Real-World Patient Experience with Linaclotide (Linzess): Efficacy, Discontinuation, and Withdrawal Symptoms

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Abstract

Background: Linaclotide (Linzess) is a guanylate cyclase-C agonist used for the treatment of irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC). While clinical trials support its effectiveness and safety, real-world data from patients remain essential for understanding long-term outcomes, discontinuation causes, and withdrawal experiences.

Objective: To assess the effectiveness of Linaclotide use, reasons for discontinuation, and post-discontinuation symptoms through a patient-reported survey.

Methods: An online survey (social media) was conducted with 86 respondents who had used linaclotide. Questions focused on duration of use, reason for prescription, symptom improvement, causes of discontinuation, and post-discontinuation gastrointestinal and systemic symptoms.

Results:

Among 86 respondents, 48% used linaclotide for less than three months and 37% for more than six months. The primary indication was constipation (71%) followed by irritable bowel syndrome (29%). Complete symptom resolution was reported by 35% of patients, while 47% had partial improvement and 18% reported no benefit. Discontinuation was common, with 49% stopping due to side effects and 29% due to cost or insurance issues. After discontinuation, abdominal pain (46%) and constipation (34%) were the most frequent gastrointestinal symptoms, whereas systemic withdrawal-like symptoms included headache (24%), anxiety or depression (24%), fatigue (20%), and sweating (12%).

Conclusion: While many patients experience some benefit from linaclotide, side effects, affordability, and symptom recurrence after discontinuation remain challenges. Post-

discontinuation withdrawal-like symptoms may occur and warrant clinical recognition and management.

Keywords: Linaclotide; constipation; IBS-C; side effects; Linzess

Introduction

Chronic idiopathic constipation (CIC) and irritable bowel syndrome with constipation (IBS-C) are prevalent gastrointestinal disorders that significantly affect patients' quality of life. Despite a wide range of available treatments, many patients remain dissatisfied due to suboptimal symptom relief, adverse effects, or financial constraints[1]. Linaclotide (brand name Linaclotide), a guanylate cyclase-C (GC-C) agonist, is a relatively newer addition to the therapeutic armamentarium for these conditions. It acts by stimulating intestinal secretion and transit, thereby alleviating symptoms such as bloating, abdominal pain, and constipation[2].

Clinical trials have established the safety and efficacy of linaclotide in both CIC and IBS-C. However, randomized controlled trials (RCTs) are conducted under tightly regulated conditions, often excluding individuals with complex medical histories or those at higher risk of adverse events. As a result, real-world experiences often diverge from those observed in clinical trials. Patient adherence, tolerability, and outcomes in everyday settings may reflect different realities particularly when it comes to long-term use, discontinuation, and potential post-discontinuation effects[3].

While the pharmacological profile of linaclotide suggests limited systemic absorption and a primarily local action in the gut, emerging anecdotal reports suggest that some patients may experience a constellation of systemic symptoms upon stopping the medication. These include fatigue, headache, anxiety, and other withdrawal-like features that are not well-documented in clinical literature[4].

This article aims to bridge that gap by presenting real-world data collected through a patient-reported survey. The objective was to capture firsthand user experiences with Linaclotide focusing on its effectiveness, the duration of use, reasons for discontinuation, and any gastrointestinal or systemic symptoms observed after cessation. By analyzing trends and patterns reported by actual users, this study seeks to provide clinicians with insights that may improve patient counseling, adherence, and overall management strategies in those prescribed linaclotide.

Methods:

An anonymous online poll (Social media) collected data from 86 respondents with prior or current Linaclotide use.

Inclusion criteria

- Adults aged **18 years or older**.
- Patients with a **self-reported history of linaclotide use** (current or past).
- Individuals diagnosed with **chronic idiopathic constipation (CIC)** or **irritable bowel syndrome with constipation (IBS-C)** for which linaclotide was prescribed.
- Participants able to **read and understand the questionnaire language**.
- Willingness to provide **informed consent** before participation.

Exclusion criteria

- **Individuals younger than 18 years.**
- **Patients who have never used linaclotide.**
- **Patients with constipation secondary to organic causes (e.g., colorectal cancer, intestinal obstruction, inflammatory bowel disease).**
- **Individuals with severe psychiatric illness or cognitive impairment affecting the ability to provide reliable responses.**
- **Incomplete or duplicate survey responses.**

The questionnaire included:

- Duration of use
- Reason for prescription
- Symptom response (improved, partial, no improvement)
- Reason for discontinuation (if any)
- Most bothersome gut symptom post-discontinuation
- Systemic symptoms after discontinuation (potential withdrawal signs)

Responses were analyzed descriptively and presented as percentages of total responses.

Results

1. Duration of Linaclotide Use

- **< 3 months:** 48% (41 responses)
- **3–6 months:** 15% (13 responses)
- **> 6 months:** 37% (32 responses)

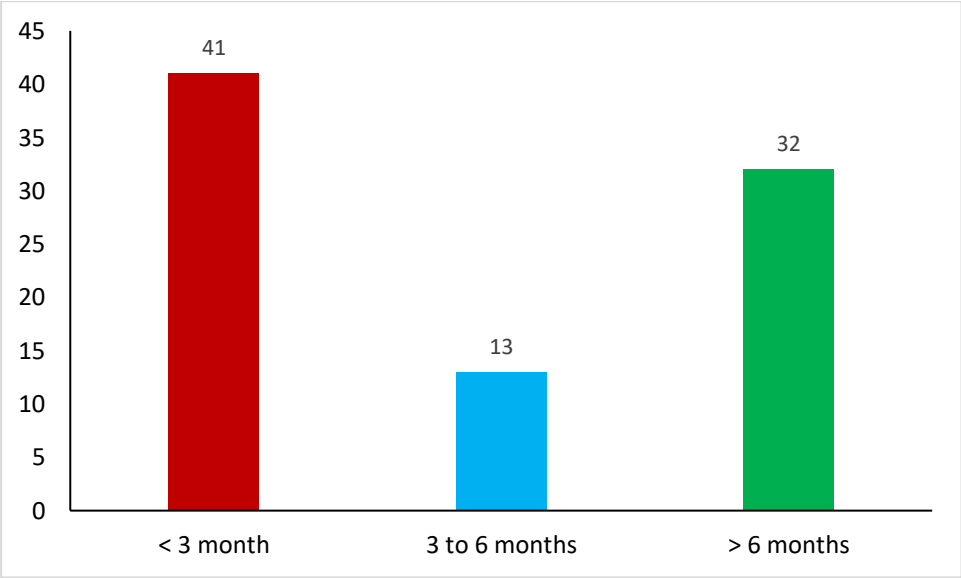

Figure 1 illustrates the duration of Linaclotide

2. Indication for Use

- **Chronic constipation:** 71% (55 responses)
- **Irritable bowel syndrome (IBS):** 29% (22 responses)

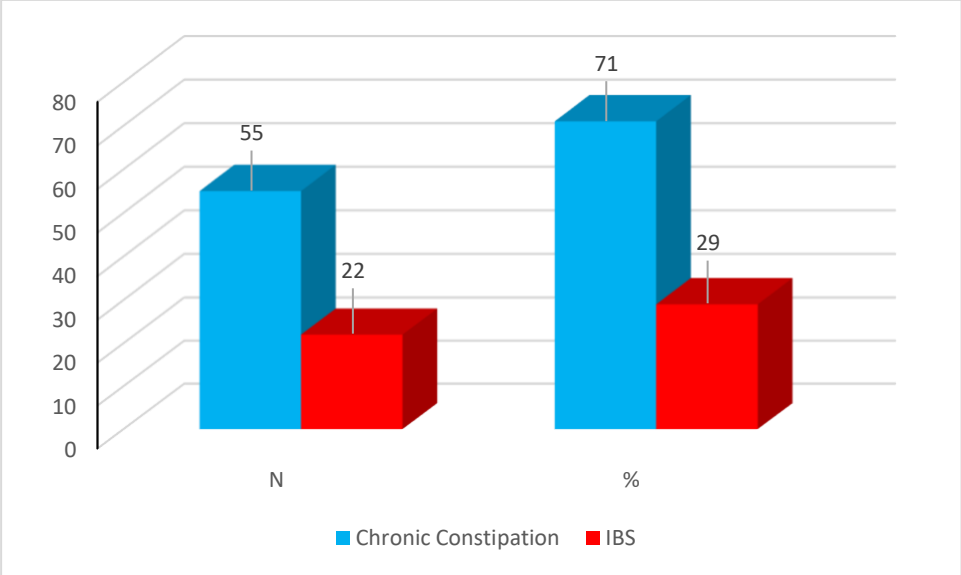

Figure 2 describes the reasons for the prescription of Linaclotide

3. Effectiveness

- **Symptoms improved completely:** 35% (25 responses)
- **Partial improvement:** 47% (34 responses)
- **No improvement:** 18% (13 responses)

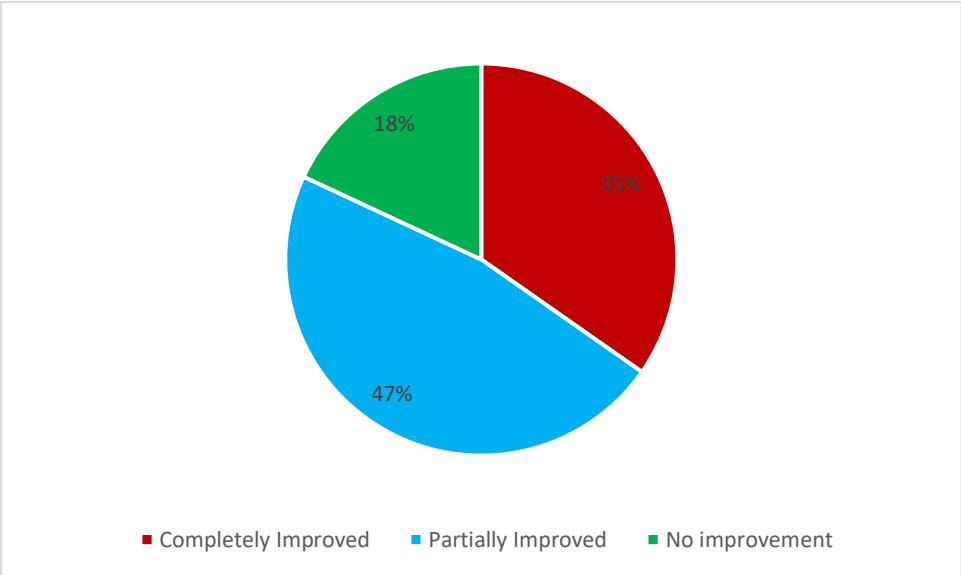

Figure 3 presents the recovery rate of patients

4. Reasons for Discontinuation

Among those who stopped the drug:

- **Side effects:** 49% (35 responses)
- **Cost/Insurance barriers:** 29% (21 responses)
- **Ineffectiveness:** 18% (13 responses)
- **Recovery/improvement:** 4% (3 responses)

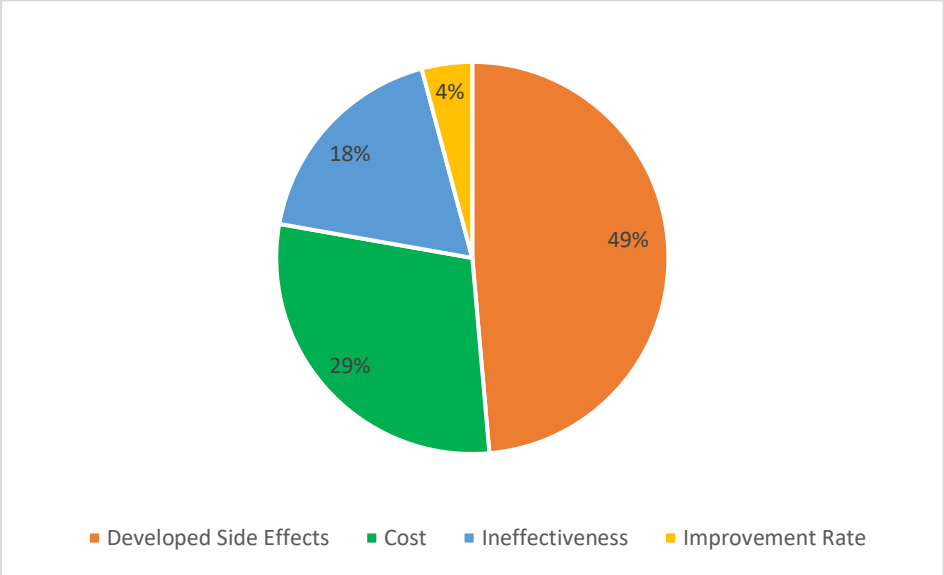

Figure 4 shows the leading causes of discontinuity

5. Post-discontinuation Gut Symptoms

- **Abdominal pain:** 46% (27 responses)
- **Constipation:** 34% (20 responses)
- **Bloating:** 20% (12 responses)

6. Systemic Withdrawal Symptoms

- **Headache:** 24% (12 responses)
- **Anxiety/Depression:** 24% (12 responses)
- **Fatigue:** 20% (10 responses)

- **Sweating:** 12% (6 responses)
- **Insomnia:** 6% (3 responses)
- **Chest tightness:** 6% (3 responses)
- **Palpitations:** 2% (1 responses)
- **Anger:** 4% (2 responses)

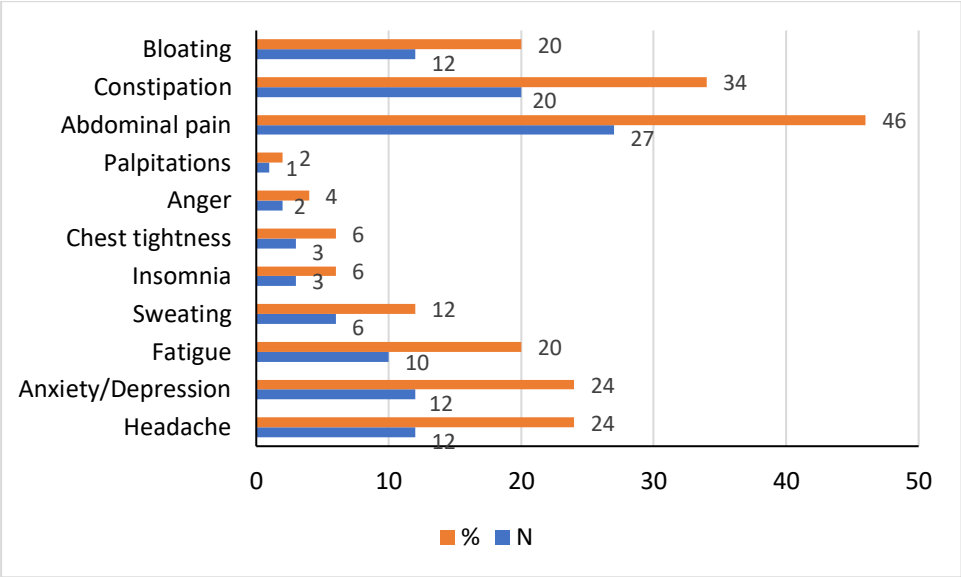

Figure 5 presents the reasons for post-withdrawal symptoms

Detailed responses to the survey questions from participants are described in Table I**.**

Table I. Survey Questions and Participant Responses

Survey Question	**Response Options**	**N= 86 (%)**
How long have you been using Linaclotide?	< 3 months	42 (48%)
	3–6 months	13 (15%)
	> 6 months	32 (37%)
Why were you prescribed Linaclotide?	Constipation	56 (72%)
	IBS	22 (28%)
Did your symptoms improve with Linaclotide?	Yes	26 (36%)

Table I. Survey Questions and Participant Responses

Survey Question	Response Options	N= 86 (%)
	No	13 (18%)
	Partially	34 (47%)
Why did you stop Linaclotide?	Developed side effects	36 (49%)
	Cost/Insurance issues	21 (29%)
	Not effective anymore	13 (18%)
	Got better	3 (4%)
Most bothersome gut symptom after stopping?	Abdominal pain	27 (46%)
	Constipation	20 (34%)
	Bloating	12 (20%)
Most bothersome withdrawal symptom?	Headache	12 (24%)
	Anxiety and Depression	12 (24%)
	Fatigue	10 (20%)
	Sweating	6 (12%)
	Insomnia	3 (6%)
	Chest tightness	3 (6%)
	Anger	2 (4%)
	Palpitations	1 (2%)

Discussion:

Efficacy and Tolerance:

This survey revealed that although 82% of patients experienced some improvement, only 35% saw complete symptom resolution. These findings are consistent with clinical trial data, where linaclotide has shown modest benefits in bowel frequency and abdominal symptoms[5].

However, partial improvement in nearly half of the users may indicate either suboptimal dosing, incomplete disease control, or patient expectations not fully met by current treatment protocols.

Side Effects and Treatment Discontinuation:

Nearly half of all users discontinued Linaclotide due to side effects, a figure that exceeds those reported in trials, where diarrhea is the most commonly cited adverse event (up to 20%)[6]. The high discontinuation rate emphasizes the need for better management strategies for tolerability such as dose titration, alternate-day dosing, or supportive care for diarrhea and cramping. Moreover, cost and insurance-related discontinuation (29%) underscores the financial burden many patients face when prescribed newer GI medications[7]. Clinicians should proactively address these issues by considering formulary alternatives or patient assistance programs.

Post-Discontinuation Gut and Systemic Symptoms:

Patients who stopped Linaclotide frequently reported rebound symptoms, including abdominal pain (46%), constipation (34%), and bloating (20%). These may reflect a recurrence of the underlying disorder, possibly exacerbated by withdrawal of prosecretory and motility-stimulating effects of the drug[8]. Additionally, non-GI symptoms such as headache, fatigue, anxiety, and sweating are typically not associated with Linaclotide pharmacology reported by up to 24% of respondents[9]. Although speculative, these symptoms may represent a withdrawal-like syndrome, potentially due to central nervous system adaptations, autonomic imbalance, or psychological stress from symptom recurrence. Further prospective studies are needed to confirm if these effects are causal, coincidental, or patient-perceived.

Limitations:

This survey has several limitations:

- Non-random, self-reported data introduces selection and recall bias.
- Lack of demographic or clinical background (e.g., age, comorbidities, concurrent meds).
- No objective measures of symptom severity or weight changes.

Despite these, the consistent trends in real-world user feedback offer valuable clinical clues.

Conclusion:

While linaclotide offers therapeutic benefit for many patients with constipation and IBS-C, side effects, cost, and rebound symptoms after discontinuation are significant challenges. Gastroenterologists should counsel patients on both the expected benefits and possible adverse events, and provide support during both initiation and discontinuation. Recognition of potential withdrawal-like symptoms and strategies for tapering or switching therapies may improve outcomes and adherence.

Conflict of interest:

The authors declare that there is no conflict of interest, neither financial nor personal.

Ethical Approval:

This is survey-based research. Therefore, there is no need for ethical approval. Only informed consent was obtained from the participants.

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