarin, carbamazepine, and lithium, there are no conclusive reports of this effect being clinically significant. Similarly, magnesium hydroxide may decrease absorption of warfarin, digoxin, and chlorpromazine, but no conclusive research confirms this belief. I think the key would be to avoid taking these agents at the same time during the day. For example, take one agent in the morning and the other in the evening, which may minimize any interactions. No clinically significant interactions with PEG or lubiprostone have been reported.

Treatment

Are there algorithms for treatment?

Lembo: There are no evidence-based algorithms for the treatment of chronic constipation. Therefore, treatments are based on
Optimal Treatment of Chronic Constipation in Managed Care: Review and Roundtable Discussion

Prescription Coverage

There are currently only a few prescription drugs for constipation that would actually have to be covered by managed care, isn’t that correct?

Lembo: That would be correct. Lubiprostone is one of them. PEG has just been moved to OTC status, so managed care plans are likely not going to be paying for that agent for the treatment of constipation, although PEG coverage will continue for bowel evacuant purposes. A more recently approved product is methylnaltrexone for opiate-induced constipation, but it is being studied for other types of constipation.

Lembo: Methylnaltrexone is only approved for end-of-life therapy (i.e., in patients who have a prognosis of 6 months or less to live). Alvimopan, also recently approved by the FDA, is an oral peripheral opioid antagonist. Because alvimopan is an oral medication, it is likely to be better accepted for patients with opioid-induced constipation.

Chronic Constipation Versus Irritable Bowel Syndrome With Constipation

How do you differentiate between IBS-C and chronic constipation?

Lembo: Sometimes it can be difficult to make a clear distinction between the 2 entities. There is significant overlap between IBS-C and chronic constipation because they share features of decreased, altered motility in the lower gastrointestinal tract. The way they are distinguished clinically is by the presence and severity of abdominal pain. The more pain that’s present, especially when it’s a predominant feature, the more consistent the symptoms are with IBS-C. A lack of pain and discomfort would be more consistent with chronic constipation. And, in between, there is overlap between the two (Figure 2).

Again, the criteria for chronic constipation and IBS are not the same. Rome III Criteria for chronic constipation specifically state that to receive a diagnosis of chronic constipation, “criteria for IBS are not fulfilled” (Table 1); again, these IBS-C criteria include the presence of pain or discomfort. The problem occurs when people with chronic constipation symptoms have discomfort in their abdomen, which is not uncommon. If you look at the IBS-C and chronic constipation groups as a whole, what helps distinguish between them—besides the discomfort of abdominal pain—is the frequency of bowel movements. Bowel movement frequency is usually greater in the IBS-C group than in the chronic constipation group.

Do treatments differ between IBS-C and chronic constipation?

Lembo: In terms of treatment, you will treat constipation similarly in both cases. However, in the IBS-C group, you would also try to treat the pain, which would not be a treatment factor in chronic constipation. So, with IBS-C, once stool frequency and

consensus opinion. These opinions take efficacy data, costs, and potential adverse reactions into account. Typical recommendations start with fiber and then add osmotic agents followed by either stimulants or lubiprostone.

Where do the prescription medications, such as lubiprostone, fit into treatment?

Lembo: OTC products are usually the first line of therapy. Managed care organizations realize that these may not be effective for all patients and managed care allows for the use of lubiprostone, often as the next step in therapy if OTC agents fail.

Is treatment of chronic constipation in pregnancy different?

Lembo: The American Gastroenterological Association Institute published a Position Statement on the Use of Gastrointestinal Medications in Pregnancy.52 In this statement, short-term use of osmotic laxatives is considered to be low-risk treatment in pregnancy, but long-term use of saline osmotic laxatives, like magnesium citrate or sodium phosphate, should be avoided because they can be harmful to the fetus. PEG, which has a pregnancy class C rating, is considered to be low-risk treatment, and it’s the preferred treatment for chronic constipation in pregnancy. Docusate sodium is also considered to be a low-risk agent. Senna and bisacodyl should be recommended only for short-term use. Castor oil and mineral oil should be avoided because they can be harmful. Although the statement does not mention lubiprostone, it also has a pregnancy class C rating, and it has been associated with increased fetal loss of life in one animal model. Because there are limited data for humans, it should be avoided in pregnant women. It is recommended that a pregnancy test be obtained prior to initiating lubiprostone in women who are of childbearing potential, and women should be advised to use an effective contraceptive while on this medication.

A few prescription drugs for constipation that would actually have to be covered by managed care, isn’t that correct?

Lembo: That would be correct. Lubiprostone is one of them. PEG has just been moved to OTC status, so managed care plans are likely not going to be paying for that agent for the treatment of constipation, although PEG coverage will continue for bowel evacuant purposes. A more recently approved product is methylnaltrexone for opiate-induced constipation, but it is being studied for other types of constipation.

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consistency are improved, you would use a visceral analgesic if there are still symptoms of pain and discomfort. For example, a tricyclic antidepressant would be an option. Antispasmodics may help pain, but you have to use them sparingly because they are constipating. Even though laxatives may help bowel function, they probably don't do much for pain in this group. Similarly, there are good data suggesting that fiber can certainly help bowel function, but it doesn't help the pain associated with IBS-C. Lubiprostone is the only FDA-approved medication for IBS-C. If other therapies do not work, it is the next logical treatment step for this condition.

**Though antidepressants help IBS-C pain, aren’t they associated with causing constipation?**

Lembo: Yes, so you would want to use them sparingly and when pain is the predominant feature, but only after bowel habits have been improved. A Clinical Crossroads article published in JAMA presents more information about the overlap and stresses the fact that you have to watch for constipation with tricyclics.37 For example, selective serotonin-reuptake inhibitors may be a better alternative for someone with IBS-C because they are less constipating.

**Care in the Nursing Home**

**How do describe treatment strategies for people in nursing homes, particularly those who are bedridden or immobile?**

Lembo: The management of patients with constipation in nursing homes is similar to the treatment of other patients. Constipation in nursing home patients is usually multifactorial. Being bedridden, having multiple comorbid conditions, using multiple medications, using narcotics, and other factors all contribute to the high prevalence of constipation in nursing home residents. In one study—which may still be the only study showing the incidence of constipation among new nursing home residents—7% developed significant constipation within their first 3 months in the nursing home.70 It is particularly challenging, and particularly important, that they don't become impacted or develop complications of constipation. Along with impaction, obstruction and stercoral ulcers are additional concerns. Therefore, I believe that most patients should be placed on some type of prophylactic treatment to prevent constipation.

Eoff: The American Medical Directors Association does provide clinical practice guidelines and a treatment algorithm for those in long-term care.69 These may be useful as many residents may have Medicare Part D coverage, which can affect a facility's medication use and reimbursements.

**Do all facilities start new residents on prophylactics?**

Lembo: Not all, but many do, especially if there is any evidence of trouble or changes in bowel habits. Because constipation is very common, facilities are particularly attuned to the development of constipation and its sequelae, such as fecal impaction.

Eoff: Everybody recommends some exercise and some modification of diet for patients who are able to incorporate those changes into their daily lives. But then you have the bedridden patient who can't exercise at all. Although you want to make sure that they get enough dietary fiber, that alone isn't typically going to help bedridden patients if they're constipated. You need to look at another agent to help with constipation and its accompanying symptoms. For those who are mobile, more alternatives are readily available to try. The American Medical Directors Association does provide clinical practice guidelines and a treatment algorithm for those in long-term care.71

**Pharmacist's Role**

**What role do you see the pharmacist playing in constipation care?**

Eoff: One way that the pharmacist can play an integral role is by reviewing with patients all of the medications they are using and then assessing whether these agents may be creating constipation and whether alternatives are available. Another task is to assist patients in taking a comprehensive, current medication history and to provide them with documentation that they can maintain, update, and share with other providers. Pharmacists can also promote lifestyle changes, such as moderate exercise and increased dietary fiber. Finally, pharmacists can be on the alert for "red flags"—those things that may warrant more extensive investigation into the etiology of the constipation as opposed to just idiopathic constipation. These would be some of the main pharmacist responsibilities as patients seek to manage their constipation. Again, most patients will get some positive effects from OTC agents, but it is important that they understand how to use them appropriately. Be sure to ask whether they have allowed enough time for the product to work and have used the product as directed. Another important aspect of working with patients concerns their out-of-pocket costs. OTC medications can be an appropriate first choice of therapy for chronic constipation, generally with savings in direct drug costs compared with prescription medication. Yet, with the exception of polyethylene glycol (PEG), the data demonstrating effectiveness of OTCs are limited, and the drug therapy ultimately most cost-effective for each patient will depend on individual patient response to therapy.

**It is important for pharmacists and providers to partner and be consistent in educating the patient. Is there a formal way of communicating information related to constipation?**

Eoff: There are more formal communication processes for institutionalized and nursing home patients, but less formal processes in a retail pharmacy setting. It is in the retail pharmacy where the patient will show up and say, “I have been using this product and it’s not working.” If the patient has gone through the gamut of OTC medicines, then usually the pharmacist’s recommendation will be to discuss these problems with a primary care provider. If there are any red flags or warning signs, the patient may be advised to see a gastroenterologist for an evaluation. The pharmacist’s important role is not only to advise patients on agents, but also to link them back into the health care system when necessary.
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Optimal Treatment of Chronic Constipation in Managed Care: Review and Roundtable Discussion


58 Lembo AJ. Linaclotide significantly improved bowel habits and reduced abdominal symptoms in adults with chronic constipation: data from a large four-week, randomized, double-blind, placebo-controlled study. Presented at: Digestive Disease Week 2008; May 17-22, 2008; San Diego, CA.


Continuing Education

Optimal Treatment of Chronic Constipation in Managed Care:
Review and Roundtable Discussion

This is a self-study journal supplement designed for physicians and pharmacists. Participation should take approximately 1 hour. To complete this activity and receive credit, the participant should:

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2. Read and review the educational supplement, and
3. Complete the posttest and evaluation form. Please go to the AMCP.org CME/CE Center to complete the Posttest and Evaluation.

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1. Posttest form for this program, “Optimal Treatment of Chronic Constipation in Managed Care: Review and Roundtable Discussion,” on the AMCP.org Online Learning Center site. To receive CE credit, you must receive a score of at least 70%. You will have 2 opportunities to pass the posttest.
2. Activity evaluation form.

Upon successful completion of this activity, you will automatically receive your CE statement. Your CE credits will be automatically archived and tracked for you on the AMCP.org (CE/CME Center) site. All information is kept confidential. Note: There is no fee to participate in this activity. Credit is available from November 1, 2008 through November 1, 2009.
1. Which of the following is not a possible secondary cause of constipation?
   a. Eating disorders
   b. Hyperthyroidism
   c. Multiple sclerosis
   d. Analgesic use
   e. All are possible causes

2. The distinguishing factor/s that separate/s IBS-C from chronic constipation include/s:
   a. Number of bowel movements is less and stools are lumpier in chronic constipation
   b. IBS-C is more prevalent in men
   c. Blood pressure rises slightly higher with chronic constipation
   d. Abdominal pain/discomfort is part of the definition of IBS-C but is not included in the definition of chronic constipation

3. Constipation ______ with age.
   a. Increases
   b. Decreases

4. The most common subtype of constipation is:
   a. Dyssynergic defecation
   b. Slow-transit constipation
   c. Normal-transit constipation
   d. None of the above

5. Alarm symptoms accompanying constipation that require the need for diagnostic testing include:
   a. IBS
   b. Iron deficiency anemia
   c. Rectal bleeding
   d. All of the above

6. A study by Johanson et al. demonstrated that during the first 24 hours of lubiprostone treatment, approximately ______% of patients reported spontaneous bowel movements.
   a. 15.9
   b. 57
   c. 90
   d. <14

7. True or False. Because most OTC medications are relatively mild, constipation during pregnancy can be treated with the same agents used by nonpregnant females.
   True ______ False ______

8. Which constipation symptom is most commonly reported by patients?
   a. Hard stools
   b. Bloating and gas
   c. Decreased frequency of bowel movements
   d. Straining

9. Which diagnostic test is most helpful in distinguishing between normal-transit and slow-transit constipation?
   a. Defecography
   b. Colonic transit
   c. Anorectal manometry
   d. None of the above

10. Each year, ______ is spent on OTC laxatives.
    a. $1 billion
    b. $800 million
    c. <$100 million
    d. $4 million

To complete this activity, go to www.amcp.org (CE/CME Center), where you will access the posttest and evaluation form.