Bowel Cleansing Agents
Drug Class Review
56:12 Cathartics and Laxatives

Polyethylene Glycol 3350
(GaviLAX [OTC]; GlycoLax [OTC]; HealthyLax [OTC]; MiraLax [OTC]; PEGyLAX)

Polyethylene Glycol Electrolyte Solution
(Colyte; GaviLyte-C; GaviLyte-G; GaviLyte-N; GoLYTELY; MoviPrep; NuLYTELY; TriLyte)

Polyethylene Glycol Electrolyte Solution/Bisacodyl
(GaviLyte-H and Bisacodyl; HalfLytely and Bisacodyl [DSC]; PEG-Prep and Bisacodyl)

Sodium Phosphates
(Fleet Enema Extra [OTC]; Fleet Enema [OTC]; Fleet Pedia-Lax Enema [OTC]; LaCrosse Complete [OTC]; OsmoPrep)

Sodium Picosulfate/Magnesium Oxide/Citric Acid
(Prepopik™)

Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate
(Suprep® Bowel Prep Kit)

Final Report
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Executive Summary

**Introduction:** The oral bowel cleansing agents are indicated prior to gastrointestinal surgeries and endoscopic, colonoscopic and radiological procedures to reduce the risk of fecal contamination and other complications. In general, osmotic laxatives, such as polyethylene glycol (PEG), are most frequently used to clear out formed stool from the GI tract prior to procedures. Agents included in this review: polyethylene glycol electrolyte solution, polyethylene glycol electrolyte solution/bisacodyl, sodium phosphates, sodium picosulfate/magnesium oxide/citric acid and sodium sulfate/potassium sulfate/magnesium sulfate. All of the agents are available as oral powder for reconstitution alone or in combination with oral tablets. Current US guidelines recommend split-dose polyethylene glycol electrolyte solution regimens as first-line bowel cleansing therapy for elective colonoscopy.

**Clinical Efficacy:** Comparative clinical evidence for the bowel cleansing agents demonstrates similar rates of efficacy across the agents. No differences in efficacy between high-volume PEG-ELS therapy and low-volume PEG-ELS therapy were reported. Clinical trials comparing split-dose regimens to single day therapy demonstrate increased rates of bowel cleanliness in the split-dose regimen treatment groups. When compared to no bowel cleansing therapy, procedural preparation with a bowel cleansing agent demonstrated similar rates of anastomotic leaks and no differences in mortality, length of hospital stay or re-intervention rates.

**Adverse Drug Reactions:** The most frequently reported adverse effects include gastrointestinal discomfort including distention, nausea and vomiting. Rare but serious adverse effects have been reported with the bowel cleansing agents including electrolyte imbalance and renal dysfunction. PEG preparations without electrolytes used in large doses for bowel preparation increase the risk for ionic shifts. Use of PEG preparations with electrolytes reduces the risk for electrolyte shifts and related adverse events. The sodium phosphate preparations are associated with acute phosphate nephropathy and are not recommended for use in patients with chronic kidney disease, congestive cardiac failure or liver failure.

**Summary:** When administered correctly, the bowel cleansing agents are safe and effective. Overall, selection of a bowel cleansing agent should be based on indication, individual patient characteristics and the advantages and disadvantages (eg, tolerability, efficacy and potential adverse effects) associated with each of the bowel cleansing therapies.
Introduction

The oral bowel cleansing agents are a group of cathartic and laxative agents used specifically prior to gastrointestinal surgeries and in endoscopic, colonoscopic and radiological procedures to reduce the risk of fecal contamination.\textsuperscript{1-3} This report will focus on the polyethylene glycol and sodium sulfate/sodium phosphates/potassium sulfate/magnesium sulfate combination agents labeled for use in bowel cleansing prior to procedures: polyethylene glycol electrolyte solution, polyethylene glycol electrolyte solution/bisacodyl, sodium phosphates, sodium picosulfate/magnesium oxide/citric acid and sodium sulfate/potassium sulfate/magnesium sulfate. All of the agents are available as oral powder for reconstitution alone or in combination with oral tablets and are generally recommended for use the day-prior-to and/or the day-of the scheduled procedure.\textsuperscript{4,5} Table 1 provides a summary of the agents reviewed in this report.
Table 1. Comparison of the Bowel Cleansing Agents

<table>
<thead>
<tr>
<th>Agents</th>
<th>Available doses</th>
<th>Indications</th>
<th>Dose range</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium Citrate (Citroma [OTC])</td>
<td>Oral Solution: 1.745 g/30 mL (296 mL) [contains polyethylene glycol, saccharin sodium; lemon flavor, cherry flavor, low sodium] Oral Tablet: 100 mg</td>
<td>Relieves occasional constipation Off-Label: Evacuation of bowel prior to certain surgical and diagnostic procedures or overdose situations</td>
<td>195-300 mL given once or in divided doses</td>
<td>To increase palatability, chill the solution prior to administration. Administer each dose with 8 oz of water. Use caution; accumulation of magnesium in renal impairment may lead to magnesium toxicity.</td>
</tr>
<tr>
<td>Polyethylene Glycol 3350 (PEG; GaviLAX [OTC]; GlycoLAX [OTC]; HealthyLax [OTC]; MiraLax [OTC]; PegLyLAX)</td>
<td>Oral Packet: 1 count, 14 count, 30 count, 100 count Oral Powder: 119 g, 238 g, 250 g, 255 g, 500 g, 510 g, 527 g, 850 g</td>
<td>Treatment of occasional constipation in adults Off-label: Bowel preparation before colonoscopy; Constipation in children</td>
<td>Occasional constipation: Oral: 17 g of powder (~1 heaping tablespoon) dissolved in 4-8 ounces of beverage, once daily; do not use for &gt;1 week unless directed by healthcare provider Bowel preparation before colonoscopy (off-label use): Oral: Mix 17 g of powder (~1 heaping tablespoon) in 8 ounces of clear liquid and administer the entire mixture every 10 minutes until 2 L are consumed (start within 6 hours after administering 20 mg bisacodyl delayed-release tablets)</td>
<td>Generic available. Preparation for Administration: Dissolve powder in 4-8 ounces of water, juice, cola, or tea; 2-4 days may be required to produce bowel movement. Prolonged, frequent, or excessive use may lead to electrolyte imbalance. Use with caution in patients with renal impairment.</td>
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<tr>
<td>Polyethylene Glycol Electrolyte Solution (Colyte; GaviLyte-C; GaviLyte-G; GaviLyte-N; GoLYTELY; MoviPrep; NuLYTELY; TriLyte)</td>
<td>Powder for Oral Solution: PEG 3350 240 g, sodium sulfate 22.72 g, sodium bicarbonate 6.72 g, sodium chloride 5.84 g, and potassium chloride 2.98 g (4000 mL); PEG 3350 236 g, sodium sulfate 22.74 g, sodium bicarbonate 6.74 g, sodium chloride 5.86 g, and potassium chloride 2.97 g (4000 mL); PEG 3350 240 g, sodium bicarbonate 5.72 g, sodium chloride 11.2 g, and potassium chloride 1.48 g (4000 mL); PEG 3350 420 g, sodium bicarbonate 5.72 g, sodium chloride 11.2 g, and potassium chloride 1.48 g (4000 mL) Colyte: PEG 3350 227.1 g, sodium sulfate 21.5 g, sodium bicarbonate 6.36 g, sodium chloride</td>
<td>Bowel cleansing prior to colonoscopy or barium enema X-ray examination Off-Label: Whole bowel irrigation for toxic ingestions</td>
<td>CoLyte, GaviLyte-C, GaviLyte-G, GaviLyte-N, GoLYTELY, NuLYTELY, TriLyte: Oral: 240 mL (8 oz) every 10 minutes until 4 L are consumed or the rectal effluent is clear; rapid drinking of each portion is preferred to drinking small amounts continuously Nasogastric: 20-30 mL/minute until 4 L are administered or the rectal effluent is clear MoviPrep: Oral: Administer 2 L total with an additional 1 L of clear fluid prior to</td>
<td>Generic available. Rapid drinking of each portion is preferred to drinking small amounts continuously. No additional ingredients or flavors should be added to the polyethylene glycol-electrolyte solution. Chilling the solution may improve palatability. Oral medications should not be administered within 1 hour of start of therapy. Use within 48 hours of preparation; discard</td>
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<tr>
<td>Agents</td>
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<td></td>
<td>5.53 g, and potassium chloride 2.82 g (3785 mL) [cherry, lemon, lime, and orange flavor packs]</td>
<td>colonscopy as follows: Split dose (2 day regimen) (preferred method): Dose 1- Evening before colonscopy (10-12 hours before dose 2) 240 mL (8 oz) every 15 minutes until 1 L (entire contents of container) is consumed. Then fill container with 480 mL (16 oz) of clear liquid and consume prior to going to bed; Dose 2- On the morning of the colonoscopy (beginning at least 3.5 hours prior to procedure) 240 mL (8 oz) every 15 minutes until 1 L (entire contents of container) is consumed. Then fill container with 480 mL (16 oz) of clear liquid and consume at least 2 hours before the procedure. Evening only dose (1 day regimen) (alternate method): Dose 1- Evening before colonoscopy (at least 3.5 hours before bedtime) 240 mL (8 oz) every 15 minutes until 1 L (entire contents of container) is consumed; Dose 2- ~90 minutes after starting dose 1 240 mL (8 oz) every 15 minutes until 1 L (entire contents of container) is consumed. Then fill container with 1 L (32 oz) of clear liquid and consume all of the liquid prior to going to bed.</td>
<td>any unused portion. Use with caution in patients with renal impairment, ulcerative colitis, patients &gt;60 years of age, patients with G6PD deficiency</td>
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<td>Agents</td>
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<td><strong>Polyethylene Glycol Electrolyte Solution/Bisacodyl</strong>&lt;br&gt;(GaviLyte-H and Bisacodyl; HalfLytely and Bisacodyl [DSC]; PEG-Prep and Bisacodyl)</td>
<td>GaviLyte-H and Bisacodyl:&lt;br&gt; Powder for solution, oral (GaviLyte-H): PEG 3350 210 g, sodium bicarbonate 2.86 g, sodium chloride 5.6 g, potassium chloride 0.74 g (2000 mL) [contains 3 flavor packs: cherry, lemon, orange] AND Tablet, delayed release, oral (Bisacodyl): 5 mg (1 count)&lt;br&gt;HalfLytely and Bisacodyl: Discontinued&lt;br&gt;PEG-Prep and Bisacodyl: Powder for solution, oral (PEG-Prep): PEG 3350 210 g, sodium bicarbonate 2.86 g, sodium chloride 5.6 g, potassium chloride 0.74 g (2000 mL) [contains 3 flavor packs: cherry, lemon, orange] AND Tablet, delayed release, oral (Bisacodyl): 5 mg (1 count)</td>
<td>Bowel cleansing prior to colonoscopy</td>
<td>Bisacodyl: 5 mg as a single dose. After bowel movement or 6 hours (whichever occurs first), initiate polyethylene glycol-electrolyte solution&lt;br&gt; Polyethylene glycol-electrolyte solution: 8 ounces every 10 minutes until 2 L are consumed</td>
<td>No generic kit available.&lt;br&gt; Administer bisacodyl tablet with water; do not chew or crush tablet.&lt;br&gt; Do not take antacids within 1 hour of taking bisacodyl.&lt;br&gt; If severe bloating, distention, or abdominal pain occurs, administration should be slowed or temporarily discontinued until symptoms resolve.&lt;br&gt; Drink only clear liquids the day of and during the bowel preparation.&lt;br&gt; HalfLytely was discontinued in November 2011 because of reports associating it with ischemic colitis.</td>
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<tr>
<td><strong>Sodium Phosphates</strong>&lt;br&gt;(Fleet Enema Extra [OTC]; Fleet Enema [OTC]; Fleet Pedia-Lax Enema [OTC]; LaCrosse Complete [OTC]; OsmoPrep)</td>
<td>Injection, solution [concentrate; preservative free]: Phosphorus 3 mmol and sodium 4 mEq per 1 mL (5 mL, 15 mL, 50 mL)&lt;br&gt; Oral Solution: Monobasic sodium phosphate monohydrate 2.4 g and dibasic sodium phosphate heptahydrate 0.9 g per 5 mL</td>
<td>Oral solution, rectal: Short-term treatment of constipation&lt;br&gt; Oral tablets: Bowel cleansing prior to</td>
<td>Acute treatment of hypophosphatemia: Low dose, serum phosphorus losses are recent and uncomplicated: 0.08 mmol/kg over 6 hours&lt;br&gt; Intermediate dose, serum phosphorus level 0.5-1 mg/dL (0.16-0.32 mmol/L): 0.16-0.24 mmol/kg over 6 hours</td>
<td>Generic available.&lt;br&gt; Do not use additional agents, especially other sodium phosphate products.&lt;br&gt; Oral solution is contraindicated in patients with kidney disease.</td>
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<tr>
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| ML [sugar free; contains sodium 556 mg/5 mL, sodium benzoate; ginger-lemon flavor] |rectal enema solution (fleet enema, lacrosse complete): monobasic sodium phosphate monohydrate 19 g and dibasic sodium phosphate heptahydrate 7 g per 118 mL delivered dose (133 mL)  
Fleet enema extra: monobasic sodium phosphate monohydrate 19 g and dibasic sodium phosphate heptahydrate 7 g per 197 mL delivered dose (230 mL)  
Fleet pedia-lax™ enema: monobasic sodium phosphate monohydrate 9.5 g and dibasic sodium phosphate heptahydrate 3.5 g per 59 mL delivered dose (66 mL)  
oral tablet (osmoprep): monobasic sodium phosphate monohydrate 1.102 g and dibasic sodium phosphate anhydrous 0.398 g  
sodium phosphate 1.5 g per tablet; gluten free |colonoscopy  
IV: source of phosphate in large volume IV fluids and parenteral nutrition; treatment and prevention of hypophosphatemia |Parenteral nutrition: IV: 10-15 mmol/1000 kcal (hicks, 2001) or 20-40 mmol/24 hours (mirtallo, 2004 [ASPEN guidelines])  
Laxative (Fleet): rectal: contents of one 4.5 oz enema as a single dose  
Laxative: oral solution: 15 mL as a single dose; maximum single daily dose: 45 mL  
bowel cleansing prior to colonoscopy: oral tablets (osmoprep): a total of 32 tablets and 2 quarts of clear liquids (8 ounces of clear liquids with each dose) divided as follows: evening before colonoscopy: 4 tablets every 15 minutes for 5 doses (total of 20 tablets); 3-5 hours prior to colonoscopy: 4 tablets every 15 minutes for 3 doses (total of 12 tablets) |Use with caution due to increased risk of renal impairment in the elderly, use with caution in patients with gastrointestinal disorders, patients with a history of seizures  
The parenteral product may contain aluminum; toxic aluminum concentrations may be seen with high doses, prolonged use, or renal dysfunction.  
Contraindications  
intravenous preparation: diseases with hyperphosphatemia, hypocalcemia, or hypernatremia  
Tablets: acute phosphate nephropathy (biopsy proven), bowel obstruction, bowel perforation, gastric bypass or stapling surgery, toxic colitis, toxic megacolon 
Otc labeling (oral solution): dehydration, heart failure, renal impairment, electrolyte abnormalities; use for bowel cleansing, use in children <5 years  
U.S. boxed Warning: acute phosphate nephropathy has been reported with use of oral products as a colon cleanser prior to colonoscopy. |
| sodium Picosulfate/ Magnesium Oxide/ Citric Acid (Prepopik™) |Powder for solution, oral [kit]: prepopik™: sodium Picosulfate 10 mg, magnesium oxide 3.5 g, and citric acid 12 g per packet (2s) [orange flavor] |bowel cleansing prior to colonoscopy  
Canadian labeling: additional uses (not in U.S. labeling): bowel cleansing prior to x-ray examination, endoscopy, or surgery |Split-dose regimen (preferred): 150 mL (5 oz) the evening before the colonoscopy (5 PM-9 PM), followed by a second 150 mL (5 oz) dose ~5 hours before the colonoscopy.  
Day-before regimen (alternative): 150 mL (5 oz) in the early evening before the colonoscopy (4 PM-6 PM), followed by a second 150 mL (5 oz) dose 6 hours later (10 PM-12 AM) the night before the colonoscopy. |No generic available.  
Following the first dose, administer five 8-ounce clear liquid drinks (eg, water, clear broth, apple juice, white cranberry juice, white grape juice, ginger ale, plain gelatin [not purple or red], frozen juice bars [not purple or red]) within 5 hours. Following the second dose, administer three 8-ounce clear liquid drinks within 5 hours of administration. Clear liquids may be consumed up until 2 hours prior to the colonoscopy. |
<table>
<thead>
<tr>
<th>Agents</th>
<th>Available doses</th>
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</thead>
<tbody>
<tr>
<td>Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate (Suprep® Bowel Prep Kit)</td>
<td>Oral Solution: Suprep® Bowel Prep Kit: Sodium sulfate 17.5 g, potassium sulfate 3.13 g, and magnesium sulfate 1.6 g per 180 mL (180 mL) [contains sodium benzoate]</td>
<td>Bowel cleansing prior to gastrointestinal examination</td>
<td>Split-dose regimen: Total volume of liquid consumed over the course of treatment: 2880 mL (96 oz) Evening before colonoscopy: Drink the entire contents of 1 bottle, diluted to a final volume of 480 mL (16 oz). Then drink 2 additional containers of water each (filled to the 16-ounce line) over the next hour, for an additional volume of 960 mL (32 oz). Morning of the colonoscopy (10-12 hours after the evening dose): Repeat entire process with the second bottle: Drink entire contents of second bottle diluted to a final volume of 480 mL (16 oz); then drink 2 additional containers of water (each filled to the 16-ounce line) over the next hour, for an additional volume of 960 mL (32 oz). Complete at least 2 hours before the procedure.</td>
<td>In patients who develop bloating, distension, or abdominal pain, temporarily discontinue administration or increase the dosing interval until symptoms improve. Reconstitute immediately prior to each administration; do not prepare the solution in advance. Use with caution in patients with renal impairment and/or in patients taking medications that may adversely affect renal function. Use with caution in patients with severe ulcerative colitis.</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>No generic available.</td>
</tr>
<tr>
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<td>Sodium Sulfate/Potassium Sulfate/Magnesium Sulfate/Polyethylene Glycol Electrolyte Solution (Suclear™ [DSC])</td>
<td>Discontinued: Oral kit: Suclear™: Powder for solution, oral: PEG 3350 210 g, sodium bicarbonate 2.86 g, sodium chloride 5.6 g, potassium chloride 0.74 g (2000 mL) [contains cherry, lemon-lime, orange, and pineapple flavor packs] ::Solution, oral: Sodium sulfate 17.5 g, potassium sulfate 3.13 g, and magnesium sulfate 1.6 g (177 mL) [contains sodium benzoate]</td>
<td>Bowel cleansing prior to colonoscopy</td>
<td>Split-dose (2-day) regimen: Total volume of liquid consumed over the course of treatment: 3440 mL (~115 oz) Dose 1: Evening before colonoscopy (10-12 hours prior to Dose 2): Dilute the contents of the 6-ounce oral solution bottle to a final volume of 480 mL (16 oz), and drink the contents within 20 minutes. Refill container with 16 ounces of water and drink over the next 2 hours. Refill the container with the second refill of 16 oz of water, and finish drinking before bedtime (2 refills totaling 960 mL [32 oz]). Dose 2: Morning of the colonoscopy (beginning at least 3.5 hours prior to colonoscopy): Drink the entire contents of the reconstituted powder which has been diluted to a final volume of 2000 mL (2 L [~67 oz]) at a rate of 480 mL (16 oz) every 20 minutes (four 16-ounce containers over ~1.5 hours). Complete at least 2 hours prior to colonoscopy. Day-before (1-day) regimen: Dose 1: Evening before colonoscopy, beginning at least 3.5 hours prior to bedtime Dose 2: Evening before colonoscopy (~2 hours after starting Dose 1)</td>
<td>Product has been discontinued and is not currently available in the US.</td>
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Disease Overview

The rate of surgical treatments and diagnostic procedures has increased substantially in the US and the rate will continue to increase over the next two decades with the growing population of Medicare-eligible patients.\textsuperscript{6} Over 50 million surgical and diagnostic procedures are performed in the US annually resulting in over $450 billion in associated costs annually.\textsuperscript{7} A portion of those costs result from the nearly 1 million patients who experience a postoperative complication related to cardiovascular, cerebral, gastrointestinal, pulmonary or renal dysfunction.\textsuperscript{6} The two most frequently performed procedures in the US are endoscopy of large intestine (5.7 million) and endoscopy of small intestine (3.5 million) which are associated with increased risk of gastrointestinal complications.\textsuperscript{7} The bowel cleansing agents are recommended before specific surgical and diagnostic procedures to reduce these risks. Unfortunately, complications (including lower cancer detection rates, longer procedural time and more frequent examinations) are reported in up to 25\% of all colonoscopy procedures and are most frequently related to inadequate bowel preparation. Factors that lead to inadequate bowel preparation include poor patient education, extended wait times before scheduled procedure, patient-related variables (i.e. compliance to bowel cleansing regimen) and a variety of medical conditions (such as structural abnormality or renal impairment) which may make bowel cleansing more difficult.\textsuperscript{8}

Characteristics of an ideal oral bowel cleansing agent include: convenient administration, efficient bowel cleansing, little to no adverse effects and easy tolerability.\textsuperscript{2} Currently, no available bowel cleansing agent meets all characteristics and continued research into designing the ideal agent/combination is ongoing. Adequate bowel preparation may reduce the risk of complications, such as longer procedural times, and postoperative infection by clearing out and decreasing the bacterial load in the colon and rectum. Laxatives and cathartics are used in this capacity to clear out formed stool from the gastrointestinal (GI) tract. A variety of laxatives are available which work by increasing the retention of intraluminal fluid, by decreasing the net absorption of fluid by electrolyte transport or by altering gut motility to loosen stools and increase bowel movements.\textsuperscript{3} Table 2 provides a summary of the different classes of laxatives based on mechanism of action. In general, osmotic laxatives, such as polyethylene glycol (PEG), are most frequently used to clear out formed stool from the GI tract prior to procedures.

Table 2. Laxative Classifications and Properties\textsuperscript{4,5}

<table>
<thead>
<tr>
<th>Class</th>
<th>Agents</th>
<th>Mechanism of Action</th>
<th>Properties</th>
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</thead>
<tbody>
<tr>
<td>Bulk-Producing</td>
<td>Methylcellulose (Citrucel); Psyllium</td>
<td>Holds water in stool; mechanical distention</td>
<td>Onset: 12-72 hours Site: Small and large intestine</td>
</tr>
<tr>
<td>Agents</td>
<td>(Metamucil); Wheat dextrin (Benefiber)</td>
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<tr>
<td>Lubricants</td>
<td>Castor Oil; Mineral Oil</td>
<td>Lubricates intestine; inhibits colonic absorption of water; softens stool</td>
<td>Onset: 6-8 hours Site: Colon</td>
</tr>
<tr>
<td>Osmotic Laxatives</td>
<td>Glycerin suppository</td>
<td>Local irritation; hyperosmotic action</td>
<td>Onset: 15-30 minutes Site: Colon</td>
</tr>
<tr>
<td></td>
<td>Nondigestible Sugars (lactulose, sorbitol, mannitol)</td>
<td>Delivers osmotically active molecules to colon</td>
<td>Onset: 24-48 hours Site: Colon</td>
</tr>
<tr>
<td></td>
<td>Polyethylene Glycol 3350 (Glycolax, Miralax)</td>
<td>Nonabsorbable solution which acts as an osmotic agent</td>
<td>Onset: 48 hours Site: Small and large</td>
</tr>
</tbody>
</table>
All of the osmotic laxative options are effective in preparing the bowel for surgeries and procedures but may be associated with variable adverse effects. Polyethylene glycol solutions used for bowel cleansing are large volumes of fluid and frequently cause gastrointestinal upset, nausea, bloating and distention. Other osmotic/saline laxatives in smaller volumes are available, including magnesium citrate and sodium phosphate. The magnesium citrate solutions used for bowel cleansing are generally better tolerated but may be associated with increased fluid and electrolyte abnormalities. Sodium phosphate (NaP) solution is an over-the-counter agent which was withdrawn from the US market in 2008 due to increased risk of phosphate-induced renal disease. Some combination therapies use tablet formulations in addition to smaller amounts of fluid to improve tolerability.1,9

Despite the widespread use of bowel preparation therapy, the necessity of bowel cleansing prior to surgeries and procedures is unclear. Recent evidence suggests bowel preparation is unnecessary and may increase complications. According to the evidence, complications reported with the bowel cleansing agents include dehydration, electrolyte imbalance and increased risk of liquid stool contamination resulting from bowel prep therapy. On the other hand, bowel preparation prior to surgeries and procedures allows for easier

<table>
<thead>
<tr>
<th>Category</th>
<th>Example Drugs</th>
<th>Action/Effect</th>
<th>Onset/Duration</th>
<th>Site/Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline Agents</td>
<td>Magnesium citrate, Magnesium hydroxide (Phillips’ Milk of Magnesia), Sodium phosphates (Fleet Enema)</td>
<td>Attract/retain water in intestinal lumen increasing intraluminal pressure; cholecystokinin release</td>
<td>2 minutes-3 hours</td>
<td>Colon; Small and large intestine</td>
</tr>
<tr>
<td>Peripherally Acting Opioid Antagonists</td>
<td>Alvimopan (Entereg); Methylnaltrexone (Relistor); Naloxegol (Movantik)</td>
<td>Blocks mu-opioid receptors in GI tract, thereby antagonizing the constipating effects of opioids; restricted ability to cross the BBB</td>
<td>A- unknown; M- Usually within 30 to 60 minutes</td>
<td>N- 6-12 hours Site: Peripheral mu-opioid receptors, including the GI tract</td>
</tr>
<tr>
<td>Stimulants</td>
<td>Senna (Senakot); Bisacodyl (Dulcolax tablets, suppositories)</td>
<td>Direct action on intestinal mucosa; stimulate myenteric plexus; alter water and electrolyte secretion</td>
<td>S- 6-10 hours; B- 15 minutes-1 hour</td>
<td>Colon</td>
</tr>
<tr>
<td>Surfactants/Stool Softener</td>
<td>Docusate/senna (Peri-Colace)</td>
<td>Senna – stimulant Docusate – stool softener</td>
<td>8-12 hours</td>
<td>Small and large intestine</td>
</tr>
<tr>
<td>Miscellaneous Agents</td>
<td>Linaclotide (Linzess)</td>
<td>Intestinal guanylate cyclase-C agonist; results in chloride and bicarbonate secretion into the intestinal lumen, thereby increasing intestinal fluid and decreasing transit time</td>
<td>Within first week of consistent use Site: Luminal surface of intestinal epithelium</td>
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<td>Lubiprostone (Amitiza)</td>
<td>Activates intestinal chloride channels increasing intestinal fluid</td>
<td>24-48 hours</td>
<td>Apical membrane of the GI epithelium</td>
</tr>
</tbody>
</table>

Adapted from Lexicomp Online: [online.lexi.com/lco/action/doc/retrieve/docid/patch_f/4151](http://online.lexi.com/lco/action/doc/retrieve/docid/patch_f/4151)
Manipulation of an “empty” colon, minimizes the risk for stool contamination in most instances and reduces overall healthcare expenditures by reducing the need for repeat procedures. A recent meta-analysis (2012) of 14 randomized controlled trials reported “mechanical bowel preparation does not prevent surgical site infection and should be abandoned in clinical practice.” Specific instances in which bowel cleansing might be beneficial include cases requiring whole colon palpation for evaluation of tumor involvement and in sphincteroplasty to delay stooling and allow for initial healing. Current European consensus guidelines (2012) recommend some patient populations, especially those at risk of complications from bowel cleansing therapy, undergo specific surgeries and procedures without preoperative bowel preparation pharmacotherapy. The US guidelines continue to recommend bowel cleansing therapy prior to most surgeries and procedures in the colon as the accuracy can be compromised and complication rate increased with adequate bowel preparation. See Table 3 for a summary of current clinical practice guidelines.

Table 3. Summary of Current Clinical Practice Guidelines

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<th>Guideline</th>
<th>Recommendations</th>
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<td>Optimizing Adequacy of Bowel Cleansing for Colonoscopy: Recommendations From the US Multi-Society Task Force on Colorectal Cancer (2014)³</td>
<td>Selection of a bowel-cleansing regimen should take into consideration: medical history, medications, previous bowel preparation experience</td>
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<td>• Use of a split-dose bowel cleansing regimen is strongly recommended for elective colonoscopy</td>
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<td>o A split-dose regimen of 4L PEG-ELS provides high-quality bowel cleansing</td>
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<td>o In healthy, nonconstipated individuals, a 4-L PEG-ELS formulation produces a bowel-cleansing quality that is not superior to a lower-volume PEG formulation (2 L plus an adjunct)</td>
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<td>• A same-day regimen is an acceptable alternative to split dosing, especially for patients undergoing an afternoon examination</td>
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<td>o The second dose of split preparation should begin 4–6 h before the time of colonoscopy with completion of the last dose at least 2 h before the procedure time</td>
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<td>Consensus guidelines for the safe prescription and administration of oral bowel-cleansing agents (2012)²</td>
<td>• Oral bowel-cleansing agents have traditionally been prescribed predominantly on the basis of observational data and expert opinion. An increasing body of evidence suggests bowel preparation is not required for most procedures.</td>
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<td>• The guidelines recommend minimal or no formal bowel purgation in most circumstances.</td>
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<td>• When used, the choice of oral bowel-cleansing agent requires consideration of the particular indication, the individual recipient, and the advantages and disadvantages (eg, tolerability, efficacy and potential adverse effects) of the different preparations available.</td>
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<td>o Polyethylene glycols are associated with significant fluid and electrolyte shifts</td>
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<td>o Magnesium salt preparations are relatively contraindicated in patients with stage 4 and 5 chronic kidney disease</td>
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<td>o Sodium picosulfate preparations should be used with caution in patients at risk of, or suffering from, hypovolemia, including those patients taking high-dose diuretics, those with congestive cardiac failure and advanced cirrhosis, and those with chronic kidney disease</td>
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<td>o The use of oral sodium phosphate preparations is strongly discouraged in patients with chronic kidney disease, pre-existing electrolyte disturbances, congestive cardiac failure or cirrhosis, or with a history of hypertension</td>
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<td>o The use of oral sodium phosphate preparations in otherwise healthy patients</td>
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<td>is currently acceptable in cases where sodium picosulfate, magnesium salts and polyethylene glycols have proven ineffective or intolerable</td>
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| Modifications in endoscopic practice for the elderly\(^{11}\)             | The Practice Committee recommends that with optimal periprocedure evaluation and care, diagnostic and therapeutic endoscopic interventions can be safely performed in elderly patients and that electrolyte-balanced polyethylene glycol–based colonoscopy preparations be used for bowel preparation  
  • Split-dosage cathartic bowel preparations are recommended |
| SAGES evidence-based guidelines for the laparoscopic resection of curable colon and rectal cancer\(^{12}\) | The authors suggest that preoperative mechanical bowel preparation be used to facilitate manipulation of the bowel during the laparoscopic approach and to facilitate intraoperative colonoscopy when needed.  
  No specific product recommendations are provided. |
| ASGE guideline: endoscopy in the diagnosis and treatment of inflammatory bowel disease\(^{13}\) | Sodium phosphate-based bowel preparations can cause mucosal changes mimicking IBD and should be avoided before colonoscopy. |

Key: PEG-ELS = polyethylene glycol electrolyte solution, L = liter, h = hour
Pharmacology/Pharmacokinetics

The osmotic laxative agents increase stool frequency by causing retention of fluid in the gut which distends the colon and increases peristaltic activity. Other mechanisms have been implicated in the laxative effects of the osmotic agents including production of inflammatory mediators which increase intestinal motility. Although very efficacious in the treatment of constipation and bowel cleansing, the osmotic laxatives are associated with dependence and electrolyte abnormalities with prolonged, frequent or excessive use.

Polyethylene glycols (PEG) are “non-absorbable iso-osmotic solutions” which travel through the GI tract without net absorption or secretion. When used in smaller doses (250-500 mL daily), PEG is indicated in the short-term treatment (≤2 weeks) of occasional constipation. PEG preparations without electrolytes used in large doses for bowel preparation increase the risk for ionic shifts. Polyethylene Glycol–Electrolyte Solutions (PEG-ELS) used in large doses for bowel preparation cause catharsis with an isotonic mixture of sodium sulfate, sodium bicarbonate, sodium chloride and potassium chloride to avoid potential ionic shifts. The PEG-ELS preps are typically dosed 240 mL every 10 minutes until 4 L is consumed or the rectal effluent is clear.

Saline Laxatives are considered those with magnesium cations or phosphate anions (magnesium sulfate, magnesium hydroxide, magnesium citrate, sodium phosphate). The magnesium salts are typically dosed at 40-120 mEq of Mg2+ and cause 300-600 mL of stool within 6 hours. Picosulfate is a prodrug metabolized in the lumen to a stimulant that promotes peristalsis and is often used in combination with magnesium salts. The magnesium salts are associated with a bitter taste and may cause nausea and vomiting. The phosphate salts are absorbed to a greater extent than the magnesium-based agents and larger doses are required to induce purging. The phosphate-based agents are associated with acute phosphate nephropathy, especially at higher doses, and use should be avoided in patients at increased risk (elderly, renal dysfunction, inadequate fluid intake, etc). The saline laxatives should be used with caution in patients with renal insufficiency, cardiac disease, preexisting electrolyte abnormalities and in those receiving diuretic therapy.

Nondigestible Sugars and Alcohols. Lactulose, sorbitol and mannitol are non-absorbable sugars which are hydrolyzed to short-chain fatty acids in the gut, draw water into the lumen and stimulate colonic motility. Typical doses range from 15-60 mL in divided doses and effects may not take place for up to 24-48 hours after the initial dose. Abdominal discomfort, flatulence and taste aversion are the most frequent adverse events reported with the agents. In general, the agents are equally efficacious in the treatment of constipation and are not recommended for use in bowel preparation. Lactulose is also recommended in the treatment of hepatic encephalopathy.
Clinical Efficacy

Clinical evidence comparing the osmotic laxatives indicated in bowel cleansing prior to surgeries and procedures is extensive and summarized in the most recent US clinical practice guidelines. In general, the available comparative evidence suggests the bowel cleansing agents are equally effective in procedural bowel preparation. A number of OTC products may also be used for bowel cleansing, however the comparative clinical safety and efficacy evidence available for these agents is limited as the FDA's oversight of OTC products is limited by therapeutic class rather than for individual agents.1

According to available clinical evidence1, 28 trials comparing high-volume PEG-ELS agents (defined as greater than 3 liters of solution; n = 3,456) to low-volume PEG-ELS agents (<3 liters of solution; n = 3,752) are available for evaluation.14−41 Of the 28 trials, 21 provided bowel cleansing efficacy outcomes. Overall, the high-volume agents and low-volume agents demonstrated similar rates of bowel cleanliness (OR, 1.03; 95% CI, 0.80–1.32). Six trials compared the efficacy of split dose bowel prep therapy (2 L administered the day before and 2 L administered the day of the procedure) compared to standard bowel prep therapy and reported significantly increased rates of cleanliness in the split-dose regimens compared to standard therapy (OR, 4.38; 95% CI, 1.88-10.21).

The PEG-ELS agents have also been compared to sodium phosphate (NaP) preparations in a number of meta-analyses and clinical trials.1 Forty-eight trials were identified for evaluation (n = 11,368; PEG n = 5529; NaP n = 5839).26,29,31,42-82 Of the 48 trials, 33 provided bowel cleansing efficacy outcomes. Overall, the PEG agents and NaP agents demonstrated similar rates of bowel cleanliness (OR, 1.02; 95% CI, 0.77–1.36). Of note, patients receiving NaP reported increased willingness to repeat the regimen compared to patients receiving PEG (OR, 2.61; 95% CI,1.48–4.59). Three trials compared the efficacy of NaP split dose bowel prep therapy compared to NaP the day before the procedure or the same day of the procedure and reported significantly increased rates of cleanliness in the split-dose regimens (OR, 2.35; 95% CI, 1.27–4.34). Although effective and well tolerated, NaP is not recommended as first-line therapy do to risk of rare, but serious adverse events (i.e. Acute phosphate nephropathy).

Combination therapy with sodium picosulfate and a magnesium salt (either magnesium oxide or magnesium citrate; SPM) was compared to PEG-ELS and NaP in a number of clinical trials.1 The efficacy of SPM vs PEG was evaluated in eleven clinical trials (n = 3,097; PEG n = 1,715; SPM n = 1,385).28,65,83-91 Of the 11 trials, 10 provided bowel cleansing efficacy outcomes. Overall, the PEG agents and SPM agents demonstrated similar rates of bowel cleanliness (OR, 0.92; 95% CI, 0.63–1.36). The efficacy of SPM vs PEG was evaluated in eight clinical trials (n = 1,792; NaP n = 826; SPM n = 966).28,43,65,92-96 Of the 8 trials, 3 provided bowel cleansing efficacy outcomes. 97,106,107 Again, the NaP agents and SPM agents demonstrated similar rates of bowel cleanliness (OR, 0.60; 95% CI, 0.22–1.65). One trial compared SPM split-dose regimen to standard therapy and found the split-dose regimen had significantly increased rates of bowel cleanliness compared to standard therapy (OR, 3.54; 95% CI, 1.95–6.45).

The use of bowel cleansing agents has been recommended based on observational data and expert opinion in an attempt to reduce the risk of adverse complications related to
anastomotic leakage. However, an increasing body of evidence suggests bowel preparation may not be required for most procedures.97,98 99-102 A recent clinical trial (n = 1300) reported no differences in clinical anastomotic leaks or intra-abdominal abscesses in patients receiving bowel preparation compared to patients who received no bowel preparation (2.6% vs 4.3%, effect difference 1.7%, 95% CI 0.7 to 2.7).103 A second trial (n = 1431) reported no differences in rate of anastomotic leaks in patients receiving bowel preparation compared to no bowel preparation while the rate of intra-abdominal abscesses was higher in the group not receiving bowel preparation (4.7% vs 2.2%, p < 0.02).104 Other end points, including mortality, length of hospital stay and re-intervention rates, were similar between the treatment groups.7. A recent meta-analysis (2009) evaluating the morbidity and mortality rates associated with mechanical bowel preparation in colorectal surgery is available. According to the review, there is “no evidence to support the perceived benefit from mechanical bowel preparation.”105 Similar outcomes have been reported in bowel cleansing studies during gynecologic and urologic procedures.8,106,107
Safety

When administered correctly, the bowel cleansing agents are safe and effective. The most frequently reported adverse effects include gastrointestinal discomfort including distention, nausea and vomiting. Rare but serious adverse effects have been reported with the bowel cleansing agents including electrolyte imbalance and renal dysfunction. Polyethylene glycol electrolyte solutions are considered iso-osmotic, are not generally associated with electrolyte shifts and are considered first-line therapy. Sodium phosphate preparations are associated with severe electrolyte shifts and acute phosphate nephropathy, are considered second-line therapy and are not recommended for use in patients with chronic kidney disease, congestive cardiac failure, liver failure, hypertension or patients taking renin-angiotensin blockers or diuretics. Bioavailability of some medications may be affected by bowel cleansing (such as oral contraceptives) and oral medications should not be administered within 1 hour of start of therapy. Glycemic control in patients with diabetes undergoing bowel prep therapy can be concerning; these patients should be closely monitored and intravenous glucose/insulin therapy may be required in some cases.

In 2009, the UK National Patient Safety Agency (NPSA) issued a warning regarding the potential risk of harm associated with oral bowel cleansing therapy reporting “one death and 218 patient safety incidents occurring over a 5-year period. Six per cent of the 218 patient safety incidents resulted in moderate harm.” In order to limit the potential adverse events associated with bowel preparation therapy, individual patient characteristics should be considered before initiating treatment. Absolute contraindications to all of the bowel cleansing agents include: gastrointestinal obstruction or perforation, ileus, ileostomy, severe acute inflammatory bowel disease, toxic megacolon, reduced levels of consciousness, hypersensitivity or inability to swallow without aspiration.

Specific concerns related to bowel cleansing therapy are outlined below:

- Hypovolaemia and intravascular volume depletion, including syncope, myocardial ischaemia acute kidney injury secondary to acute tubular necrosis.
  - The risk is greatest with sodium phosphate preparations but also reported with sodium picosulphate
- Hypokalaemia
  - The frequency of hypokalaemia reported in clinical studies is variable (9%-56%)
  - Hypokalaemia may occur due to increased gastrointestinal loss of secreted potassium or, with the use of sodium phosphate, increased urinary loss as a result of hyperphosphaturia
  - Co-administration of a carbohydrate-electrolyte solution with sodium phosphate has been reported to reduce the risk of hypokalaemia.
- Hyponatraemia
  - The ingestion of large volumes of water, especially seen with PEG preparations, predisposes patients to hyponatraemia
- Phosphate nephropathy
  - Acute phosphate nephropathy may occur in up to 1 in 1000 patients who receive sodium phosphate preparations
- Oral sodium phosphate preparations provoke a transient mild hyperphosphataemia, which is most profound in older patients or in patients with inadequate hydration, hypertension with arteriosclerosis or in patients receiving NSAIDs, diuretics or renin-angiotensin inhibitors. Heart failure, cirrhosis and advancing age are additional risk factors.
- Oral sodium phosphate preparations are no longer available as over-the-counter medications for oral bowel cleansing

- Hypocalcaemia
  - Hypocalcaemia is a direct result of hyperphosphataemia and has been reported to occur in 58% of patients who receive oral sodium phosphate.

- Hypernatraemia
  - Hypernatraemia is uncommon, but can occur as a result of the sodium load in oral sodium phosphate preparations in combination with inadequate water intake.

- Hypermagnesaemia
  - Preparations containing magnesium salts may cause a transient rise in serum magnesium levels; this is a concern in patients with kidney disease.
Summary

The oral bowel cleansing agents are indicated prior to gastrointestinal surgeries and endoscopic, colonoscopic and radiological procedures to reduce the risk of fecal contamination and other complications. Current US guidelines recommend split-dose polyethylene glycol electrolyte solution regimens as first-line bowel cleansing therapy for elective colonoscopy. PEG preparations without electrolytes used in large doses for bowel preparation increase the risk for ionic shifts. Use of PEG preparations with electrolytes reduces the risk for electrolyte shifts and related adverse events. Comparative clinical evidence for the bowel cleansing agents demonstrates similar rates of efficacy across the agents. Clinical trials comparing split-dose regimens to single day therapy demonstrate increased rates of cleanliness in the split-dose regimen treatment groups. When administered correctly, the bowel cleansing agents are safe and effective. Rare but serious adverse effects have been reported with the bowel cleansing agents including electrolyte imbalance and renal dysfunction. The sodium phosphate preparations are associated with acute phosphate nephropathy and are not recommended for use in patients with chronic kidney disease, congestive cardiac failure or liver failure. Overall, selection of a bowel cleansing agent should be based on indication, individual patient characteristics and the advantages and disadvantages (eg, tolerability, efficacy and potential adverse effects) of each bowel preparation therapy.
References


59. Kastenberg D, Barish C, Burack H, et al. Tolerability and patient acceptance of sodium phosphate tablets compared with 4-L PEG solution in colon cleansing: combined results of 2 identically designed,


