

Drug Therapy Guidelines

Antiemetic Agents:
 Zofran®/ODT® (ondansetron/ondansetron ODT/ondansetron oral solution), Zuplenz® (ondansetron oral film), Kytril® (granisetron), granisetron, Sancuso® (granisetron topical), Anzemet® (dolasetron), Emend® (aprepitant), Akynzeo® (netupitant/palonosetron), Varubi® (rolapitant)

Applicable

Medical Benefit		Effective: 6/15/18
Pharmacy- Formulary 1	x	Next Review: 6/19
Pharmacy- Formulary 2	x	Date of Origin: 4/99
Pharmacy- Formulary 3/Exclusive	x	Review Dates: 4/99, 10/00, 9/01, 9/02, 10/03, 9/04, 8/05, 8/06, 11/07, 12/08, 7/09, 12/09, 6/10, 9/10, 6/11, 6/12, 6/13, 6/14, 6/15, 6/16, 6/17, 6/18
Pharmacy- Formulary 4/AON	x	

I. Medication Description

Ondansetron, granisetron, and dolasetron are selective serotonin 5-HT₃ receptor antagonists. 5-HT₃ receptors are found centrally in the chemoreceptor trigger zone and peripherally at vagal nerve terminals in the intestines. Emesis during chemotherapy and radiation therapy appears to be associated with the release of serotonin from enterochromaffin cells in the small intestine. Blocking these nerve endings in the intestines prevents signals to the central nervous system.

Aprepitant, netupitant, and rolapitant are selective high-affinity antagonists of human substance P/neurokinin 1 (NK₁) receptors. They have little or no affinity for serotonin (5-HT₃), dopamine, and corticosteroid receptors, the targets of existing therapies for chemotherapy-induced nausea and vomiting (CINV) and postoperative nausea and vomiting (PONV).

II. Position Statement

For all formularies, prescriptions for ondansetron (4 mg and 8 mg regular or orally disintegrating tablets) for quantities up to 90 tablets per each 30 days will not require prior authorization.

For Formularies 1, 2, 3, and 4, prior authorization is not required if the quantity requested falls within limits outlined below **AND** one of the following:

- Medication is prescribed by an oncologist (including therapeutic radiology, hematology, radiation oncology, oncology, pediatric hematology-oncology, surgical oncology, hematology-oncology, gynecology-oncology, nurse practitioner- hematology, nurse practitioner- oncology) **OR**
- Member has a paid claim for a cancer drug in the past 30 days of their prescription drug history

Coverage is determined through a prior authorization process for all other requests.

III. Policy

- **Coverage of Zofran/ondansetron solution, Kytril, granisetron, and Anzemet** may be provided for the following indications:
 - Prevention of nausea and vomiting associated with initial and repeat courses of emetogenic chemotherapy

- Prevention of nausea and vomiting associated with highly emetogenic chemotherapy, including high dose cisplatin
- Prevention and treatment of nausea and vomiting associated with radiation
- Prevention and treatment of post-operative nausea and vomiting
- **Coverage of Zuplenz** will be provided when the following criteria are met:
 - When requesting coverage of a brand medication for which an A/B rated generic is available, there is sufficient evidence that the use of the A/B rated generic equivalent has resulted in inadequate results **AND**
 - The member is unable to take plan-preferred medications (ondansetron tablets or ondansetron ODT) **OR** when at least ONE of the following criteria have been met:
 - The plan-preferred medications are contraindicated or will likely cause an adverse reaction by or physical or mental harm to the member.
 - The plan-preferred medications are expected to be ineffective based on the known clinical history and conditions of the member and the member's prescription drug regimen.
 - The member has tried the plan-preferred medications or another prescription drug in the same pharmacologic class or with the same mechanism of action and such prescription drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event.
 - The member is stable on the medication selected by their healthcare professional for the medical condition under consideration (where "stable" is defined as receiving the medication for an adequate period of time, have achieved optimal response, and continued favorable outcomes are expected UNLESS the medication was initially selected solely due to the availability of a drug sample or a coupon card and the member does not otherwise meet the definition of "stable").
 - The plan-preferred medication is not in the best interest of the member because it will likely cause a significant barrier to the member's adherence or to compliance with the member's plan of care, will likely worsen a comorbid condition of the member, or will likely decrease the member's ability to achieve or maintain reasonable functional ability in performing daily activities.
- **Coverage of Sancuso** will be provided for prevention of nausea and vomiting associated with moderately and/or highly emetogenic chemotherapy regimens of up to 5 consecutive days.
- **Coverage of Akynzeo or Varubi for CINV prophylaxis OR Emend for CINV or PONV prophylaxis** will be provided when the following criteria are met:
 - When requesting coverage of a brand medication for which an A/B rated generic is available, there is sufficient evidence that the use of the A/B rated generic equivalent has resulted in inadequate results **AND**
 - The member has previously failed a trial with a plan-preferred medication (5HT₃ antagonist) **OR** when at least ONE of the following criteria have been met:
 - The plan-preferred medications are contraindicated or will likely cause an adverse reaction by or physical or mental harm to the member.
 - The plan-preferred medications are expected to be ineffective based on the known clinical history and conditions of the member and the member's prescription drug regimen.
 - The member has tried the plan-preferred medications or another prescription drug in the same pharmacologic class or with the same mechanism of action and such prescription drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event.
 - The member is stable on the medication selected by their healthcare professional for the medical condition under consideration (where "stable" is defined as receiving the medication for an adequate period of time, have achieved optimal response, and continued

favorable outcomes are expected UNLESS the medication was initially selected solely due to the availability of a drug sample or a coupon card and the member does not otherwise meet the definition of “stable”).

- The plan-preferred medication is not in the best interest of the member because it will likely cause a significant barrier to the member’s adherence or to compliance with the member’s plan of care, will likely worsen a comorbid condition of the member, or will likely decrease the member’s ability to achieve or maintain reasonable functional ability in performing daily activities.

IV. Quantity Limitations

The quantities of tablets, capsules or packs that may be received at one time (amount dispensed per copay, per fill) are outlined below:

- Akynzeo: 1 capsule
- Anzemet: 7 tablets
- Emend:
 - 40mg: 1 capsule
 - 80mg: 8 capsules
 - 125mg: 2 capsules
 - Trifold packs: 2 packs
 - 125mg powder for oral suspension: 2 cartons
- Kytril/granisetron: 14 tablets
- Ondansetron/ODT, Zofran/ODT:
 - 4mg: 90 tablets
 - 8mg: 90 tablets
 - 24mg: 7 tablets
 - 4mg/5ml solution: 100ml
- Sancuso: 2 patches
- Varubi: 2 tablets
- Zuplenz: 21 films

V. Coverage Duration

Timeframe for approvals will vary based on member’s diagnosis and the medication requested.

VI. Coverage Renewal Criteria

Coverage may be renewed based on original prior authorization criteria and documentation that member has received clinical benefit from the drug.

VII. Billing/Coding Information

- Ondansetron/Zofran 4 mg, 8 mg, 24 mg tablets
- Ondansetron ODT/Zofran ODT 4 mg, 8 mg tablets
- Ondansetron/Zofran oral solution 4 mg/5ml (50 ml bottle)
- Zuplenz (ondansetron soluble film) 4mg, 8 mg
- Sancuso (granisetron transdermal – 34.3 mg)
- Kytril/Granisetron 1 mg tablets

- Anzemet 50mg, 100mg tablets
- Akynzeo (300mg netupitant/0.5mg palonosetron) capsules
- Varubi 90mg tablets
- Emend 40mg capsules, 80mg capsules, 125mg capsules, 125mg and 80mg Tripack, 125mg powder for oral suspension

VIII. Summary of Policy Changes

- 9/1/11:
 - Removal of ondansetron ODT from prior authorization in quantities up to 21 tablets per fill
 - Addition of specific dosage and administration information for each medication
 - Addition of Contraindication for dolasetron injection
- 9/15/12: Increase quantities of ondansetron/ODT 4mg and 8mg tablets to up to 90 tablets per fill without need for prior authorization due to decreasing cost of generic
- 9/15/13:
 - Apomorphine contraindication added
 - Emend-CYP3A4 interacting drugs added
 - Removed the term “cancer” to describe chemotherapy in Section III
- 9/15/14:
 - clarified when prior authorization is required on each benefit
 - Granisol added to policy
- 12/29/14: Akynzeo added to policy
- 7/1/15: formulary distinctions made
- 9/15/15: no policy changes
- 9/21/15: Varubi added to policy
- 7/19/16: updated Emend formulations
- 11/7/16: updated with new Emend formulations
- 5/1/17:
 - step therapy criteria added
 - removed Granisol as product is off-market
- 6/21/17: no policy changes
- 6/15/18: no policy changes

IX. References

1. Clinical Pharmacology. Tampa, FL: Gold Standard, Inc, Accessed 3/2018.
2. Micromedex (Thomson Healthcare), Accessed 3/2018.
3. Anzemet® (Prescribing information), Sanofi-Aventis, Revised 6/2016.
4. Emend® (Prescribing information), Merck, Revised 5/2017.
5. Kytril® (Prescribing information), Genentech/Roche, April 2011.
6. UpToDate online, Hyperemesis gravidarum, Accessed 7/2005.
7. Zofran® (Prescribing information), Glaxo Smith Kline, Revised 10/2017.
8. Sancuso® (Prescribing information), ProStrakan, Revised 1/2017.
9. Zuplenz® (Prescribing information), Praelia Pharmaceuticals. Revised 9/2014.
10. Granisol™ (Prescribing information), Therapax. Revised 11/2010.
11. Akynzeo® (Prescribing Information), Eisai Inc. Revised 12/2016.
12. Varubi package insert. Waltham, MA; Tesaro, Inc.; Revised 3/2018.

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary medication will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.