Drug Class Review Monograph – GPI Class 52 – Gastrointestinal Agents

Review Time Frame: 02/2016 – 01/2017
Previous Class Review: 11/2016

Background:
Gastrointestinal agents encompass many different classes of drugs that are used to treat various gastrointestinal disorders such as:

- **Gallstone Solubilizing Agents** suppress the amount of cholesterol synthesized by the liver or inhibit the amount of cholesterol absorbed from the intestines.
- **Gastrointestinal Anti-allergy Agents** work at the surface of the mast cell to inhibit its degranulation. This, in turn, prevents the release of histamine and slow-reacting substance of anaphylaxis (SRS-A), mediators of type I allergic reactions.
- **Antiflatulents** act to disperse and prevent the formation of mucus-surrounded gas pockets in the GI tract.
- **Gastrointestinal stimulants** increase motility of the gastrointestinal smooth muscle without acting as a laxative.
- **Intestinal Acidifiers** increase osmotic pressure, causing fluid accumulation that softens the stool and distends the colon, thereby enhancing peristalsis.
- **Gastrointestinal Chloride Channel Activators** activate chloride channels in the intestine and increases secretion of intestinal fluid that helps in passing of the stool.
- **Inflammatory Bowel Agents** include aminosalicylates which work by via inhibition of arachidonic acid in the bowel mucosa by the enzyme cyclooxygenase, ultimately diminishing the production prostaglandins, thereby reducing colonic inflammation. Other inflammatory bowel agents include integrin receptor antagonists, interleukin receptor antagonists, and tumor necrosis factor alpha inhibitors.
- **Short bowel syndrome agents** are glucagon-like peptide-2 (GLP-2) analogs. GLP-2, which is a peptide secreted by L-cells of the distal intestine in response to a meal, increases intestinal and portal blood flow and inhibits gastric acid secretion.
- **Irritable Bowel Syndrome (IBS) Agents** include work as a selective antagonists at the 5-hydroxytryptamine (5-HT3) receptor which modulates the regulation of visceral pain, colonic transit, and GI secretions. Other IBS agents include guanylate cyclase-C receptor agonists and mu-opioid receptor agonists.
- **Peripheral Opioid Receptor Antagonists** bind to the peripheral opioid receptors, such as those in the gastrointestinal tract, and block unwanted effects caused by opioids.
- **Bile acid synthesis disorder agents** include cholic acid, an endogenous bile acid that enhances bile flow and provides the physiologic feedback inhibition of bile acid synthesis.
- **Farnesoid X receptor (FXR) agonists** activate FXR receptors. This decreases the intracellular hepatocyte concentrations of bile acids and promotes cholestasis, thus reducing hepatic exposure to bile acids.
- **Phosphate Binder Agents** bind dietary phosphate and prevent its absorption, thereby lowering serum phosphorous concentrations such as calcium carbonate combines with dietary phosphate, forming an insoluble calcium phosphate complex, which lowers serum phosphorous concentrations. Lanthanum carbonate dissociates to lanthanum ions in the acidic environment of the upper GI tract. The lanthanum ions bind dietary phosphate released from...
food during digestion. Sevelamer carbonate binds dietary phosphate within the gastrointestinal tract, thereby preventing phosphate absorption.

New treatment guideline recommendations:
• None identified

Newly approved drugs:
• Viberzi (eluxadoline) May 27, 2015
  • Approved 01/19/2017: Trulance (plecanatide) 3 mg tablets; anticipated to be commercially available by end of Q1 2017.

Newly approved formulations:
• Xifaxan (rifaximin)—newly approved indication of irritable bowel syndrome with diarrhea (IBS-D) May 27, 2015
  • Approved 09/23/2016: Stelara (ustekinumab) 130 mg/26 mL intravenous infusion; currently commercially available.

Newly approved generics:
• Alosetron 0.5mg, 1mg May 4, 2015

Discontinued drugs:
• None identified

FDA Safety Alerts/black box warnings:
• None identified

Pipeline alerts:
Agents pending FDA approval include:
• None identified. Naldemedine, a peripherally selective mu-opioid receptor antagonist for the treatment of opioid-induced constipation in adults with chronic non-cancer pain (PDUFA: 3/23/17).

References:
5. WWW.FDA.GOV.