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Medication Policy Manual

Policy No: dru163

Topic: Aloxi[®], palonosetron

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Next Review Date: November 2009

IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Palonosetron (Aloxi[®]) is a 5-HT₃ antagonist medication used to prevent nausea and vomiting.

Policy/Criteria

- I.** Most contracts require prior authorization approval of oral palonosetron prior to coverage. Oral palonosetron may be considered medically necessary when both criteria A and B below are met.
 - A.** Oral palonosetron is used for the prevention and/or treatment of nausea/vomiting associated with chemotherapy and/or radiation therapy.

AND

- B.** Treatment with at least one generic 5-HT₃ antagonist (ondansetron or granisetron) is not effective or not tolerated.

II. Administration, Quantity Limitations, and Authorization Period

- A.** Regence considers oral palonosetron to be a self-administered medication.
- B.** When prior authorization is approved, oral palonosetron may be authorized in quantities of up to four capsules per month. Quantities exceeding four capsules per month may be approved when appropriate for the prescribed chemotherapy and/or radiation treatment regimen, not to exceed 30 capsules per month (e.g., if chemotherapy is given on an every 3-week cycle, two capsules per month may be authorized, or if radiation therapy is scheduled three times per week, twelve capsules per month may be authorized).
- C.** Authorization may be reviewed at least every six months to confirm that current medical necessity criteria are met and that the medication is effective.

III. Oral palonosetron is considered investigational when used for all other conditions, including but not limited to:

- A.** Hyperemesis gravidarum.
- B.** Nausea and vomiting of pregnancy (NVP).
- C.** Post-operative nausea and vomiting (PONV).

Position Statement

- All of the 5-HT₃-antagonist antiemetic medications are effective in preventing nausea and vomiting. [24-26, 30]
- No single 5-HT₃-antagonist antiemetic medication has been shown to work better or be better tolerated than another when given in equally potent doses whether given by mouth, by injection, or via a topical patch. [12, 31-36]
- Two of the 5-HT₃-antagonist antiemetic medications, ondansetron and granisetron, are available as generics and provide the best value in preventing nausea and vomiting.

Chemotherapy and Radiation Therapy

- The American Society of Clinical Oncology (ASCO) provides recommendations for antiemetic use during chemotherapy: [12]
 - * Acute Emesis (0 - 24 hours after chemotherapy) - A single dose of a 5-HT₃-receptor antagonist just prior to highly emetogenic chemotherapy agents (e.g., cisplatin, cyclophosphamide, and lomustine) and moderately emetogenic chemotherapy (e.g., carboplatin, iphosphamide, and idarubicin), as part of an antiemetic regimen.
 - * For consecutive days of highly and moderately emetogenic chemotherapy, a 5-HT₃-receptor antagonist during each day of chemotherapy.
 - * Delayed Emesis (24 to 72 hours after chemotherapy) - For moderately emetogenic chemotherapy, dexamethasone or a 5-HT₃-receptor antagonist is recommended for up to two to three days. 5-HT₃-receptor antagonists are no longer recommended for delayed emesis due to highly emetogenic chemotherapy.
 - * An antiemetic, including a 5-HT₃-receptor antagonist, may be considered in high dose or pediatric chemotherapy.
- ASCO also provides recommendations for antiemetic use during radiation therapy: [12]
 - * A single dose of a 5-HT₃-receptor antagonist before each fraction of radiation when there is high, intermediate, or low risk of radiation-induced emesis.

- * A dopamine receptor or a 5-HT₃-receptor antagonist as needed for minimal-risk radiation therapy.
- There are no well-designed studies to support antiemetic therapy for periods greater than 24 hours after the last dose of radiation therapy.
- A small (n = 39) double-blind, randomized parallel study evaluated the efficacy of 1 mg granisetron IV vs. 3 mg IV. Of the group getting 3 mg, 90% showed complete response vs. 60% in the group receiving 1 mg. The approved U.S. dose of 2 mg was not evaluated. ^[27]

Nausea and Vomiting of Pregnancy (NVP) versus Hyperemesis Gravidarum

- NVP occurs in the majority of pregnant women, is commonly limited in duration, and does not adversely affect pregnancy outcomes.
 - * Non-pharmacological treatment of NVP is preferred over pharmacological therapies and includes dietary modifications; eating small, bland, frequent, low fat, high carbohydrate meals; avoiding emetogenic odors; avoiding iron supplements; and relaxation.
 - * Hyperemesis gravidarum, which is more rare than uncomplicated NVP, is severe, persistent, uncontrollable nausea and vomiting during pregnancy resulting in dehydration and weight loss. Electrolyte and metabolic disturbances, nutritional deficiency, and ketosis may also occur.
 - * Treatment of hyperemesis gravidarum may include non-pharmacological therapies and parenteral hydration with glucose, electrolytes, and vitamins, often in an inpatient setting. Antiemetics, corticosteroids, and sedatives are used for the acute vomiting.

Antiemetics in Pregnancy and Hyperemesis Gravidarum

- Diphenhydramine, dimenhydrinate, meclizine, doxylamine, and metoclopramide (rated FDA Pregnancy category B) have not been associated with an increased risk of teratogenicity when used in humans, and have demonstrated some level of efficacy in NVP or hyperemesis gravidarum in clinical trials.
- There is extensive experience indicating that the combination of doxylamine and pyridoxine is safe in pregnancy. Doxylamine and pyridoxine are available as Diclectin[®] in Canada. Canadian physicians use this product as first line therapy for NVP. Doxylamine and pyridoxine are currently available without a prescription in the U.S.
- Ondansetron, granisetron, dolasetron, and palonosetron are also rated FDA Pregnancy category B. ^[24-26, 30-31] Studies using ondansetron during pregnancy are limited and there are currently no clinical trials evaluating dolasetron, granisetron, or palonosetron in NVP or hyperemesis gravidarum.
- Ondansetron has not demonstrated superiority over other antiemetics in the treatment of hyperemesis gravidarum. There are no controlled trials that evaluate the safety of high-dose or long-term use of ondansetron in pregnancy.
- Doses of ondansetron used in clinical trials for the treatment of hyperemesis gravidarum ranged from 4mg to 10mg IV daily, up to TID. ^[6, 15-16]
- Ondansetron may be considered medically necessary for the treatment of hyperemesis gravidarum. There is no useful evidence supporting the use of dolasetron, granisetron, or palonosetron for this indication.

Postoperative Nausea and Vomiting

- Efficacy and benefits in preventing/treating postoperative nausea and vomiting with a 5-HT₃-receptor antagonist have not been demonstrated beyond 24 hours.

Safety

- Headache was the most commonly observed adverse effect with 5-HT₃-receptor antagonists in clinical trials. [24-26, 30-31]

5-HT₃ receptor antagonists: Use in Other Conditions

- There are preliminary trials which have used ondansetron in the treatment of memory impairment in schizophrenic patients [17], neuropathic pain [18], pruritus of cholestasis [19], ataxia and incoordination secondary to brain injury [20], Tourette's disorder [21], fatigue with primary biliary cirrhosis [22], fatigue in chronic Hepatitis C, [23] cocaine dependence [28] and schizophrenia [29]. The trials were all of short duration, they enrolled small populations, and several included ondansetron given by injection.

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Cross References
Anzemet [®] , dolasetron dru069
Emend [®] , aprepitant dru091
Kytril [®] , granisetron dru068
Sancuso [®] , granisetron topical patch dru164
Zofran [®] , ondansetron dru046

Codes	Number	Description
N/A		