Drug Class Review Monograph – GPI Class 52 – Gastrointestinal Agents

Review Time Frame: 02/2016 – 01/2017

Previous Class Review: 11/2016

Background:

Gastrointestinal agents ~~include~~ encompass many different classes of drugs that are used to treat various gastrointestinal disorders ~~such as~~. These classes include:~~:~~

- Gallstone ~~S~~solubilizing ~~A~~agents suppress the amount of cholesterol synthesized by the liver or inhibit the amount of cholesterol absorbed from the intestines.
- Gastrointestinal ~~A~~anti-allergy ~~A~~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~~ gastrointestinal tract.
- Gastrointestinal stimulants increase motility of the gastrointestinal smooth muscle~~,~~ without acting as a laxative.
- Intestinal a~~A~~cidifiers increase osmotic pressure, causing fluid accumulation that softens the stool and distends the colon, thereby enhancing peristalsis.
- Gastrointestinal ~~C~~chloride ~~C~~channel ~~A~~activators activate chloride channels in the intestine and increase~~s~~ secretion of intestinal fluid that helps in passing of ~~the~~ stool.
- Inflammatory ~~B~~bowel ~~A~~agents include aminosalicylates which work ~~by~~ via inhibition of arachidonic acid in the bowel mucosa by the enzyme cyclooxygenase, ultimately ~~. Inhibition of cyclooxygenase effectively diminishes 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 ~~B~~bowel ~~S~~syndrome (IBS) a~~A~~gents include~~work as a~~ selective antagonists at the 5-hydroxytryptamine (5-HT_3) receptor which ~~-~~modulate~~s~~ the regulation of visceral pain, colonic transit, and ~~GI~~ gastrointestinal secretions. Other IBS agents include guanylate cyclase-C receptor agonists and mu-opioid receptor agonists.
- Peripheral ~~O~~opioid ~~R~~receptor ~~A~~antagonists bind~~s~~ 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 choleresis, thus reducing hepatic exposure to bile acids.
- Phosphate ~~B~~binder ~~A~~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 phosphorus concentrations. Lanthanum carbonate dissociates to lanthanum ions in the acidic environment of the upper GI tract. The lanthanum ions bind dietary phosphate released from~~

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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.
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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:

1. Farrell RJ. Overview of the medical management of mild to moderate Crohn disease in adults. Rutgeerts P, Grover S (Eds.), UpToDate. Waltham, MA. Accessed January 2017~~6~~.
2. Wald A. Management of chronic constipation in adults. Talley NJ, Grover S (Eds.), UpToDate. Waltham, MA. Accessed January 2017~~6~~.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017~~5~~. ~~URL~~Available at: http://www.clinicalpharmacology-ip.com/. ~~Updated~~ Accessed January 2017~~6~~.
4. US Script Oracle PBM: Medi-Span® Master Drug Data Base. January ~~-~~2017.~~6~~
5. WWW.FDA.GOV.
~~5.~~6. Shionogi Inc. Shionogi announces acceptance of new drug application in the US for naldemedine for the treatment of opioid-induced constipation. Available at: http://www.shionogi.com/newsroom/article.html#122502. Published June 6, 2016. Accessed January 27, 2017.

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