Drug Class Review Monograph – GPI Class 50 – Antiemetics

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

Background:
Antiemetic agents are drugs used for the prevention and treatment of nausea, vomiting, and motion sickness. There are five neurotransmitter receptor sites that are of primary importance in the vomiting reflex: muscarinic (M1), dopamine (D2), histamine (H1), 5-hydroxytryptamine (HT)-3 – serotonin, and neurokinin 1 (NK1) receptor – substance P. Anti-emetics are classified based upon their primary site of action, with some agents affecting multiple receptors. Classes of anti-emetics that antagonize the neurotransmitter receptors known to be involved in the physiology of nausea and vomiting include:

- Anticholinergics (e.g., scopolamine) - antagonizes acetylcholine at muscarinic receptors and predominantly used as prophylaxis against motion sickness;
- Antihistamines (e.g., dimenhydrinate, meclizine) - antagonizes the effects of histamine on H1-receptors and primarily used for motion sickness;
- Dopamine receptor antagonists (e.g., prochlorperazine, chlorpromazine) - act predominantly by antagonizing D2-dopamine receptors in the area postrema of the midbrain;
- Serotonin receptor antagonists (5-HT3 receptor antagonists) - blocks the serotonin 5-HT3 receptors which are found centrally in the chemoreceptor trigger zone and peripherally at vagal nerve terminals in the intestines and antagonizes the effects of serotonin;
- Neurokinin receptor antagonists - prevents acute and delayed vomiting by inhibiting the substance P/NK1 receptor; augments the antiemetic activity of 5-HT3 receptor antagonists and corticosteroids to inhibit acute and delayed phases of chemotherapy-induced emesis.

New treatment guideline recommendations:
- No new treatment guideline recommendations identified. The American Society of Clinical Oncology recommends that all patients who receive highly emetogenic chemotherapy regimens (including anthracycline plus cyclophosphamide) should be offered a three-drug combination of an NK1 receptor antagonist, a 5-HT3 receptor antagonist, and dexamethasone. The oral combination of netupitant and palonosetron plus dexamethasone is an additional treatment option in this setting.

Newly approved drugs:
- Varubi (rolapitant) 90mg tablet on 09/1/2015

Newly approved formulations:
- Emetrol (aprepitant) 125mg oral solution on 12/17/2015 - anticipated launch date is April 2016 per Merck National Service Center

Approved 11/07/2016: Bonjesta (doxylamine succinate;
pyridoxine hydrochloride) 20 mg doxylamine succinate and 20 mg pyridoxine hydrochloride extended-release tablets; currently not commercially available-anticipated launch date unknown.

- Approved 08/09/2016: Sustol (granisetron) 10 mg/0.4 mL extended-release solution for injection; commercially available.
- Approved 08/22/2016: Palonosetron (palonosetron) 0.25 mg/2 mL (0.125mg/mL) injection in a single-dose vial; currently not commercially available-anticipated launch date unknown.
- Approved 07/01/2016: Syndros (dronabinol) 5 mg/mL oral solution; anticipated to launch in Q2 2017.
- Approved 03/01/2016: Palonosetron (palonosetron) 0.25 mg/5 mL and 0.075 mg/1.5 mL injection; currently not commercially available-anticipated launch date unknown.

Newly approved generics:
- Approved 08/19/2016: Diclegis (doxylamine succinate and pyridoxine hydrochloride) 10 mg/10 mg delayed release tablets; currently not commercially available-anticipated launch date unknown.
- Scopolamine transdermal therapeutic system 1mg/3 days on 01/30/2015-launch date is currently not available according to the generic manufacturer, PerrigoApproved 06/09/2016: Emend (fosaprepitant dimeglumine) for injection, 150 mg/vial; currently not commercially available-anticipated launch date unknown.

Discontinued drugs:
- Antivert tablet 50mg

FDA Safety Alerts/black box warnings:
- None identified

Pipeline alerts:
Agents pending FDA approval include:
- Cinvanti (aprepitant) injection: for the prevention of chemotherapy-induced nausea and vomiting (CINV); FDA expected to review application by 11/12/2017.

References: