# American Gastroenterological Association Technical Review on the Pharmacological Management of Irritable Bowel Syndrome

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Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder characterized by abdominal pain and/or discomfort associated with altered defecation.[1] Other common symptoms include bloating, straining, rectal urgency, and the sensation of incomplete evacuation. These symptoms occur in approximately 11% of the world's population.[2–4] Women report symptoms of IBS more frequently than men; likewise, younger people are more susceptible than older people. IBS negatively impacts health-related quality of life[5] and results in a significant financial burden through reduced work productivity and increased use of health-related resources.[6]

Q4 The diagnosis of IBS is based on the presence of symptoms and, when clinically appropriate, exclusion of organic disease. In the absence of alarm symptoms (eg, rectal bleeding, unintentional weight loss, family history of colon cancer), diagnostic testing does not increase the sensitivity of the diagnosis.[7,8] The current Rome III criteria for IBS require the presence of recurrent abdominal pain and/or discomfort at least 3 days per month in the past 3 months that is associated with 2 or more of the following: improvement with defecation, onset associated with a change in frequency of stool, or onset associated with a change in form (appearance) of stool. Further subclassification is based on the predominant stool consistency: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), IBS with mixed pattern (IBS-M), and unsubtyped IBS.[1] Symptoms have to be present for at least 6 months. Current pharmacological treatments are generally aimed at improving one or more of the predominant symptoms, such as abdominal pain, constipation, or diarrhea. There is a lack of treatment data on IBS-M alone; however, some of the trials include these patients in a nonconstipating IBS group.

In this technical review, the American Gastroenterological Association (AGA) reviews commonly used pharmacological therapies for IBS. Selecting appropriate therapy for patients with IBS is a common clinical dilemma, particularly in a heterogeneous patient population with a range of symptoms. This review provides evidence-based information to guide clinicians and patients to the most appropriate therapy. However, the list of therapies in this review is not exhaustive and does not include nonpharmacological and alternative therapies. In this technical review, the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system was used to assess the quality of evidence for the most commonly used pharmacological therapies for IBS.[9–11] GRADE has been adopted by several national and international societies, including the AGA, and is becoming the common methodology for the streamlined development of clear, transparent, and actionable guidelines.[9,11]

## Methods

### Overview

This technical review was conducted to inform the AGA guidelines for the management of IBS. Methods for deriving focused clinical questions, systematically reviewing and rating the quality of evidence for each outcome, and rating the overall quality of evidence were based on the GRADE framework, which has been described in more detail previously.[12–26] Using the PICO format, which frames a clinical question by defining a specific patient population (P), intervention (I), comparator (C), and outcome(s), we outlined a total of 9 questions (see Table 1).

### Types of Participants, Interventions, and Comparators

We included studies of adults (18 years of age and older) with IBS using symptom-based diagnostic criteria. The interventions were linaclotide, lubiprostone, polyethylene glycol (PEG) laxative, rifaximin, alosetron, loperamide, tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and antispasmodics. The comparators were placebos. It should be noted that there is a lack of comparative effectiveness studies in IBS.

***Abbreviations used in this paper:*** **AGA, American Gastroenterological Association; CI, confidence interval; CSBM, complete spontaneous bowel movement; FDA, Food and Drug Administration; GRADE, Grading of Recommendations Assessment, Development and Evaluation; IBS, irritable bowel syndrome; IBS-C, irritable bowel syndrome with constipation; IBS-D, irritable bowel syndrome with diarrhea; IBS-M, irritable bowel syndrome with mixed pattern; PEG, polyethylene glycol; PICO, population, intervention, comparator, and outcome(s); QOL, quality of life; RCT, randomized controlled trial; RR, relative risk; SBM, spontaneous bowel movement; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.**


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**Table 1.** PICO Questions

| Population(s) | Intervention(s) | Comparator | Outcome(s) |
|---|---|---|---|
| Adults with IBS-C | Linaclotide | Placebo or control | Beneficial<br>1. Symptom relief (FDA responder)<br>2. Global relief<br>3. Abdominal pain<br>4. CSBM or SBM<br>5. IBS-QOL<br>Harms<br>6. Diarrhea leading to treatment discontinuation |
| Adults with IBS-C | Lubiprostone | Placebo or control | Beneficial<br>1. Symptom relief (FDA responder)<br>2. Global relief<br>3. Abdominal pain<br>4. CSBM or SBM<br>5. IBS-QOL<br>Harms<br>6. Diarrhea leading to treatment discontinuation |
| Adults with IBS | Rifaximin | Placebo or control | Beneficial<br>1. Symptom relief (FDA responder)<br>2. Global relief<br>3. Abdominal pain<br>4. Bloating<br>5. IBS-QOL<br>Harms<br>6. Adverse effects leading to treatment discontinuation |
| Adults with IBS | Alosetron | Placebo or control | Beneficial<br>1. Global relief<br>2. Abdominal pain<br>3. Urgency<br>4. Stool consistency<br>5. IBS-QOL<br>Harms<br>6. Ischemic colitis<br>7. Serious complications of constipation |
| Adults with IBS | TCAs | Placebo or control | Beneficial<br>1. Global relief<br>2. Abdominal pain<br>Harms<br>3. Anticholinergic effects |
| Adults with IBS | SSRIs | Placebo or control | Beneficial<br>1. Global relief<br>2. Abdominal pain<br>Harms<br>3. Sexual dysfunction |
| Adults with IBS | Antispasmodics | Placebo or control | Beneficial<br>1. Global relief<br>2. Abdominal pain<br>Harms<br>3. Adverse effects leading to treatment discontinuation |
| Adults with IBS | PEG laxatives | Placebo or control | Beneficial<br>1. Symptom relief (FDA responder)<br>2. Global relief<br>3. Abdominal pain<br>4. CSBM or SBM<br>5. IBS-QOL<br>Harms<br>6. Diarrhea |
| Adults with IBS-C | Linaclotide | Lubiprostone | No studies |