

Clinical Policy: Oral Antiemetics (5-HT3 Antagonists)

Reference Number: CP.PMN.11

Effective Date: 09.01.06

Last Review Date: 05.18

Line of Business: Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

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(s)

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 (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that 5-HT3 receptor antagonist oral antiemetics are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chemotherapy-Induced Nausea and Vomiting (must meet all):

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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 \geq 18 years (Akynzeo, Kytril, Zuplenz) or \geq 2 years (Anzemet);
3. Member meets one of the following:
 - a. For Anzemet, Kytril, and Zuplenz: Failure of a trial of ondansetron in the last 60 days 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 in the last 60 days 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 chemotherapy up to 72 hours after completion of chemotherapy

B. Postoperative Nausea/Vomiting (must meet all):

1. Prescribed for prevention of postoperative nausea/vomiting;
2. Request is for Zuplenz;
3. Age \geq 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 \geq 18 years;
4. Failure of ondansetron in the last 60 days at maximum indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed one of the following:

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- 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

1. Refer to 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- or Radiation-Induced Nausea and Vomiting (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Documentation supports that member is currently receiving chemotherapy or radiation therapy;
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 chemotherapy 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:

1. Reauthorization is not permitted. Members will need to be re-evaluated against the initial approval criteria.

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 3 months (whichever is less); or

2. Refer to CP.PMN.53 if requested indication is NOT listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 - CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation Key

5-HT3: serotonin 5-hydroxytryptamine, type 3

FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ondansetron (Zofran [®] , Zofran [®] ODT)	<p>For prevention of chemotherapy-induced nausea/vomiting</p> <p><u>For moderately emetogenic chemotherapy:</u> 8 mg PO BID. Give first dose 30 minutes before the start of emetogenic chemotherapy, with a subsequent dose 8 hours after the initial dose. Further doses may be given every 12 hours for 1 to 2 days after completion of chemotherapy</p> <p><u>For highly emetogenic chemotherapy:</u> 24 mg PO once given 30 minutes before administration of single-day highly emetogenic chemotherapy</p> <p>Postoperative Nausea/Vomiting 16 mg PO as a single dose given 1 hour before anesthesia induction</p> <p>Radiation-Induced Nausea and Vomiting <i>For radiotherapy:</i> 8 mg PO TID</p> <p><i>For total body irradiation:</i> 8 mg PO 1 to 2 hours prior to each fraction of radiotherapy each day</p>	24 mg/day PO
aprepitant (Emend [®])	<p>For prevention of chemotherapy-induced nausea/vomiting</p> <p>On Day 1, give 125 mg PO 1 hour before chemotherapy. On Days 2 and 3, give 80 mg PO 1 hour before chemotherapy or if no chemotherapy is scheduled on Days 2 and 3, administer in the morning</p>	125 mg/day PO

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

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
Dolasetron (Anzemet)	Tablets: 50 mg, 100 mg
Netupitant/palonosetron (Akynzeo)	Capsule: 300 mg/0.5 mg
Granisetron (Kytril)	Tablet: 1 mg
Ondansetron (Zuplenz)	Oral soluble film: 4 mg, 8 mg

VII. References

1. Clinical Pharmacology. Tampa, FL: Gold Standard; 2018. Available at www.clinicalpharmacology.com. Accessed February 6, 2018.
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4. Anzemet Prescribing Information. Bridgewater, NJ: Sanofi-Aventis; October 2014. Available at <https://dailymed.nlm.nih.gov>. Accessed February 6, 2018.

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5. Granisetron Prescribing Information. Columbus, OH: Roxane Laboratories, Inc.; March 2016. Available at <https://dailymed.nlm.nih.gov>. 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>.
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Reviews, Revisions, and Approvals	Date	P&T Approval Date
References updated. Removed ondansetron from policy since it is a preferred agent.	12.14	12.14
Guideline converted to new template; Approval criteria for covered diagnosis clarified and reworded; Added that ondansetron must have been used in the last 60 days for chemo/radiation therapy, and within the last 10 days for post-operative nausea/vomiting; For renewal: added that documentation of chemotherapy/ radiation therapy is required; Clarified that renewal for post-operative nausea and vomiting will not be approved; Reviewed and updated references.	11.15	11.15
Converted to new integrated template; removed all references to Sancuso as it is not an oral antiemetic; references updated.	08.16	11.16
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.	09.05.17	11.17
2Q 2018 annual review: added aprepitant as a step therapy requirement for Akynzeo; references reviewed and updated.	02.08.18	05.18

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program

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approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence.

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Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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