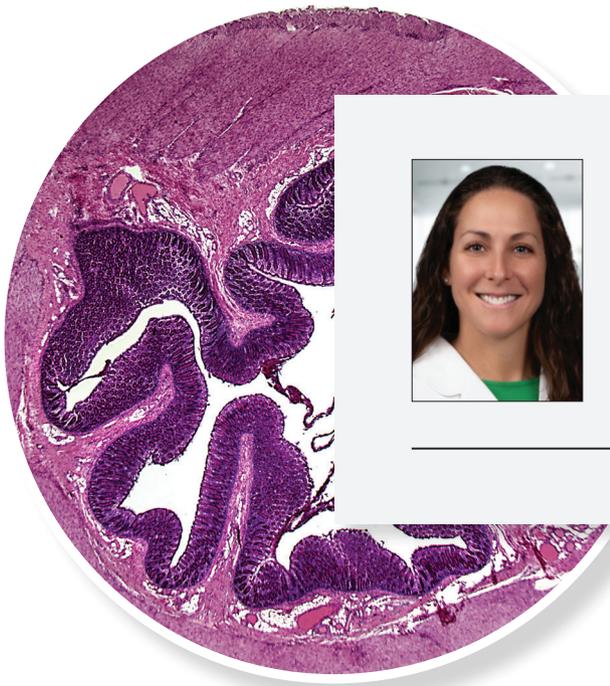


Case Study Series

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Making Patient Quality of Life the Focus of IBS-C Management



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About the Patient

AB, a 22-year-old female graduate student enrolled in a Master of Public Health (MPH) program, first presented to the clinic in August 2024 with a 6-year history of persistent gastrointestinal symptoms. Her chief complaints were abdominal bloating, excessive gas, abdominal pain, and constipation. She reported that these daily symptoms worsened after eating and intensified in the evening, but improved “somewhat” with bowel movement. Bowel movements occurred every 2 to 3 days and were characterized by hard stools, significant straining, and a persistent sensation of incomplete evacuation. She noted a marked reduction in appetite and expressed considerable frustration over the chronicity of her symptoms.

In recent months, the severity of her symptoms had begun to interfere with academic performance. She reported frequent difficulty concentrating, missed assignment deadlines, and recurrent requests for extensions. Additionally, she missed at least 1 class per week because of symptom burden, which she described as increasingly disruptive to her studies and overall quality of life.

AB had previously consulted 2 gastroenterologists and visited the emergency department. Her diagnostic workup included upper endoscopy, abdominal ultrasound, computed tomography scan, and laboratory testing, all of which were unremarkable. She had tried a low-fermentable oligo-, di-, monosaccharides, and polyols (FODMAP) diet, food sensitivity testing, and various over-the-counter agents such as fiber supplements, magnesium, and probiotics. These interventions failed to

provide meaningful symptom relief. She reported partial improvement with polyethylene glycol (MiraLAX), noting softer stools and reduced straining; however, its use was associated with increased abdominal bloating and discomfort, limiting its tolerability.

AB had not previously received a formal diagnosis of irritable bowel syndrome with constipation (IBS-C).

During the consultation, the psychosocial impact and stigma often associated with irritable bowel syndrome (IBS) were acknowledged. AB was reassured that her symptom profile met diagnostic criteria for IBS-C, and that a formal diagnosis was warranted. It was emphasized that, although over-the-counter therapies may offer partial relief by targeting isolated symptoms, their limited scope often fails to produce meaningful improvements in overall quality of life—consistent with AB’s prior experience. In contrast, US Food and Drug Administration (FDA)–approved pharmacologic agents for IBS-C have demonstrated efficacy across multiple symptom domains in large, randomized controlled trials.

The complex, multifactorial pathophysiology of IBS-C was reviewed, highlighting the relevance of distinct mechanisms of action among available FDA-approved therapies. AB was counseled that a trial-and-error approach is often necessary in IBS-C management, and that switching to an agent with a different mechanism of action may be beneficial if initial therapy proves inadequate. We discussed data supporting the importance of therapeutic persistence, as symptom improvement may occur gradually across different domains. Treatment with linaclotide 290 µg orally once daily (FDA-approved dose

On the Cover: Light micrograph of a cross section of a colon. Credit: Alvin Telsler / Science Source

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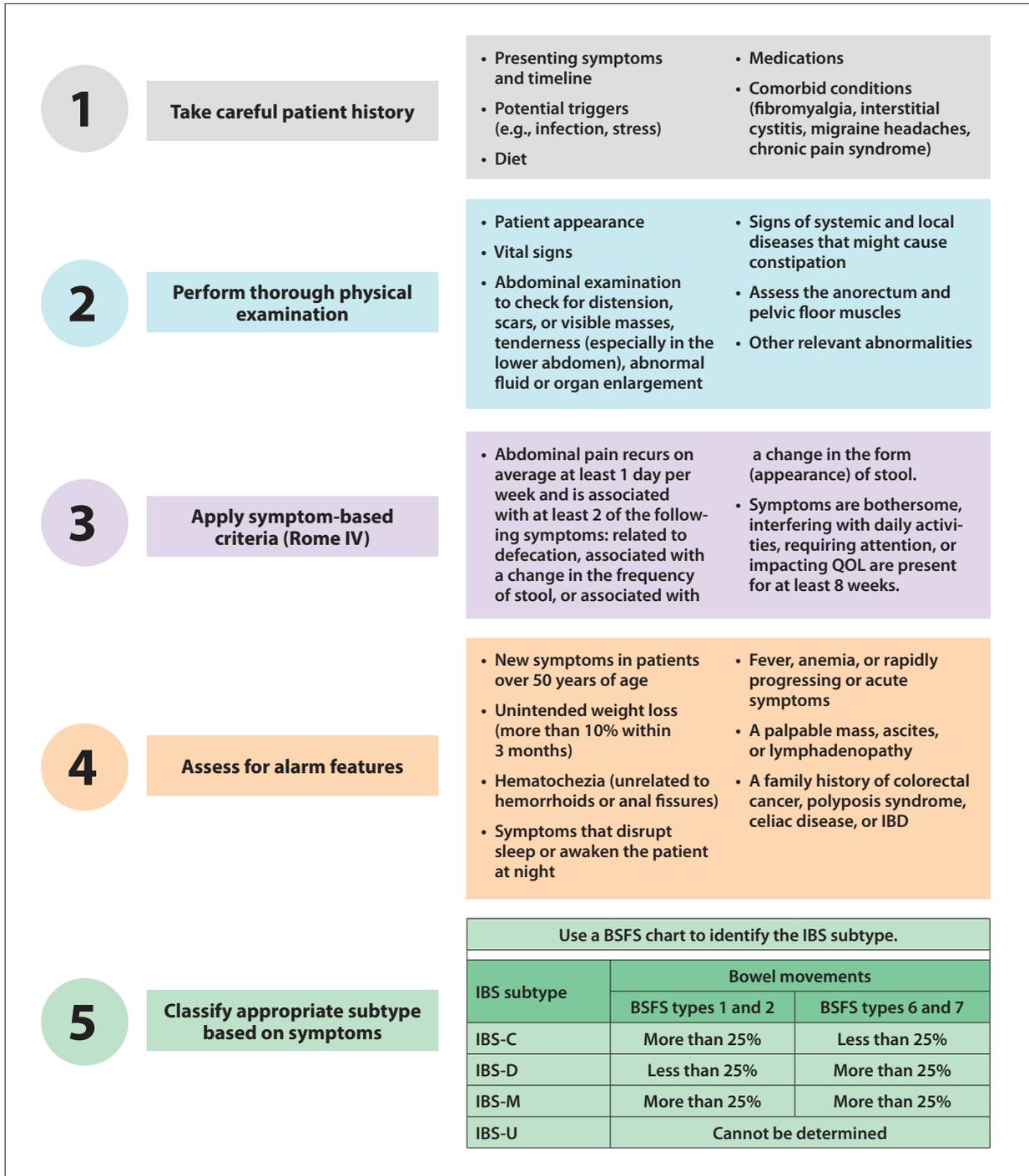


Figure 1. Making a positive IBS diagnosis: 5 key features.

BSFS, Bristol Stool Form Scale; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; IBS-C, IBS with constipation; IBS-D, IBS with diarrhea; IBS-M, IBS with mixed or alternating bowel habits; IBS-U, IBS without a significant pattern of abnormal stool or unclassified.

for IBS-C) was initiated and a structured follow-up was scheduled at 8 weeks to assess treatment response and guide ongoing management.

AB continued linaclotide for approximately 6 weeks. She experienced a notable improvement in bowel move-

ment frequency, achieving daily defecation for the first time in several years. However, she continued to report a persistent sensation of incomplete evacuation despite the increased frequency. Importantly, her abdominal symptoms, including bloating and discomfort, remained

unchanged. The lack of improvement in these domains contributed to continued academic interference and poor overall quality of life.

Given the inadequate response to linaclotide, AB was transitioned to tenapanor and a follow-up visit was scheduled for 2 months later. At follow-up, she reported significant clinical improvement. Bowel movement frequency remained consistent at once daily, and now accompanied by a sensation of complete evacuation. Abdominal symptoms, including pain, bloating, and discomfort, were markedly reduced. These improvements translated into meaningful gains in academic functioning. AB reported enhanced concentration, uninterrupted participation in her MPH program, and no missed classes or assignment extensions over the preceding month. She expressed a renewed sense of control over her symptoms and optimism regarding her academic and personal well-being.

Making a Positive Diagnosis of IBS: 5 Key Features

Given the absence of validated diagnostic tests or biomarkers, IBS-C is not a diagnosis of exclusion. Providers should use a positive, symptom-based diagnostic approach, which is also endorsed by the American College of Gastroenterology (ACG).¹ Figure 1 demonstrates a 5-step approach to making a confident IBS diagnosis.¹⁻⁴

Step 1. Take careful history

This involves asking the patient their primary reason for the consultation.

- What is their chief complaint?
- How long have they been experiencing these symptoms?
- How have these symptoms impacted their quality of life?
- Have they noticed any triggers that exacerbate these symptoms or anything that alleviates them?
- Have they sought other consultations?
- Have they tried any interventions to address these?
- What has been their experience with these interventions?

Note that patients typically seek a gastroenterology consultation primarily for severe abdominal symptoms (bloating and pain) that are interfering with their quality of life. While conducting the initial workup, constipation comes up as an issue.

Step 2. Perform a thorough physical examination

- Check patient appearance.
- Check vital signs.
- Perform abdominal examination to check for distension, scars, or visible masses; gently press to detect tenderness, especially in the lower abdomen; tap to assess for abnormal fluid or organ enlargement; and listen for bowel sounds.

- Check for signs of systemic and local diseases that might cause constipation.
- Assess the anorectum and pelvic floor muscles.
- Rule out other relevant abnormalities.

Step 3. Apply symptom-based Rome criteria

According to the Rome IV criteria, IBS is a disorder of gut-brain interaction in which abdominal pain recurs on average at least 1 day per week and is associated with at least 2 of the following symptoms: related to defecation, associated with a change in the frequency of stool, or associated with a change in the form (appearance) of stool.²⁻⁴ In clinical practice, these symptoms should be present for at least 8 weeks and are bothersome, interfering with daily activities, requiring attention, or impacting quality of life. This is a much more practical application of Rome criteria compared with the strict requirements for clinical research—symptoms present for the previous 3 months, with an onset at least 6 months prior.

Step 4. Rule out alarm features

Certain alarm features are suggestive of an underlying organic gastrointestinal disorder and should prompt immediate investigation and treatment. These include:

- New symptoms in patients over 50 years of age
- Unintended weight loss (more than 10% within 3 months)
- Hematochezia (unrelated to hemorrhoids or anal fissures)
- Symptoms that disrupt sleep or awaken the patient at night
- Fever, anemia, or rapidly progressing or acute symptoms (*Note that limited diagnostic workup is done [complete blood count at a minimum] to rule out anemia.*)
- A palpable mass, ascites, or lymphadenopathy
- A family history of colorectal cancer, polyposis syndrome, celiac disease, or inflammatory bowel disease (IBD)

Step 5. Classify appropriate subtype based on symptoms

- Bristol Stool Form Scale (BSFS) is a useful tool for classification of the appropriate IBS subtype.³
- IBS-C involves more than 25% BSFS types 1 and 2 and less than 25% BSFS types 6 and 7 bowel movements.
- IBS with diarrhea (IBS-D) involves less than 25% BSFS types 1 and 2 and more than 25% BSFS types 6 and 7 bowel movements.
- IBS with mixed or alternating bowel habits (IBS-M) involves more than 25% BSFS types 1 and 2 and more than 25% BSFS types 6 and 7 bowel movements.
- IBS without a significant pattern of abnormal stool or unclassified (IBS-U) has no identifiable pattern of bowel movements.

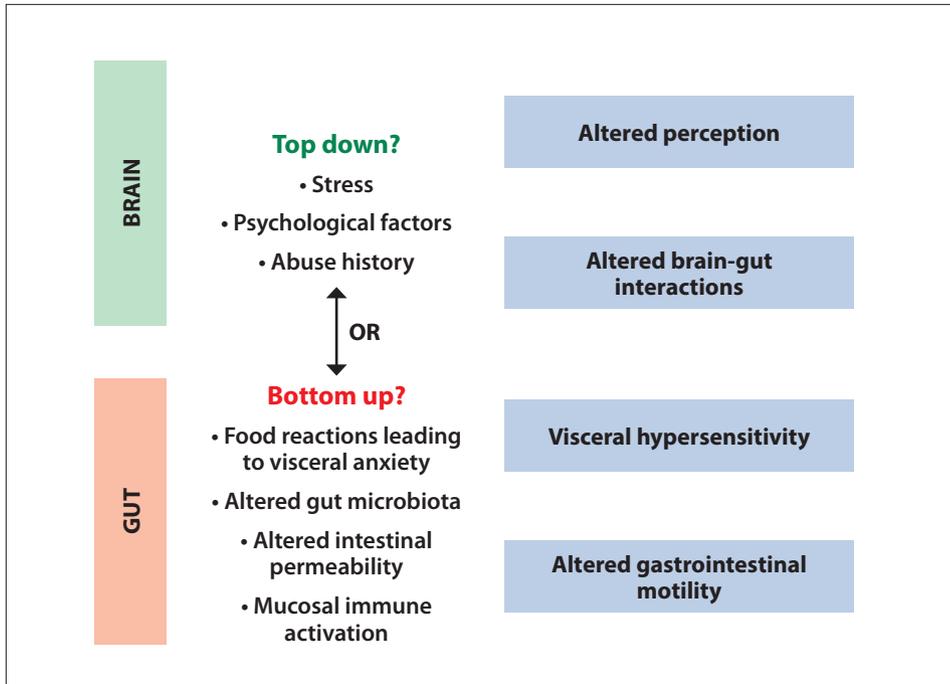


Figure 2. IBS: gut-brain or brain-gut?

IBS, irritable bowel syndrome.

Courtesy of Kimberly Orleck, PA-C.

Educating the Patient: What Does an IBS-C Diagnosis Mean?

Despite suffering for years and possibly going through several providers and extensive testing that mostly turns out normal, most patients have not heard of IBS-C. Therefore, educating the patient becomes paramount.

Acknowledge the Stigma Associated With IBS

Bowel symptoms are considered socially taboo and the absence of biomarkers or definitive tests fuels the misperception that IBS is not “real” or a legitimate medical condition.⁵ Clinicians should proactively address this stigma by validating the patient’s experience and make the patient more comfortable discussing personal bowel habits. It is essential to reassure patients that the absence of abnormal laboratory or imaging findings does not negate the reality of their symptoms. Acknowledging both the physical discomfort and emotional distress associated with IBS fosters trust and supports a confident, symptom-based diagnosis.

Educate About the Complex Multifactorial Pathophysiology of IBS

Explain to patients that IBS is a chronic condition that has a complex, multifactorial pathophysiology, and the exact underlying issues responsible for each patient’s symptoms cannot be determined.⁶⁻¹⁵ Proposed etiologies of IBS include visceral hypersensitivity, gastrointestinal motility, increased intestinal permeability, diet, gut microbiome, immune activation, genetic factors, and psychosocial fac-

tors/stress. Although IBS is described as a disorder of the gut-brain interaction, the precise nature of this interaction is not known (Figure 2).¹⁶

The chronic and fluctuating nature of IBS means that symptom exacerbations, or “flares”, may be triggered by diverse and sometimes unrelated factors, including specific foods, psychological stress, infections, or antibiotic exposure. Regardless of the underlying cause of each patient’s symptoms, the foundational principles of IBS-C management remain consistent.

In the Clinic . . .

Patients with IBS-C have often undergone extensive testing—laboratory panels, stool studies, imaging, and even colonoscopy—only to be told, perhaps by multiple providers, that “everything looks normal.” Their persistent symptoms exacerbate their frustration and they are often looking to providers not to simply state a diagnosis but to explain why they are experiencing these symptoms.

Explain to patients that normal test results do not equate to the absence of disease. This will make them feel heard and understood, validating what they are experiencing.

Take the time to articulate the multifactorial and complex pathophysiology of IBS-C and be honest about the fact that it is not possible to know the specific cause of each patient’s symptoms. Reassure patients that there are options to help them achieve a better quality of life.

Table 1. Over-the-Counter Options Fail to Treat Cardinal Symptoms of IBS-C

Over-the-counter options	Improve bowel symptoms	Improve abdominal symptoms	Approved by the FDA
Stool softeners	??	x	x
Soluble fiber	✓	??	x
Laxatives			
Osmotic	✓	x	x
Stimulant	✓	x	x
Saline	✓	x	x

FDA, US Food and Drug Administration; IBS-C, irritable bowel syndrome with constipation.

Make Quality of Life Considerations Part of the Initial Workup

Patients often seek gastroenterology consultation because of severe abdominal symptoms, particularly bloating and pain, that significantly impair daily functioning. Constipation frequently emerges during the initial evaluation as a contributing factor but may not be the primary reason for seeking care.

Surveys like IBS in America have also elucidated the bothersome impact of IBS-C symptoms on patients’ quality of life—including mental and emotional health, sexual health and intimacy, employment or education, sense of independence, relationships with friends or family, and household finances.^{17,18} Furthermore, greater symptom severity is associated with greater financial distress, including concerns about out-of-pocket medical expenses, ability to work, and financial future.¹⁹ It is therefore critical to make quality of life considerations part of the initial workup and consider approaches to IBS-C management that have the promise to improve patient quality of life.

Providers should engage patients in open-ended dialogue to explore how IBS-C symptoms affect their daily lives. Although no standardized quantitative tool exists for this purpose, qualitative inquiry can yield valuable insights. The impact of IBS-C varies widely depending on a patient’s age, life stage, and social context.

For a college student like AB, uninterrupted focus on academic tasks—papers, lectures, and examinations—is essential for success. For a parent, the ability to participate in their child’s activities, such as soccer games, school concerts, or PTA meetings, without the distraction of pain and bloating is critical to maintaining family engagement. Adults with demanding travel schedules may prioritize predictable bowel habits to avoid disruptions during work-related commitments. Meanwhile, active

older adults often value social participation, and symptoms such as abdominal distension may be particularly distressing when attending plays, community events, or family gatherings.

Determining the most bothersome symptom and quality of life impact for the patient at baseline will help with conducting a meaningful follow-up to evaluate the impact of treatment intervention and tailoring management strategies to address these individualized concerns.

Over-the-Counter Approaches Do Not Have a Significant Impact on Quality of Life

Patients have generally tried dietary interventions like probiotics and a low-FODMAP diet, as well as over-the-counter options such as psyllium fiber, osmotic laxatives (polyethylene glycol), and stimulant laxatives (senna, cascara sagrada, castor oil, bisacodyl) prior to being seen by a gastroenterologist. These, however, fail to treat all the cardinal symptoms of IBS and are not approved by the FDA for the treatment of IBS-C (Table 1).²⁰

Intake of fermentable foods through the low-FODMAP diet can help with some IBS symptoms but not all, and it is not for all patients.²¹ Probiotics have limited benefit and are not featured in any guidelines for IBS.¹ Psyllium fiber is associated with modest benefits for global IBS symptoms and is strongly recommended by the ACG for overall symptom improvement.¹ It is important to note that dietary fiber may exacerbate symptoms in some patients; gradual introduction is recommended. Osmotic laxatives like polyethylene glycol improve stool frequency and consistency but do not reliably improve abdominal pain or bloating and are therefore given a weak recommendation by ACG for overall symptom improvement in IBS. ACG makes no recommendations regarding stimulant laxatives.¹

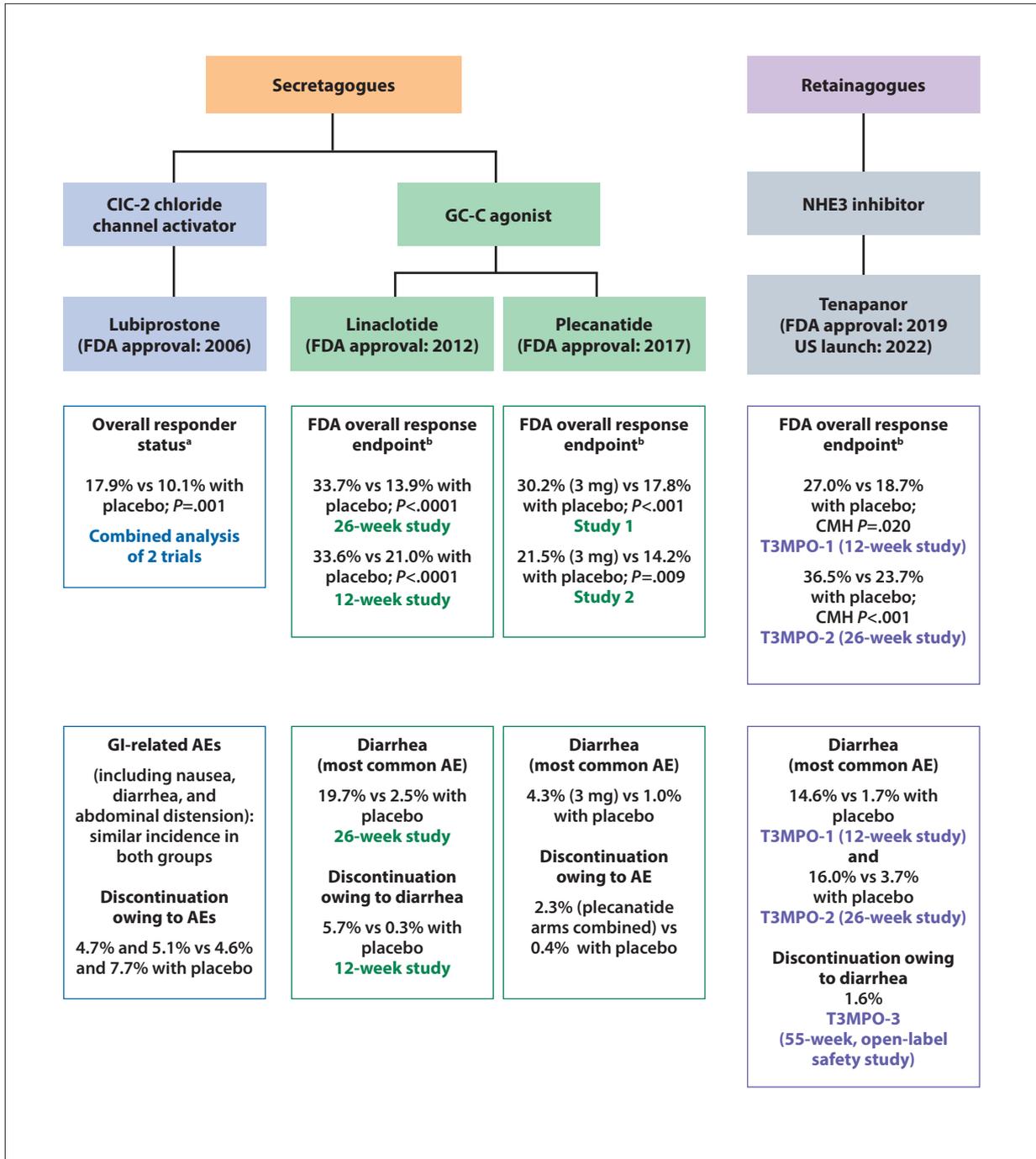


Figure 3. Currently available FDA-approved treatment options for IBS-C and their efficacy and safety data.

^aOverall responder status was calculated from the weekly assessments of symptom relief. Monthly responders were defined as patients who rated their IBS symptoms as being at least moderately relieved for all 4 weeks of the month or significantly relieved for at least 2 weeks of the month, with no ratings of moderately or severely worse. A patient was considered an overall responder if they were monthly responders for at least 2 of the 3 months of the study.

^bDefined as an improvement of at least 30% from baseline in average daily worst abdominal pain score and an increase of at least 1 CSBM from baseline, both in the same week for 6 or more out of 12 weeks.

AE, adverse event; CMH, Cochran-Mantel-Haenszel; CSBM, complete spontaneous bowel movement; FDA, US Food and Drug Administration; GC-C, guanylate cyclase-C; IBS-C, irritable bowel syndrome with constipation; NHE3, sodium/hydrogen exchanger isoform 3.

Adapted from Brenner DM. *Gastroenterol Hepatol (N Y)*. 2023;19(12)(suppl 6):749-756.²²

Table 2. Indication, Dosage, and Administration of Currently Available FDA-Approved Medications for IBS-C

FDA-approved agent	FDA-approved indication for	Dosage	Administration
Lubiprostone	Women >18 years of age	8 µg orally twice daily	With food and water
Linaclotide	Adults	290 µg orally once daily	On empty stomach at least 30 minutes prior to a meal at approximately the same time each day
Plecanatide	Adults	3 mg orally once daily	With or without food
Tenapanor	Adults	50 mg orally twice daily	Immediately prior to breakfast or the first meal of the day and immediately prior to dinner

FDA, US Food and Drug Administration; IBS-C, irritable bowel syndrome with constipation.

Because all of these options do not significantly improve ALL symptom domains in IBS, they are unable to improve patient quality of life in a meaningful way.

In the Clinic . . .

Recognize that over-the-counter medications do not improve patient's quality of life and that is the reason why patients are seeking help.

Improved Quality of Life is Possible With FDA-Approved IBS-C Medications

The complex, multifactorial pathophysiology of IBS-C has led to FDA-approved medications with distinct mechanisms of action (Figure 3).²²⁻³² Of these, tegaserod, a 5-hydroxytryptamine type 4 agonist, was approved in 2002 but is no longer commercially available.³³ This was followed by approval of 3 secretagogues—lubiprostone (in 2006), linaclotide (in 2012), and plecanatide (in 2017). In 2019, the first-in-class retainagogue, tenapanor, was approved (launched in the United States in 2022).

The specific FDA-approved indications of these agents and their recommended dosages are listed in Table 2.²²⁻²⁶ Linaclotide and tenapanor are being evaluated in pediatric patients for IBS and preliminary results of these studies presented at Digestive Disease Week 2025 are promising.³⁴⁻³⁶

Distinct Mechanism of Action = Possibility for Patients to Achieve Desired Outcome

Secretagogues increase the secretion of chloride and bicarbonate ions into the intestinal lumen, promoting water secretion and thereby accelerating colonic transit, improving stool consistency, and increasing the frequency of

bowel movements. The only retainagogue, tenapanor, is a locally acting inhibitor of sodium/hydrogen exchanger isoform 3 (NHE3); the NHE3 antiporter is responsible for the absorption of dietary sodium.³⁷⁻⁴⁰ NHE3 inhibition reduces the absorption of dietary sodium, causing water retention in the intestinal lumen and accelerating intestinal transit. In animal models, NHE3 inhibition is associated with a reconstitution of the tight junctions between intestinal epithelial cells (decreasing intestinal permeability) and antagonism of transient receptor potential vanilloid 1 channels—actions hypothesized to be responsible for the reduction in visceral hypersensitivity and improvement in abdominal symptoms seen in the phase 3 trials. The distinct mechanism of action of these medications offers options for providers to switch to an agent with a different mechanism of action if a particular agent is associated with inadequate response.

Improvement Across a Range of Abdominal and Bowel Symptoms and Acceptable Safety Profile

Unlike over-the-counter medications, the FDA-approved medications have been evaluated in pivotal, large, randomized, and placebo-controlled clinical trials and follow-up studies across a range of abdominal and bowel symptoms (Table 3) and have consistently shown improvement compared with placebo.^{27-32,41-44}

In a combined analysis of two 12-week phase 3 trials, the **lubiprostone** group was associated with significantly greater overall response compared with the placebo group (17.9% vs 10.1%; $P=.001$) and this increased over the first 3 months of treatment (month 1: 10.8% vs 7.5%; month 2: 18.3% vs 11.4%; month 3: 22.0% vs 14.5%).²⁷ Abdominal discomfort or pain, bloating, constipation severity, stool consistency, and straining significantly improved in overall responders compared with nonresponders.

In both a 26-week and a 12-week study, the **linaclotide** group was associated with significantly greater

Table 3. Available FDA-Approved Medications for IBS-C Have Been Evaluated Across a Range of Abdominal and Bowel Symptoms

FDA-approved medication	Primary endpoint studied	Other endpoints studied
Lubiprostone	Overall responder status ^a	<ul style="list-style-type: none"> • Abdominal discomfort or pain • Bloating • Constipation severity • Stool consistency • Straining
Linaclotide	FDA combined endpoint ^b	<ul style="list-style-type: none"> • Abdominal pain response • Reduction in abdominal pain of 30% or greater • CSBM response • Increase of at least 1 CSBM from baseline
Plecanatide	FDA combined endpoint ^b	<ul style="list-style-type: none"> • Abdominal pain • Stool frequency/consistency • Change in BSFS score • Change in CSBM • Change in straining score • Novel trisymptom composite endpoint^c
Tenapanor	FDA combined endpoint ^b	<ul style="list-style-type: none"> • Abdominal pain response • Abdominal discomfort response • Rate of abdominal bloating response • Abdominal cramping response • Abdominal fullness response • Abdominal score^d • CSBM

^aCalculated from the weekly assessments of symptom relief. A patient was considered an overall responder if they were a monthly responder for at least 2 of the 3 months of the study. Monthly responders were defined as patients who rated their IBS symptoms as being at least moderately relieved for all 4 weeks of the month or significantly relieved for at least 2 weeks of the month, with no ratings of moderately or severely worse.

^bDefined as an improvement of at least 30% from baseline in average daily worst abdominal pain score and an increase of at least 1 CSBM from baseline, both in the same week for 6 or more out of 12 weeks.

^cConsisting of abdominal pain, abdominal bloating, and CSBMs.

^dAverage of weekly scores for abdominal pain, discomfort, and bloating symptoms.

BSFS, Bristol Stool Form Scale; CSBM, complete spontaneous bowel movement; FDA, US Food and Drug Administration; IBS-C, irritable bowel syndrome with constipation.

FDA overall response compared with the placebo group (26-week study: 33.7% vs 13.9%; $P<.0001$; 12-week study: 33.6% vs 21.0%; $P<.0001$).^{28,29} For at least 6 of 12 treatment weeks, linaclotide compared with placebo was associated with greater abdominal pain response (48.9% vs 34.5%) and complete spontaneous bowel movement (CSBM) response (47.6% vs 22.6%).²⁸ For at least 6 of the 12 treatment weeks, linaclotide was associated with a greater reduction (compared with placebo) in abdominal pain of 30% or greater (50.1% vs 37.5%; $P=.0003$) and an increase of at least 1 CSBM from baseline (48.6% vs 29.6%; $P<.0001$).²⁹

The FDA-approved 3 mg dose of **plecanatide** was also associated with significantly greater FDA overall response than placebo (Study 1: 30.2% vs 17.8%; $P<.001$; Study 2: 21.5% vs 14.2%; $P=.009$).³⁰ Pivotal trials also reported impact of plecanatide on stool frequency/consistency, straining, and abdominal symptoms, and a

reanalysis reported a novel trisymptom composite endpoint (consisting of abdominal pain, abdominal bloating, and CSBMs).⁴¹⁻⁴³ Among patients with IBS-C classified as having moderate-to-severe bloating, plecanatide was associated with reduced bloating severity (least-squares mean change, -1.7 vs -1.3 ; $P=.002$), reduced abdominal pain (-1.7 vs -1.3 ; $P=.006$), and increased CSBM frequency (1.4 vs 0.8; $P<.0001$). A systemic review and meta-analysis reported impact of plecanatide on abdominal pain (pooled effect size, -0.49 ; 95% CI, -0.88 to -0.09 ; $P=.03$); change in BSFS score (pooled effect size, 0.82; 95% CI, -0.53 to 2.18; $P=.12$); change in CSBM (pooled effect size, 0.53; 95% CI, -1.77 to 2.83; $P=.42$); and change in straining score outcome (pooled effect size, 0.39; 95% CI, -1.21 to 1.99; $P=.40$).

Tenapanor was also associated with a significantly greater FDA overall response compared with placebo in both the 12-week T3MPO-1 trial (27.0% vs 18.7%;

Cochran-Mantel-Haenszel [CMH] $P=.020$) and the 26-week T3MPO-2 trial (36.5% vs 23.7%; CMH $P<.001$).^{31,32} In T3MPO-1, tenapanor (compared with placebo) was associated with greater abdominal pain response (44.0% vs 33.1%; CMH $P=.008$), abdominal discomfort response (29.0% vs 17.1%; CMH $P<.001$), rate of abdominal bloating response (27.0% vs 16.1%; CMH $P=.001$), abdominal cramping response (30.6% vs 23.1%; CMH $P=.044$), and abdominal fullness response (27.4% vs 14.4%; CMH $P<.001$).³¹ T3MPO-2 showed similar results for abdominal pain response (49.8% vs 38.3%; CMH $P=.004$) and CSBM (47.4% vs 33.3%; CMH $P<.001$).³² A post hoc analysis of pooled data from the T3MPO-1 and T3MPO-2 trials revealed that tenapanor (compared with placebo) was associated with better abdominal score (AS; least-squares mean change from baseline: -2.66 vs -2.09 ; $P<.0001$) and AS response rate for at least 6 out of 12 weeks (44.4% vs 32.4%; $P<.0001$) and for at least 9 out of 12 weeks (30.6% vs 20.5%; $P<.0001$).⁴⁴ (Note that AS was defined as average of weekly scores for abdominal pain, discomfort, and bloating symptoms.) Tenapanor was also associated with an improvement in abdominal pain as early as 1 week after treatment initiation and a decrease in other abdominal symptoms including bloating, fullness, discomfort, and cramping.

Moreover, side effects associated with these agents were generally mild or moderate in severity. Lubiprostone was associated with gastrointestinal-related events (nausea, diarrhea, and abdominal distension) in pivotal studies. Linaclotide, plecanatide, and tenapanor studies reported diarrhea as the most frequently reported adverse event. Note that in a 55-week open-label safety study (T3MPO-3), tenapanor was well tolerated with no new safety signals and only 1.6% discontinuation owing to diarrhea.⁴⁵

Bowel Symptoms Typically Improve Before Abdominal Symptoms

Tenapanor and linaclotide studies indicate that bowel symptoms typically improve prior to abdominal symptoms.^{46,47}

A post hoc analysis of pooled data from 3 tenapanor studies (T3MPO-1, T3MPO-2, and a phase 2b study) revealed that the median time to CSBM response was 2 weeks, and time to abdominal pain response was 4 weeks and time to bloating response was 5 weeks.⁴⁶ Furthermore, response rates improved over time with persistence of therapy—CSBM response probability (week 2: 52.3%; week 4: 72.5%; week 12: 76.7%); abdominal pain response (week 4: 54.6%; week 8: 67.9%; and week 12: 72.3%); and abdominal bloating response probability (week 4: 48.1%; week 8: 61.9%; and week 12: 67.7%).

A post hoc analysis of linaclotide trials revealed that more than one-half of patients with IBS-C in the linaclotide group experienced responses for abdominal pain, discomfort, bloating, or CSBM frequency within 4 weeks of starting treatment, and an additional 8% to 17% showed responses between weeks 5 and 12.⁴⁷

Start the Patient on an FDA-approved Medication for IBS-C

Note that although each of these medications has been associated with improved bowel and abdominal symptoms, there are no head-to-head trials to determine their comparative efficacy. Even the 2 network meta-analyses offering indirect comparisons report similar efficacy of these agents across most endpoints (including abdominal bloating) and prove their superiority to placebo for the treatment of global IBS-C symptoms.^{48,49} Therefore, if a patient is treatment-naïve with respect to FDA-approved IBS-C medications, then start them with any of the agents discussed. If, however, the patient has tried one class of agents and not experienced an improved quality of life, then providers can consider starting the patient on a medication with different mechanism of action and schedule a follow-up visit at 2 months.

In the Clinic . . .

- Reassure patients that improved quality of life is indeed possible with FDA-approved treatment options, as these medications have been proven to improve both bowel and abdominal symptoms across a range of studies.
- Stress the importance of persistence with therapy for at least 6 weeks to experience the full effect and evaluate efficacy.
- Reiterate that chronic nature of IBS-C necessitates long-term management.
- Explain the need for a follow-up to evaluate response and that there are options in case the patient's quality of life has not substantially improved by that time.

Follow-up Visit: Improved Quality of Life Is the ONLY Acceptable Response

There are no standardized questionnaires to conduct a follow-up visit evaluating response in IBS-C. In some ways, a standardized approach is not possible given the inherent variability in symptom presentation and the individualized nature of how these symptoms affect quality of life.

To assess response to therapy, clinicians should revisit the baseline evaluation and compare changes across 3 key

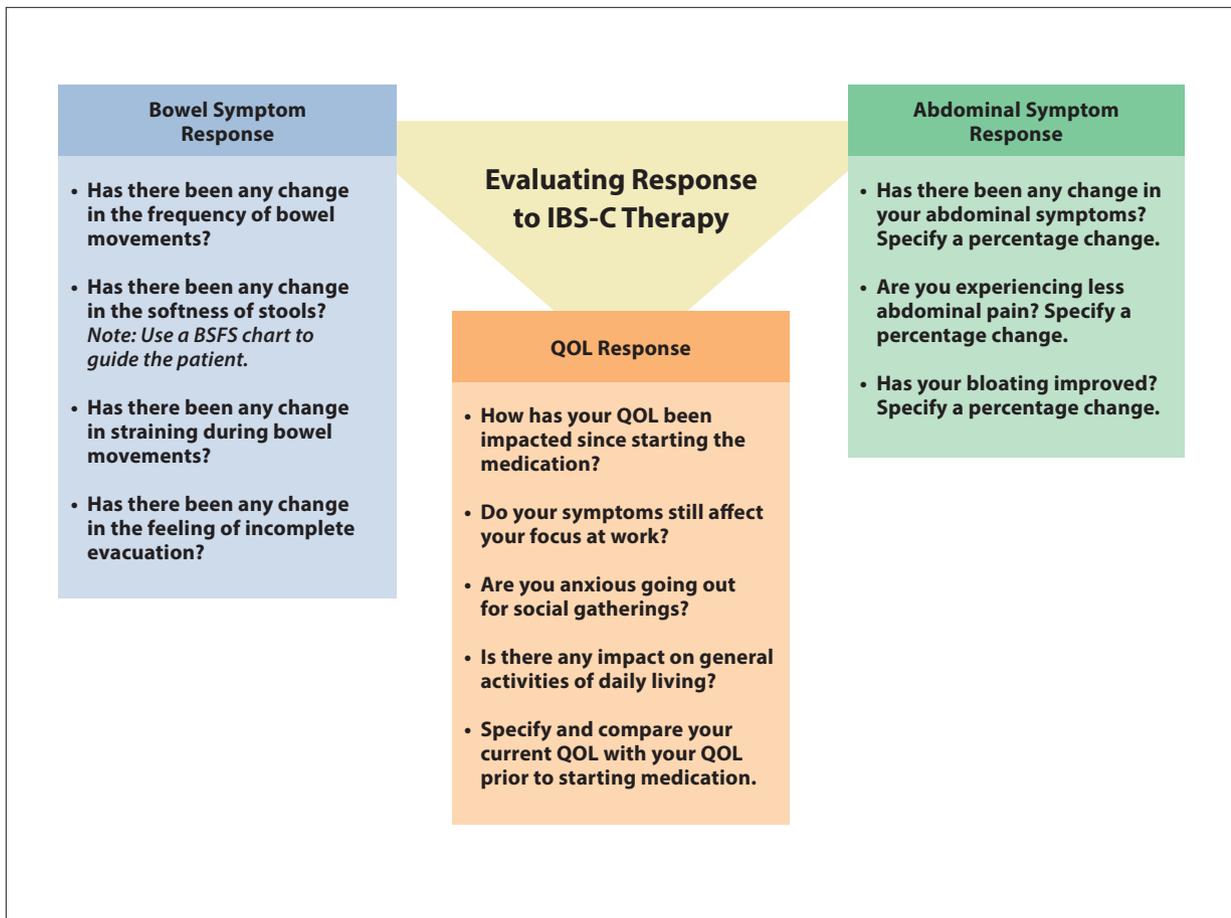


Figure 4. Evaluating response to IBS-C therapy: what you should ask patients.

BSFS, Bristol Stool Form Scale; IBS-C, irritable bowel syndrome with constipation; QOL, quality of life.

domains: abdominal symptoms, bowel function, and quality of life. It is essential to guide patients toward providing quantitative feedback rather than vague descriptors such as “somewhat better” or “a little improved.” Encourage patients to reflect deeply and express symptom changes in terms of percentage improvement for specific functional outcomes. It is also essential to ask open-ended questions rather than those requiring a mere “yes” or “no” response.

For example, if AB’s abdominal pain previously led to frequent missed academic deadlines, a targeted follow-up question would be: “How many assignment extensions have you requested because of abdominal symptoms since starting therapy?” Similarly, if she reported missing classes at least once weekly prior to treatment, clinicians should ask: “How often have you missed class because of symptoms in the past month?” These concrete metrics offer a more reliable gauge of therapeutic efficacy and help tailor ongoing management.

Figure 4 suggests questions you should consider asking patients at follow-up.

Back to the Patient

The patient in this case, AB, was experiencing debilitating symptoms for about 6 years and had unsuccessfully tried dietary and over-the-counter interventions. She had undergone extensive testing, which yielded normal findings, had been to multiple providers, and had never been informed that she has IBS-C. She sought another gastroenterology consultation when her symptoms started to interfere with her ability to focus in college with missed classes, missed assignment deadlines, and having to frequently ask for extensions for schoolwork.

At her initial visit she was informed that she has IBS-C. The complex pathophysiology of IBS-C was explained. She was educated about the inadequacy of over-the-counter options and the possibility to achieve improvement across all symptom domains and quality of life with FDA-approved treatment options. She was prepared to expect a trial-and-error approach to treatment with FDA-approved IBS-C medications with dif-

ferent mechanisms of action because the exact cause of her specific symptoms couldn't be ascertained. When a guanylate cyclase-C agonist (secretagogue) linaclotide did not provide adequate response and did not improve her quality of life, she was switched to the NHE3 inhibitor (retainagogue) tenapanor.

Detailed and thorough follow-up asking specific questions seeking quantitative responses to all symptom domains and impact on quality of life compared with baseline was key to evaluating response. Ultimately for this specific case, tenapanor resulted in improved bowel frequency, feeling of complete evacuation, and abdominal symptoms. This contributed to better focus and no interruptions as she pursued her MPH degree. She reported not having asked for any extensions for assignments in the past month and not missing a single class during that period.

The key to successful IBS-C management lies in educating the patient and preparing them for trial-and-error approach with FDA-approved IBS-C medications while expecting quality of life improvement as the ultimate achievable goal of therapy. Providers need to be proactive and thorough with follow-up evaluation of treatment response; and if medication from one class is associated with inadequate response, then change to another with a different mechanism of action.

Disclosures

Ms Orleck is a consultant/advisor for Salix, Lilly, Johnson & Johnson, AbbVie, Takeda, Pfizer, Phathom Pharmaceuticals, and Ardelyx.

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