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Drug Class Review Monograph – GPI Class 50 – Antiemetics

Review Time Frame: 02/2016 – 01/2017

Previous Class Review: 11/2016

Background:

Antiemetic ~~a~~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;

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- ~~Antihistamines~~ (e.g., dimenhydrinate, meclizine) - ~~antagonizes~~ the effects of histamine on H1-receptors and primarily used for motion sickness;

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- ~~Dopamine~~ ~~r~~Receptor ~~a~~Antagonists (e.g., prochlorperazine, chlorpromazine) - act predominantly by antagonizing D2-dopamine receptors in the area postrema of the midbrain;

- ~~Serotonin~~ ~~r~~Receptor ~~a~~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;

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- ~~Neurokinin receptor antagonists~~ - ~~p~~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.

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New treatment guideline recommendations:

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- ~~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.~~

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Newly approved drugs:

- ~~Varubi (rolapitant) 90mg tablet on 09/1/2015~~None identified

Newly approved formulations:

- ~~Emend (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);

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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.

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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, Perrigo~~ Approved 06/09/2016: Emend (fosaprepitant dimeglumine) for injection, 150 mg/vial; currently not commercially available-anticipated launch date unknown.

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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:

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2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017~~5~~. ~~URL Available at: http://www.clinicalpharmacology-ip.com/. Updated October 2015~~ Accessed February 2017.
3. ~~Trimethobenzamide. Lexi Drugs. Lexicomp. Wolters Kluwer Health, Inc. Hudson, OH. Available at: http://online.lexi.com. Accessed January 27, 2016.~~
4. Food and Drug Administration. Available at: www.fda.gov.
- 7-5. ~~Hesketh PJ, Bohlke K, Lyman GH, et al. Antiemetics: American Society of Clinical Oncology focused guideline update. J Clin Oncol. 2016 Feb 1;34(4):381-6.~~