Clinical Policy: Oral Antiemetics (5-HT3 Antagonists)

Reference Number: PA.CP.PMN.11
Effective Date: 01/18
Last Review Date: 04/18

Coding Implications
Revision Log

Description
The following oral antiemetics are serotonin 5-hydroxytryptamine, type 3 (5-HT3) receptor antagonists requiring prior authorization: dolasetron (Anzemet®), granisetron (Kytril®), netupitant/ palonosetron (Akynzeo®), and ondansetron (Zuplenz®).

FDA approved indication
Akynzeo is indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.

Anzemet is indicated for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy, including initial and repeat courses in adults and children 2 years and older.

Kytril is indicated for the prevention of:
- Nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin.
- Nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation.

Zuplenz is indicated for the prevention of:
- Nausea and vomiting associated with highly emetogenic cancer chemotherapy.
- Nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.
- Nausea and vomiting associated with radiotherapy in patients receiving total body irradiation, single high-dose fraction to abdomen, or daily fractions to the abdomen.
- Prevention of postoperative nausea and/or vomiting.

Policy/Criteria
Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of Pennsylvania Health and Wellness® that 5-HT3 receptor antagonist oral antiemetics are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chemotherapy/Radiation Induced Nausea and Vomiting (must meet all)**:**

1. Prescribed for one of the following (a or b):
   a. Prevention of chemotherapy-induced nausea/vomiting;
   b. Treatment (off-label) of chemotherapy-induced nausea/vomiting (Anzemet and Kytril only);
2. Age ≥ 18 years (Akynzeo, Kytril, Zuplenz) or ≥ 2 years (Anzemet);

3. Member meets one of the following:
   a. For Anzemet, Kytril, and Zuplenz: Failure of a trial of ondansetron at maximum indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. For Akynzeo: Failure of a trial of aprepitant in combination with ondansetron at maximum indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
      ** Aprepitant may require prior authorization*
4. Request meets one of the following (a or b):
   a. For prophylaxis, dose does not exceed:
      i. Akynzeo: 1 capsule/chemotherapy course;
      ii. Anzemet: 100 mg/chemotherapy course;
      iii. Kytril: 2 mg/chemotherapy course;
      iv. Zuplenz: 24 mg/chemotherapy course;
   b. Dose is supported by practice guidelines or peer-reviewed literature for off-label treatment of chemotherapy-induced nausea and vomiting *(prescriber must submit supporting evidence)*.

Approval duration: projected course of chemo/radiation therapy up to 72 hours after completion of chemo/radiation therapy

B. Postoperative Nausea/Vomiting (must meet all)**:**
1. Prescribed for prevention/treatment of postoperative nausea/vomiting;
2. Request is for Zuplenz;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Member is contraindicated or has experienced clinically significant adverse effects to the excipients in all PDL generic ondansetron products (regular tablet, orally disintegrating tablet, oral solution);
   b. Documentation supports member's inability to use all PDL generic ondansetron products (regular tablet, orally disintegrating tablet, oral solution);
5. Dose does not exceed 16 mg pre-operatively.

Approval duration: 3 days

C. Radiation-Induced Nausea and Vomiting (must meet all)**:**
1. Prescribed for the prevention of radiation-induced nausea/vomiting;
2. Request is for Kytril or Zuplenz;
3. Age ≥ 18 years;
4. Failure of ondansetron at maximum indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed one of the following:
   a. Kytril: 2 mg/chemotherapy course;
   b. Zuplenz: 24 mg/day.

Approval duration: projected course of radiation therapy up to 48 hours after completion of radiation therapy

D. Other diagnoses/indications – Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

II. Continued Therapy

A. Chemotherapy/Radiation Induced Nausea and Vomiting (must meet all)**:**

1. Documentation that member is currently receiving chemotherapy/radiation therapy;
2. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
3. Member is responding positively to therapy;
4. If request is for a dose increase, request meets one of the following (a or b):
    a. New dose does not exceed the following:
        i. Akynzeo: 1 capsule/chemotherapy course;
        ii. Anzemet: 100 mg/chemotherapy course;
        iii. Kytril: 2 mg/chemotherapy course;
        iv. Zuplenz: 24 mg/chemotherapy course;
    b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence)*.

Approval duration: projected course of chemo/radiation therapy up to 72 hours after completion of chemotherapy OR projected course of radiation therapy up to 48 hours after completion of radiation therapy

B. Postoperative Nausea and Vomiting – reauthorization is not permitted.

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53 if requested indication is NOT listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

Approval duration: duration of request or 3 month (whichever is less)

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label policy – PA.CP.PMN.53 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation Key
5-HT3: serotonin 5-hydroxytryptamine, type 3

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Dolasetron (Anzemet)	Chemotherapy-induced nausea/vomiting	100 mg tablet PO taken 1 hour before chemotherapy	100 mg

Netupitant/ palonosetron (Akynzeo)	Chemotherapy-induced nausea/vomiting	1 capsule PO taken approximately 60 minutes prior to chemotherapy	1 capsule
Granisetron (Kytril)	Chemotherapy-induced nausea/vomiting	2 mg PO 1 hour before chemotherapy OR 1 mg PO twice daily on the day of chemotherapy	2 mg
Ondansetron (Zuplenz)	Chemotherapy-induced nausea/vomiting	8 mg PO twice daily or 24 mg PO one time, 30 minutes before chemotherapy	24 mg
	Radiation-induced nausea/vomiting	8 mg PO three times daily OR 8 mg PO 1-2 hours before each fraction of radiotherapy administered each day OR 8 mg PO 1 hour before radiotherapy with subsequent doses every 8 hours after the first dose for 1-2 days after radiotherapy completion or for each day radiotherapy is given	8 mg
	Postoperative nausea/vomiting	16 mg PO taken 1 hour before anesthesia induction	16 mg

VI. Product Availability

Drug	**Availability**
Anzemet (dolasetron)	100 mg, 500 mg tablet
Akynzeo (netupitant; palonosetron)	300 mg/0.5mg capsule
Kytril (granisetron)	1 mg tablet
Zuplenz (ondansetron)	4 mg, 8 mg oral soluble film

VII. References

1. Clinical Pharmacology. Tampa, FL: Gold Standard; 2018. Available at www.clinicalpharmacology.com. Accessed February 6, 2018..
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8. Guidelines for Antiemetic Treatment of Chemotherapy-Induced Nausea and Vomiting: Past, Present, and Future Recommendations. *The Oncologist*, Vol. 12, No. 9, 1143-1150, September 2007; doi:10.1634/theoncologist.12-9-1143. http://theoncologist.alphamedpress.org/cgi/content/full/12/9/1143.
9. National Comprehensive Cancer Network. Antiemesis Version 2.2017. Available at: https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed February 6, 2018.

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: added aprepitant as a step therapy requirement for Akynzeo; references reviewed and updated.Converted to new template; added age restriction; separated chemo-induced from radiation-induced nausea vomiting in the Initial Approval section; specified which agents are FDA-approved or NCCN-supported for use for which indications (previously all agents were covered for all indications). Changed auth duration for radiation-induced nausea vomiting from 72 hours to 48 hours based on Zuplenz dosing recommendations.	02.08.18	