Supplemental Table 1. Commonly Reported TEAEs (\geq 5% of Patients in Either Group or \geq 3% of Patients With a GI Disorder) Categorized by Male Sex

Patients with ≥1 TEAE 11 (45.8) 5 (35.7) 16 (42.1) Gastrointestinal disorders 5 (20.8) 3 (21.4) 8 (21.1) Diarrhea 2 (8.3) 1 (7.1) 3 (7.9) Abdominal pain upper 1 (4.2) 1 (7.1) 2 (5.3) Dyspepsia 2 (8.3) 0 (0.0) 2 (5.3) Voniting 1 (4.2) 1 (7.1) 2 (5.3) Abdominal distension 1 (4.2) 0 (0.0) 1 (2.6) Abdominal pain 1 (4.2) 0 (0.0) 1 (2.6) Abdominal tenderness 1 (4.2) 0 (0.0) 1 (2.6) Fecaloma 1 (4.2) 0 (0.0) 1 (2.6) Fecaloma 1 (4.2) 0 (0.0) 1 (2.6) Nausea 0 (0.0) 1 (7.1) 1 (2.6) Injury, poisoning, and procedural complications 2 (8.3) 2 (14.3) 4 (10.5) Blood uric acid decreased 2 (8.3) 2 (14.3) 4 (10.5) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Blood phosphorus increased 0 (0.0) 1	System Organ Class (Preferred Term, MedDRA 19.1)	Lubiprostone 12 mcg BID (n=24), n (%)	Lubiprostone 24 mcg BID (n=14), n (%)	Total (N=38), N (%)
Diarrhea 2 (8.3) 1 (7.1) 3 (7.9) Abdominal pain upper 1 (4.2) 1 (7.1) 2 (5.3) Dyspepsia 2 (8.3) 0 (0.0) 2 (5.3) Vomiting 1 (4.2) 1 (7.1) 2 (5.3) Vomiting 1 (4.2) 1 (7.1) 2 (5.3) Vomiting 1 (4.2) 0 (0.0) 1 (2.6) Abdominal distension 1 (4.2) 0 (0.0) 1 (2.6) Abdominal tenderness 1 (4.2) 0 (0.0) 1 (2.6) Fecaloma 1 (4.2) 0 (0.0) 1 (2.6) Flatulence 1 (4.2) 0 (0.0) 1 (2.6) Nausea 0 (0.0) 1 (7.1) 1 (2.6) Injury, poisoning, and procedural complications 2 (8.3) 1 (7.1) 3 (7.9) Thermal burn 0 (0.0) 1 (7.1) 1 (2.6) Investigations 2 (8.3) 2 (14.3) 4 (10.5) Blood uric acid decreased 2 (8.3) 0 (0.0) 2 (5.3) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) <tr< td=""><td>Patients with ≥1 TEAE</td><td>11 (45.8)</td><td>5 (35.7)</td><td>16 (42.1)</td></tr<>	Patients with ≥1 TEAE	11 (45.8)	5 (35.7)	16 (42.1)
Abdominal pain upper 1 (4.2) 1 (7.1) 2 (5.3) Dyspepsia 2 (8.3) 0 (0.0) 2 (5.3) Vomiting 1 (4.2) 1 (7.1) 2 (5.3) Abdominal distension 1 (4.2) 0 (0.0) 1 (2.6) Abdominal pain 1 (4.2) 0 (0.0) 1 (2.6) Abdominal tenderness 1 (4.2) 0 (0.0) 1 (2.6) Abdominal tenderness 1 (4.2) 0 (0.0) 1 (2.6) Fecaloma 1 (4.2) 0 (0.0) 1 (2.6) Flatulence 1 (4.2) 0 (0.0) 1 (2.6) Nausea 0 (0.0) 1 (7.1) 1 (2.6) Injury, poisoning, and procedural complications 2 (8.3) 1 (7.1) 1 (2.6) Investigations 2 (8.3) 2 (14.3) 4 (10.5) Blood uric acid decreased 2 (8.3) 0 (0.0) 2 (5.3) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Heart rate irregular 0 (0.0) 1 (7.1) 1 (2.6) Blood phosphorus increased 0 (0.0) 1 (7.1) <td>Gastrointestinal disorders</td> <td>5 (20.8)</td> <td>3 (21.4)</td> <td>8 (21.1)</td>	Gastrointestinal disorders	5 (20.8)	3 (21.4)	8 (21.1)
Dyspepsia 2 (8.3) 0 (0.0) 2 (5.3) Vomiting 1 (4.2) 1 (7.1) 2 (5.3) Abdominal distension 1 (4.2) 0 (0.0) 1 (2.6) Abdominal pain 1 (4.2) 0 (0.0) 1 (2.6) Abdominal tenderness 1 (4.2) 0 (0.0) 1 (2.6) Abdominal tenderness 1 (4.2) 0 (0.0) 1 (2.6) Fecaloma 1 (4.2) 0 (0.0) 1 (2.6) Flatulence 1 (4.2) 0 (0.0) 1 (2.6) Nausea 0 (0.0) 1 (7.1) 1 (2.6) Injury, poisoning, and procedural complications 2 (8.3) 1 (7.1) 1 (2.6) Investigations 2 (8.3) 2 (14.3) 4 (10.5) Blood uric acid decreased 2 (8.3) 0 (0.0) 2 (5.3) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Heart rate irregular 0 (0.0) 1 (7.1) 1 (2.6) Blood phosphorus increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and connective tissue disorders 0 (0.0) </td <td>Diarrhea</td> <td>2 (8.3)</td> <td>1 (7.1)</td> <td>3 (7.9)</td>	Diarrhea	2 (8.3)	1 (7.1)	3 (7.9)
Vomiting 1 (4.2) 1 (7.1) 2 (5.3) Abdominal distension 1 (4.2) 0 (0.0) 1 (2.6) Abdominal pain 1 (4.2) 0 (0.0) 1 (2.6) Abdominal tenderness 1 (4.2) 0 (0.0) 1 (2.6) Abdominal tenderness 1 (4.2) 0 (0.0) 1 (2.6) Fecaloma 1 (4.2) 0 (0.0) 1 (2.6) Flatulence 1 (4.2) 0 (0.0) 1 (2.6) Nausea 0 (0.0) 1 (7.1) 1 (2.6) Injury, poisoning, and procedural complications 2 (8.3) 1 (7.1) 3 (7.9) Thermal burn 0 (0.0) 1 (7.1) 1 (2.6) Investigations 2 (8.3) 2 (14.3) 4 (10.5) Blood uric acid decreased 2 (8.3) 0 (0.0) 2 (5.3) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Heart rate irregular 0 (0.0) 1 (7.1) 1 (2.6) Specific gravity urine increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and connective tissue disorders	Abdominal pain upper	1 (4.2)	1 (7.1)	2 (5.3)
Abdominal distension 1 (4.2) 0 (0.0) 1 (2.6) Abdominal pain 1 (4.2) 0 (0.0) 1 (2.6) Abdominal tenderness 1 (4.2) 0 (0.0) 1 (2.6) Fecaloma 1 (4.2) 0 (0.0) 1 (2.6) Fecaloma 1 (4.2) 0 (0.0) 1 (2.6) Flatulence 1 (4.2) 0 (0.0) 1 (2.6) Nausea 0 (0.0) 1 (7.1) 1 (2.6) Injury, poisoning, and procedural complications 2 (8.3) 1 (7.1) 1 (2.6) Investigations 2 (8.3) 2 (14.3) 4 (10.5) Blood uric acid decreased 2 (8.3) 0 (0.0) 2 (5.3) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Heart rate irregular 0 (0.0) 1 (7.1) 1 (2.6) Blood phosphorus increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and corners 0 (0.0) 1 (7.1) 1 (2.6) Neck pain 0 (0.0) 1 (7.1) 1 (2.6) Renal and urinary disorders 0 (0.0) <	Dyspepsia	2 (8.3)	0 (0.0)	2 (5.3)
Abdominal pain 1 (4.2) 0 (0.0) 1 (2.6) Abdominal tenderness 1 (4.2) 0 (0.0) 1 (2.6) Fecaloma 1 (4.2) 0 (0.0) 1 (2.6) Flatulence 1 (4.2) 0 (0.0) 1 (2.6) Nausea 0 (0.0) 1 (2.6) 1 (2.6) Nausea 0 (0.0) 1 (7.1) 1 (2.6) Injury, poisoning, and procedural complications 2 (8.3) 1 (7.1) 3 (7.9) Thermal burn 0 (0.0) 1 (7.1) 1 (2.6) Investigations 2 (8.3) 2 (14.3) 4 (10.5) Blood uric acid decreased 2 (8.3) 0 (0.0) 2 (5.3) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Heart rate irregular 0 (0.0) 1 (7.1) 1 (2.6) Specific gravity urine increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and connective tissue disorders 1 (4.2) 1 (7.1) 2 (5.3) Neck pain 0 (0.0) 1 (7.1) 1 (2.6)	Vomiting	1 (4.2)	1 (7.1)	2 (5.3)
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Fecaloma 1 (4.2) 0 (0.0) 1 (2.6) Flatulence 1 (4.2) 0 (0.0) 1 (2.6) Nausea 0 (0.0) 1 (7.1) 1 (2.6) Injury, poisoning, and procedural complications 2 (8.3) 1 (7.1) 3 (7.9) Thermal burn 0 (0.0) 1 (7.1) 1 (2.6) Investigations 2 (8.3) 2 (14.3) 4 (10.5) Blood uric acid decreased 2 (8.3) 0 (0.0) 2 (5.3) Blood iron decreased 2 (8.3) 0 (0.0) 2 (5.3) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Heart rate irregular 0 (0.0) 1 (7.1) 1 (2.6) Specific gravity urine increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and connective tissue disorders 1 (4.2) 1 (7.1) 2 (5.3) Neck pain 0 (0.0) 1 (7.1) 1 (2.6)	Abdominal pain	1 (4.2)	0 (0.0)	1 (2.6)
Flatulence 1 (4.2) 0 (0.0) 1 (2.6) Nausea 0 (0.0) 1 (7.1) 1 (2.6) Injury, poisoning, and procedural complications 2 (8.3) 1 (7.1) 3 (7.9) Thermal burn 0 (0.0) 1 (7.1) 1 (2.6) Investigations 2 (8.3) 2 (14.3) 4 (10.5) Blood uric acid decreased 2 (8.3) 2 (14.3) 4 (10.5) Blood uric acid decreased 2 (8.3) 0 (0.0) 2 (5.3) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Blood phosphorus increased 0 (0.0) 1 (7.1) 1 (2.6) Blood phosphorus increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and connective tissue disorders 1 (4.2) 1 (7.1) 2 (5.3) Neck pain 0 (0.0) 1 (7.1) 1 (2.6) Renal and urinary disorders 0 (0.0) 1 (7.1) 1 (2.6)	Abdominal tenderness	1 (4.2)	0 (0.0)	1 (2.6)
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Injury, poisoning, and procedural complications 2 (8.3) 1 (7.1) 3 (7.9) Thermal burn 0 (0.0) 1 (7.1) 1 (2.6) Investigations 2 (8.3) 2 (14.3) 4 (10.5) Blood uric acid decreased 2 (8.3) 0 (0.0) 2 (5.3) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Blood phosphorus increased 0 (0.0) 1 (7.1) 1 (2.6) Heart rate irregular 0 (0.0) 1 (7.1) 1 (2.6) Specific gravity urine increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and connective tissue disorders 1 (4.2) 1 (7.1) 2 (5.3) Neck pain 0 (0.0) 1 (7.1) 1 (2.6)	Flatulence	1 (4.2)	0 (0.0)	1 (2.6)
procedural complications 0 (0.0) 1 (7.1) 1 (2.6) Investigations 2 (8.3) 2 (14.3) 4 (10.5) Blood uric acid decreased 2 (8.3) 0 (0.0) 2 (5.3) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Blood phosphorus increased 0 (0.0) 1 (7.1) 1 (2.6) Heart rate irregular 0 (0.0) 1 (7.1) 1 (2.6) Specific gravity urine increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and connective tissue disorders 1 (4.2) 1 (7.1) 2 (5.3) Neck pain 0 (0.0) 1 (7.1) 1 (2.6)	Nausea	0 (0.0)	1 (7.1)	1 (2.6)
Investigations 2 (8.3) 2 (14.3) 4 (10.5) Blood uric acid decreased 2 (8.3) 0 (0.0) 2 (5.3) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Blood phosphorus increased 0 (0.0) 1 (7.1) 1 (2.6) Heart rate irregular 0 (0.0) 1 (7.1) 1 (2.6) Specific gravity urine increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and connective tissue disorders 1 (4.2) 1 (7.1) 2 (5.3) Neck pain 0 (0.0) 1 (7.1) 1 (2.6)		2 (8.3)	1 (7.1)	3 (7.9)
Blood uric acid decreased 2 (8.3) 0 (0.0) 2 (5.3) Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Blood phosphorus increased 0 (0.0) 1 (7.1) 1 (2.6) Heart rate irregular 0 (0.0) 1 (7.1) 1 (2.6) Specific gravity urine increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and connective tissue disorders 1 (4.2) 1 (7.1) 2 (5.3) Neck pain 0 (0.0) 1 (7.1) 1 (2.6)	Thermal burn	0 (0.0)	1 (7.1)	1 (2.6)
Blood iron decreased 0 (0.0) 1 (7.1) 1 (2.6) Blood phosphorus increased 0 (0.0) 1 (7.1) 1 (2.6) Heart rate irregular 0 (0.0) 1 (7.1) 1 (2.6) Specific gravity urine increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and connective tissue disorders 1 (4.2) 1 (7.1) 2 (5.3) Neck pain 0 (0.0) 1 (7.1) 1 (2.6)	Investigations	2 (8.3)	2 (14.3)	4 (10.5)
Blood phosphorus increased 0 (0.0) 1 (7.1) 1 (2.6) Heart rate irregular 0 (0.0) 1 (7.1) 1 (2.6) Specific gravity urine increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and connective tissue disorders 1 (4.2) 1 (7.1) 2 (5.3) Neck pain 0 (0.0) 1 (7.1) 1 (2.6) Renal and urinary disorders 0 (0.0) 1 (7.1) 1 (2.6)	Blood uric acid decreased	2 (8.3)	0 (0.0)	2 (5.3)
Heart rate irregular 0 (0.0) 1 (7.1) 1 (2.6) Specific gravity urine increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and connective tissue disorders 1 (4.2) 1 (7.1) 2 (5.3) Neck pain 0 (0.0) 1 (7.1) 1 (2.6) Renal and urinary disorders 0 (0.0) 1 (7.1) 1 (2.6)	Blood iron decreased	0 (0.0)	1 (7.1)	1 (2.6)
Specific gravity urine increased 0 (0.0) 1 (7.1) 1 (2.6) Musculoskeletal and connective tissue disorders 1 (4.2) 1 (7.1) 2 (5.3) Neck pain 0 (0.0) 1 (7.1) 1 (2.6) Renal and urinary disorders 0 (0.0) 1 (7.1) 1 (2.6)	Blood phosphorus increased	0 (0.0)	1 (7.1)	1 (2.6)
increasedImage: Constraint of the second	Heart rate irregular	0 (0.0)	1 (7.1)	1 (2.6)
connective tissue disorders Connective tissue disorders Neck pain 0 (0.0) 1 (7.1) 1 (2.6) Renal and urinary disorders 0 (0.0) 1 (7.1) 1 (2.6)		0 (0.0)	1 (7.1)	1 (2.6)
Renal and urinary disorders 0 (0.0) 1 (7.1) 1 (2.6)		1 (4.2)	1 (7.1)	2 (5.3)
	Neck pain	0 (0.0)	1 (7.1)	1 (2.6)
Urine abnormality 0 (0.0) 1 (7.1) 1 (2.6)	Renal and urinary disorders	0 (0.0)	1 (7.1)	1 (2.6)
	Urine abnormality	0 (0.0)	1 (7.1)	1 (2.6)

BID = twice daily; GI = gastrointestinal; MedDRA = Medical Dictionary for Regulatory Activities; N = total population; n = subgroup of total population; TEAE = treatment-emergent adverse event.