Rifaximin and Eluxadoline Utilization for Irritable Bowel Syndrome With Diarrhea (IBS-D) in the United States and Budget Impact Analysis of Switching From Eluxadoline to Rifaximin

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BACKGROUND

- Irritable bowel syndrome (IBS) is defined as recurrent abdominal pain, on average, at least 1 day/week in the last 3 months, associated with 2 or more of the following criteria[1,2]:
  - Related to defecation
  - Associated with a change in the frequency of stool
  - Associated with a change in the form (appearance) of stool
- Diarrhea-predominant irritable bowel syndrome (IBS-D) affects approximately 40% of patients with IBS.[1]
- Accumulating evidence suggests that altered gut microbiota may contribute to IBS-D symptoms.[3-8]
- Rifaximin (Xifaxan®) and eluxadoline (Viberzi®) are 2 of the 3 agents indicated for the treatment of IBS-D in the United States (US).
  - Rifaximin is a non-aminoglycoside semi-synthetic, non-systemic antibiotic derived from rifamycin, with a recommended dosing of one 550 mg tablet 3 times a day for 14 days.[9]
  - Eluxadoline is a mu-opioid receptor agonist with 100 mg twice-daily recommended dosing (eluxadoline prescribing information).[10] In patients who are unable to tolerate the 100 mg dose, are receiving concomitant OATP1B1 inhibitors, or have mild or moderate hepatic impairment, a 75 mg twice-daily dose is recommended.
  - Rifaximin patients can receive up to 3 courses of treatment vs potentially chronic treatment with eluxadoline.

OBJECTIVE

- To evaluate the utilization of rifaximin and eluxadoline using a claims analysis and estimate the budget impact of switching from eluxadoline to rifaximin from a US payer perspective.

METHODS

Real-world utilization analysis

- A retrospective database analysis was conducted utilizing the Symphony Health's Integrated Dataverse® database from October 2011 through September 2016.
- Nine separate monthly cohorts, from January 2016 to September 2016, were identified; patients in each cohort were required to have a diagnosis for IBS-D based on International Statistical Classification of Diseases, 10th Revision (ICD-10-CM) code K58.0 in a healthcare professional's (HCP) office, and filled a prescription for rifaximin or eluxadoline within the same month of the diagnosis.
- The number of prescriptions and HCP visits were tracked for 12 months following the diagnosis month.
- Patients were excluded if they:
  - Were diagnosed with hepatic encephalopathy (HE), cirrhosis, or any other non-gastrointestinal (GI) diagnosis from October 2011 until the end of 12-month cohort tracking window, in a hospital or HCP's office
  - Filled a prescription for the same drug as their treatment (rifaximin or eluxadoline) prior to cohort start date (October 2013 to cohort start date)
  - Filled a prescription for a competitor product from the cohort start month to end of the 12-month tracking period. Competitor products included eluxadoline (for rifaximin), rifaximin (for eluxadoline), alosetron, antispasmodics, and antidiarrheals
- The average annual number of prescriptions per patient was calculated by dividing the total prescriptions for all cohorts by the total number of patients for all cohorts.
- The average annual number of HCP visits per patient was calculated by dividing the total HCP visits for all cohorts by the total number of patients for all cohorts.

Budget impact analysis

Model overview

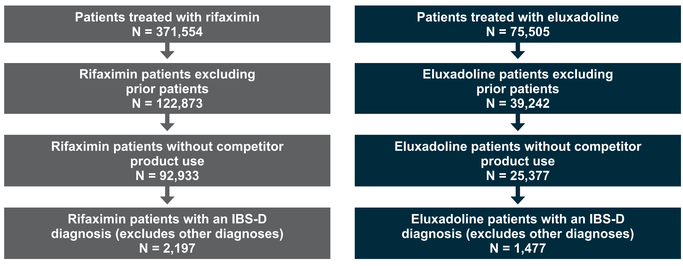
- A Microsoft® Excel-based model was developed to estimate the annual budget impact of switching from eluxadoline to rifaximin for a hypothetical 1,000,000-member US health plan for the treatment of patients with IBS-D.
- The number of patients receiving eluxadoline is determined by multiplying the plan's covered lives by the IBS-D prevalence (3.3%),[11] and the percentage of IBS-D diagnosed patients receiving eluxadoline (4%).[12]
- Annual per-patient costs for rifaximin and eluxadoline are calculated based on the annual number of prescriptions from the real-world utilization analysis and wholesale acquisition costs, obtained from Red Book.[13]
- Rifaximin: Forty-two 550 mg tablets = $1,358.44 (1 prescription for a 14-day course)
- Eluxadoline: Sixty 75 mg or 100 mg tablets = $1,046.4 (1 prescription per month)
- The annual pharmacy cost to the plan is calculated by switching all eluxadoline patients to rifaximin.
- The difference is calculated as the total budget impact. The budget impact in terms of cost per-member per-month (PMPM) is also calculated based on plan size.

RESULTS

Real-world utilization analysis

- A total of 2,197 rifaximin patients and 1,477 eluxadoline patients met all the criteria for inclusion (**Figure 1**).
- The number of prescriptions in a year were 1.4 for rifaximin and 3.7 for eluxadoline.
- Patients on rifaximin and eluxadoline had 1.6 and 1.9 HCP visits annually, respectively.

Figure 1. Sample Selection Diagram



Key: IBS-D – irritable bowel syndrome with diarrhea

Budget impact analysis

- The annual per-patient cost for rifaximin ranged from $1,358 (1 course) to $4,075 (3 courses). Eluxadoline costs ranged from $1,046 (1 month) to $12,557 (12 months).
- Based on the average duration of therapy of 1.4 courses of rifaximin vs 3.7 months of eluxadoline use from the real-world utilization analysis, annual costs were $1,970 lower for a patient treated with rifaximin.
  - For an estimated number of 1,320 patients with IBS-D using eluxadoline, the switch to rifaximin resulted in savings of $2,600,220 ($0.22 PMPM), based on the utilization patterns from the claims analysis.
- In a sensitivity analysis, where the duration varied for both treatments simultaneously, treatment with rifaximin resulted in a range from $3,029 in additional costs (3 courses of rifaximin vs 1 month of eluxadoline) to $11,198 in cost savings (1 course of rifaximin vs 12 months of eluxadoline) compared to eluxadoline (**Figure 2**).
  - The budget impact analysis results ranged from a savings of ~$15 million ($1.23 PMPM) to an additional cost of ~$4 million (–$0.33 PMPM) for the plan (**Figure 3**).
- In additional sensitivity analyses, where the prevalence of IBS-D varied between 0.7% and 14.1%, the estimated budget savings range for the plan was $553,847 to $2,366,437 ($0.05–$0.93 in PMPM) (**Table 1**).

Figure 2. Projected Net Cost per Treated Patient (Eluxadoline–Rifaximin) Based on Treatment Duration

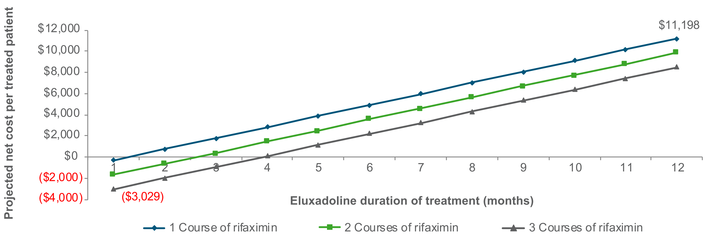


Figure 3. Projected Budget Impact of Switching From Eluxadoline to Rifaximin Based on Treatment Duration

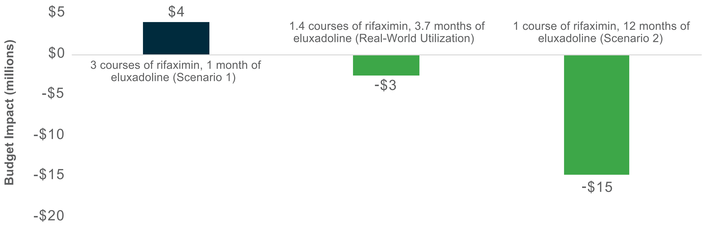


Table 1. Base Case Results and Results From Prevalence Sensitivity Analyses

Prevalence[a]	Total budget			PMPM		
	Rifaximin	Eluxadoline	Net	Rifaximin	Eluxadoline	Net
3.3% (base case)	$2,510,397	$5,110,618	–$2,600,220	$0.21	$0.43	–$0.22
0.7%[b]	$534,715	$1,088,562	–$553,847	$0.04	$0.09	–$0.05
14.1%[c]	$10,726,242	$21,836,275	–$11,110,033	$0.89	$1.82	–$0.93
3.0%[d]	$2,284,690	$4,651,127	–$2,366,437	$0.19	$0.39	–$0.20

[a] Base case value and ranges for prevalence estimates are based on Hungin et al 2005.[11]
[b] Includes medically diagnosed and IBS-D only. Medically diagnosed prevalence was multiplied by 21.3%.
[c] Includes medically diagnosed and not medically diagnosed.
[d] Includes medically diagnosed and not medically diagnosed for IBS-D only. Medically diagnosed and not medically diagnosed prevalence was multiplied by 21.3%.
Key: IBS-D – irritable bowel syndrome with diarrhea; PMPM – per-member per-month.

Limitations

- There was a steep drop in sample size in the real-world utilization analysis after requiring patients to have an IBS-D diagnosis within the same month of the prescription.
  - This could be explained by lack of proper IBS-D coding by HCPs.[11]
- To address the heterogeneity between studies regarding IBS-D prevalence, sensitivity analyses were conducted.
- The budget impact analysis addressed the pharmacy aspect and did not include other resource utilization components, such as HCP visits given the claims analysis showed similar frequency for rifaximin and eluxadoline.

CONCLUSION

- Due to the short duration of rifaximin therapy (14-day course, which may be repeated twice) vs continuous dosing of eluxadoline, rifaximin is the economically favorable therapy for IBS-D based on real-world claims budget projections.

REFERENCES

1. Lacy BE, Mearin F, Chang L, et al. Bowel disorders. *Gastroenterology*. 2016a;150:1393-1407. **2.** Lacy BE, Patel NK. Rome criteria and a diagnostic approach to irritable bowel syndrome. *J Clin Med*. 2017 Oct 26;6(11). pii: E99. **3.** Lacy BE, Moreau JC. Diarrhea-predominant irritable bowel syndrome: diagnosis, etiology, and new treatment considerations. *J Am Assoc Nurse Pract*. 2016b;28(7):393-404. **4.** Chey WD, Kurlander J, Eswaran S. Irritable bowel syndrome: a clinical review. *JAMA*. 2015;313(9):949-958. **5.** Zhuang X, Xiong L, Li L, et al. Alterations of gut microbiota in patients with irritable bowel syndrome: a systematic review and meta-analysis. *J Gastroenterol Hepatol*. 2017;32(1):28-38. **6.** Kennedy PJ, Cryan JF, Dinan TG, et al. Irritable bowel syndrome: a microbiome-gut-brain axis disorder? *World J Gastroenterol*. 2014;20(39):14105-14125. **7.** Rajilić-Stojanović M, Biagi E, Heilig HG, et al. Global and deep molecular analysis of microbiota signatures in fecal samples from patients with irritable bowel syndrome. *Gastroenterology*. 2011;141(5):1792-1801. **8.** Raskov H, Burcharth J, Pommergaard H-C, et al. Irritable bowel syndrome, the microbiota and the gut-brain axis. *Gut Microbes*. 2016;7(5):365-383. **9.** XIFAXAN (rifaximin) tablets, for oral use [prescribing information]. Bridgewater, NJ: Salix Pharmaceuticals, a division of Valeant Pharmaceuticals North America LLC; January 2018. **10.** VIBERZI (eluxadoline) tablets, for oral use, CIV [prescribing information]. Irvine, CA: Allergan USA, Inc.; November 2017. **11.** Hungin AP, Chang L, Locke GR, et al. Irritable bowel syndrome in the United States: prevalence, symptom patterns and impact. *Aliment Pharmacol Ther*. 2005 Jun 1;21(11):1365-1375. **12.** Data on file. Valeant Pharmaceuticals, Inc. October 30, 2017. **13.** Truven Health Analytics, Inc. Red Book Online®, Micromedex 2.0, Accessed January 8, 2018.

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