TREATING ADULT PATIENTS WITH IBS-D

Xifaxan®
rifaximin 550 mg tablets

Help your adult patients with IBS-D

FIND MULTISYMPTOM RELIEF WITH XIFAXAN

A SHORT-TERM THERAPY

2 weeks of treatment for up to 6 months of relief from abdominal pain and diarrhea[1-3,*]

Median of 10 weeks (range of 6 to 24 weeks).
Patients who experience recurrence can be retreated up to 2 times.
*See TARGET 1, 2, and 3 study data sections.

XIFAXAN was given a strong recommendation[†] to treat global IBS-D symptoms in the 2020 ACG Clinical Guideline on Managing IBS[4,‡]

[†]Based on a moderate quality of evidence.[§]

INDICATION

XIFAXAN® (rifaximin) 550 mg tablets are indicated for the treatment of irritable bowel syndrome with diarrhea (IBS-D) in adults.

IMPORTANT SAFETY INFORMATION

- XIFAXAN is contraindicated in patients with a hypersensitivity to rifaximin, rifamycin antimicrobial agents, or any of the components in XIFAXAN. Hypersensitivity reactions have included exfoliative dermatitis, angioneurotic edema, and anaphylaxis.

Please see additional Important Safety Information throughout and click here for full Prescribing Information.

ACG, American College of Gastroenterology; IBS-D, irritable bowel syndrome with diarrhea.
[†]Strength of recommendation: Strong=Most patients should receive the recommended course of action. Conditional=Many patients should have this recommended course of action, but different choices may be appropriate for some patients.[4]
[§]Summary of quality of evidence: High=The estimate of effect is unlikely to change with new data. Moderate=The estimate of effect is uncertain.[4]

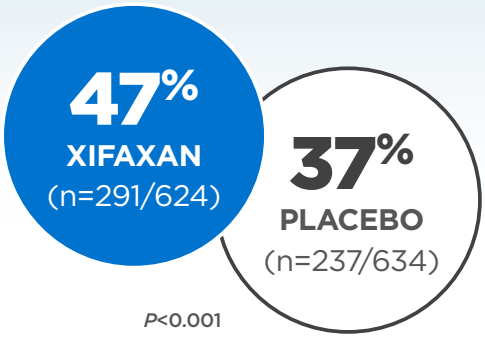
TARGET 1 & 2

In adults with IBS-D

2 weeks of XIFAXAN provided significant relief of abdominal pain and diarrhea[1,2,*]

Significant relief of abdominal pain and diarrhea

Percentage of responders during the month following 2 weeks of treatment (composite endpoint, pooled analysis)



No rescue medication was allowed in these clinical trials.

TARGET 1 and 2 study design

Two identical phase 3, randomized, double-blind, placebo-controlled trials were conducted over a 3-month period. A total of 1258 patients meeting Rome II criteria for IBS-D were to receive XIFAXAN 550 mg 3 times a day (n=624) or placebo (n=634) for 14 days.

Primary endpoint: Adequate relief of IBS-D signs and symptoms for at least 2 of 4 weeks during the month following 14 days of treatment, with adequate relief defined as a response of "yes" to the weekly Subject Global Assessment (SGA) question: "In regards to your IBS-D symptoms, compared to the way you felt before you started study medication, have you, in the past 7 days, had adequate relief of your IBS-D symptoms? [Yes/No]."

Primary endpoint results: Adequate relief of IBS-D signs and symptoms was experienced during the first month in:

- **TARGET 1: 41% (n=126/309) of XIFAXAN-treated patients vs 31% (n=98/314) of placebo-treated patients (*P*<0.05)**
- **TARGET 2: 41% (n=128/315) of XIFAXAN-treated patients vs 32% (n=103/320) of placebo-treated patients (*P*<0.05)**

Composite endpoint: Responder defined by a ≥30% decrease from baseline in abdominal pain, with a weekly mean stool consistency score of <4 (loose stool) for ≥2 weeks during the month following 2 weeks of treatment.

*Patients who experience recurrence can be retreated up to 2 times.[1]

IMPORTANT SAFETY INFORMATION *(continued)*

- *Clostridium difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including XIFAXAN, and may range in severity from mild diarrhea to fatal colitis. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued.
- There is an increased systemic exposure in patients with severe (Child-Pugh Class C) hepatic impairment. Caution should be exercised when administering XIFAXAN to these patients.

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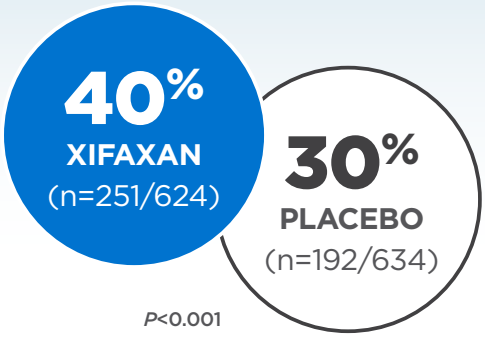
TARGET 1 & 2

XIFAXAN provided relief of bloating and urgency[2,5]

Percentage of **BLOATING** responders based on weekly responses in a pooled analysis of TARGET 1 and 2[2]

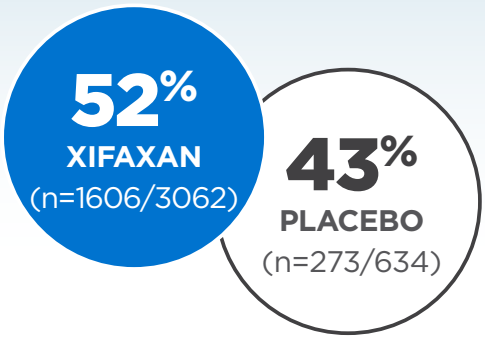


P<0.001

Key secondary endpoint: The proportion of patients who achieved adequate relief of IBS-D–related bloating (ie, responders) for at least 2 of 4 weeks during the month following 14 days of treatment.[2]

A bloating responder was defined as a patient who responded "yes" to the weekly question: "In regards to your IBS-D symptom of bloating, compared to the way you felt before you started study medication, have you, in the past 7 days, had adequate relief of your IBS-D symptom of bloating? [Yes/No]." Responses were given during the first 4 weeks of the treatment-free period following 2 weeks of active treatment (primary evaluation period).[2]

Percentage of **URGENCY** responders based on weekly responses in a pooled post hoc analysis of TARGET 1, 2, and 3[5]



Post hoc analysis endpoint: Change from baseline to each week during the 12-week study duration for sense of urgency.[5]

An urgency responder was defined as a patient with ≥30% decrease from baseline in the percentage of days with urgency for at least 2 of 4 weeks during the month following 14 days of treatment.[5] Urgency was determined based on patient response of "yes" to the daily question: "Have you felt or experienced a sense of urgency today (past 24 hours)? [Yes/No]."[6-8]

Stool frequency (number of bowel movements per day) was assessed as a secondary endpoint, but there was no meaningful difference between XIFAXAN and placebo.[6-9]

IMPORTANT SAFETY INFORMATION (*continued*)

- Caution should be exercised when concomitant use of XIFAXAN and P-glycoprotein (P-gp) and/or OATPs inhibitors is needed. Concomitant administration of cyclosporine, an inhibitor of P-gp and OATPs, significantly increased the systemic exposure of rifaximin. In patients with hepatic impairment, a potential additive effect of reduced metabolism and concomitant P-gp inhibitors may further increase the systemic exposure to rifaximin.

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TARGET 3

In patients who experienced IBS-D symptom recurrence, repeat treatment with XIFAXAN…

Open-label phase
(N=2438)

44% **XIFAXAN 1st treatment responders**
(n=1074/2438)

36% of open-label responders (n=382/1074) had no reported symptom recurrence within 6 months

36% of open-label responders did not experience relapse during the 18-week observation phase before being withdrawn from the trial for any reason

Symptom recurrence 64%
(n=692/1074)

10 weeks
Median time to recurrence during treatment-free observation
(range of 6 to 24 weeks)

Double-blind repeat treatment
(n=636 randomized)

Primary endpoint

38% experienced significant improvement in stool consistency and abdominal pain
(n=125/328, *P*<0.05 **vs 31.5% for placebo, n=97/308**)

…significantly improved their abdominal pain and diarrhea vs placebo[1,3]

TARGET 3 study design

This trial included an open-label phase followed by a randomized, placebo-controlled phase, with the aim of determining the efficacy and safety of repeat treatment with XIFAXAN in patients with IBS-D who had responded to a 2-week course of XIFAXAN and subsequently experienced IBS-D symptom recurrence.

A responder was defined as a patient experiencing a ≥30% improvement from baseline in the weekly average abdominal pain score (based on daily self-reports) and a ≥50% reduction in the number of days in a week with a daily stool consistency of Bristol Stool Form Scale type 6 or 7 (mushy or watery) for ≥2 of the 4 weeks after treatment.

Recurrence was defined as the return of abdominal pain or lack of stool consistency for 3 weeks of a rolling 4-week period.

Primary endpoint: The proportion of patients who were responders to repeat treatment in both IBS-D–related abdominal pain and stool consistency during the 4 weeks following the first repeat treatment course.

IMPORTANT SAFETY INFORMATION (*continued*)

- In clinical studies, the most common adverse reactions for XIFAXAN in IBS-D (≥2%) were nausea (3%) and ALT increased (2%).

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XIFAXAN is the #1 prescribed medication approved for IBS-D[10,*]

In adults with IBS-D

XIFAXAN has a well-established safety profile[1]

Side effects at rates similar to placebo

Adverse event	TARGET 1 and 2		TARGET 3	
	XIFAXAN (n=624)	Placebo (n=634)	XIFAXAN (n=328)	Placebo (n=308)
Nausea	3%	2%	2%	1%
ALT increased†	NA	NA	2%	1%

- Constipation was observed in 0.3%—0.6% of patients treated with XIFAXAN[3,11]
- Did not cause any clinically relevant antibiotic resistance after 1 to 3 treatment cycles[12]
  - *Clostridium difficile*-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including XIFAXAN, and may range in severity from mild diarrhea to fatal colitis. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued.[1]

XIFAXAN is the only FDA-approved, nonsystemic IBS-D treatment that alters the microbiome[1,13]

- Less than 0.4% is absorbed from the GI tract[1]
- There is an increased systemic exposure in patients with severe hepatic impairment; caution should be exercised when administering XIFAXAN to these patients[1]

Mechanism of action is unknown and does not imply clinical efficacy

XIFAXAN is a short-term therapy for lasting relief[1-3,‡]

rfx

One 550-mg tablet 3 times a day with or without food[1]

2 weeks of treatment, not continuous, daily prescription medication[1]

2x

Patients who complete initial treatment can be retreated **up to 2 times** for recurrence[1]

ALT, alanine aminotransferase; NA, not available.
*Based on aggregated total of all prescribers as of June 2023.
†Most of the events of ALT increase were due to transient increases that resolved over time and were not temporally associated with study drug treatment.[8]
‡Median of 10 weeks (range of 6 to 24 weeks).[1-3]
§The ICD-10 code and all other patient-access–related information are provided for informational purposes only. It is the treating physician's responsibility to determine the proper diagnosis, treatment, and applicable ICD-10 code. Salix Pharmaceuticals does not guarantee coverage or reimbursement for the product.

IMPORTANT SAFETY INFORMATION (*continued*)

- INR changes have been reported in patients receiving rifaximin and warfarin concomitantly. Monitor INR and prothrombin time. Dose adjustment of warfarin may be required.

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XIFAXAN has a straightforward prior authorization (PA) process

Branded PAs are common

Initiate a pull-through protocol to proactively submit PAs to ensure timely and efficient outcomes

When a PA is required, complete the following steps:

STEP 1 — Provide patient and insurance information

STEP 2 — Include prescriber information
(eg, practice name, your name, NPI #, DEA/License #)

STEP 3 — Provide accurate information, including:

- **Age, diagnosis, dosing**
  Age of patient, IBS-D, XIFAXAN 550 mg, three times a day/14 days, 42 tablets[1]
- **ICD-10 code for IBS-D**[14,*]
  K58.0 *Irritable bowel syndrome with diarrhea*
- **Previous therapies tried and failed**
  (eg, antidiarrheals, antispasmodics, loperamide, Rx SSRIs, TCAs)
- **Rationale for prescribing XIFAXAN**

STEP 4 — Remember your signature and the date

Remember to check for accurate and complete prescribing in EHR/EMR and on Rx, and consider XIFAXAN 550 mg for your system's EHR preference list or favorites. For PA support for XIFAXAN, go to **covermymeds.com** or call **1-866-452-5017**.

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Access additional resources

XIFAXAN Copay Card

IBS-D clinical tools and educational resources

IMPORTANT SAFETY INFORMATION *(continued)*

- XIFAXAN may cause fetal harm. Advise pregnant women of the potential risk to a fetus.

To report SUSPECTED ADVERSE REACTIONS, contact Salix Pharmaceuticals at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see additional Important Safety Information throughout and click here for full Prescribing Information.

References: 1. XIFAXAN [prescribing information]. Bridgewater, NJ: Salix Pharmaceuticals. **2.** Pimentel M et al. *N Engl J Med*. 2011;364(1):22-32. **3.** Lembo A et al. *Gastroenterology*. 2016;151(6):1113-1121. **4.** Lacy BE et al. *Am J Gastroenterol*. 2021;116(1):17-44. **5.** Lacy BE et al. *Clin Ther*. 2023;45(3):198-209. **6.** Data on file. Target 1 CSR May 2010. Salix Pharmaceuticals, Bridgewater, NJ. **7.** Data on file. Target 2 CSR May 2010. Salix Pharmaceuticals, Bridgewater, NJ. **8.** Data on file. Target 3 CSR August 2014. Salix Pharmaceuticals, Bridgewater, NJ. **9.** Data on file. Integrated Summary of Efficacy. Salix Pharmaceuticals, Bridgewater, NJ. **10.** Data on file. LAAD June 2023. Salix Pharmaceuticals, Bridgewater, NJ. **11.** Schoenfeld P et al. *Aliment Pharmacol Ther*. 2014;39(10):1161-1168. **12.** Pimentel M et al. *Dig Dis Sci*. 2017;62(9):2455-2463. **13.** Rezaie A et al. *Am J Gastroenterol*. 2019;114(12):1886-1893. **14.** CMS. 2024 ICD-10-CM. Accessed July 17, 2024. https://www.cms.gov/medicare/coding-billing/icd-10-codes/2024-icd-10-cm

Salix Pharmaceuticals

Salix Pharmaceuticals, 400 Somerset Corporate Blvd., Bridgewater, NJ 08807

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