Effective Date: 12/02/2020
Last P&T Approval/Version: 01/26/2022
Next Review Due By: 01/2023
Policy Number: C20780-A

Antiemetics

PRODUCTS AFFECTED

Akynzeo (fosnetupitant/palonosetron; netupitatnt/palonosetron), Aloxi (palonosetron), aprepitant, Emend (aprepitant/fosaprepitant), Cinvanti (aprepitant), fosaprepitant, granisetron, Sancuso (granisetron) patch, Sustol(granisetron) PFS, Varubi (rolapitant)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
Acute and delayed chemotherapy-induced nausea/vomiting associated with initial and repeat courses of cancer chemotherapy, Chemotherapy-induced nausea/vomiting prophylaxis, Post-operative nausea/vomiting (PONV) prophylaxis

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review
A. FOR CHEMOTHERAPY INDUCED NAUSEA/VOMITING PROPHYLAXIS:
1. Documentation of the treatment plan including the names all of chemotherapy and or radiation agents; frequency; length, cycle and duration of therapy

AND

3. Product being request has an FDA labeled indication or compendia support use for diagnosis, age, and dose
   AND.
4. Prescriber attests that medication will be used in combination (when indicated per FDA label or guideline) with other antiemetic agents (5HT3 antagonist) OR used in combination with corticosteroid such a dexamethasone, unless documentation of contraindication to dexamethasone is provided, per FDA label or NCCN guideline and will NOT be used with additional agents if FDA label or guideline does not support concurrent therapy
   AND
5. Prescriber attests to review of concurrent medication therapy for drug-drug interactions
   AND
6. FOR ALOXI ONLY: FOR HIGH EMETIC IV CHEMOTHERAPY AND CONCURRENTLY RECEIVING APREPITANT OR FOSAPREPITANT ONLY: Documentation of trial and failure or labeled contraindication of preferred serotonin-receptor antagonists (ondansetron and IV granisetron)
   AND
7. FOR SANCUSO AND SUSTOL: Documentation of trial and failure or labeled contraindication of preferred serotonin-receptor antagonist [ondansetron and granisetron (any dosage form)]
   AND
8. FOR VARUBI ONLY: (a)Documentation that the member has experienced inadequate response or contraindication to aprepitant/ foasaprepitant AND generic oral ondansetron OR generic oral granisetron with dexamethasone AND (b) Prescriber attests that Varubi (rolapitant) will not be administered any less than a 2-week interval between doses

   (NOTE: the proper succession for these criteria can be found within compendia monographs, FDA label or NCCN guidelines; IF compendia monographs, FDA label or NCCN guidelines have aformulary/preferred product at therapeutic parity with requested agent a formulary/preferred product should be used first where state regulations allow) Molina reviewers and delegates will comply with all regulations and requirements applicable to the review of the request, providing exception to our standard criteria as may be required under state regulations and requirements.

B .FOR POST-OPERATIVE NAUSEA/VOMITING PROPHYLAXIS:

1. Documentation of expected surgery date (within the next 30 days)
   AND
2. Product being request has an FDA labeled indication or compendia support use for diagnosis, age and dose
   AND
3. Prescriber attestation to a historical trial and failure or labeled contraindication to preferred serotonin-receptor antagonists (ondansetron and IV granisetron) *

CONTINUATION OF THERAPY:

A. CHEMOTHERAPY INDUCEDNAUSEA/VOMITTING (PROPHYLAXIS):

1. Documentation of continuation of chemotherapy requiring antiemetics.
   AND
2. Documentation that the member has not developed any contraindications or other significant adverse drug effects (hypersensitivity reactions, serotonin syndrome).

B. FOR POST-OPERATIVE NAUSEA/VOMITING PROPHYLAXIS: N/A MUST SUBMITNEW REQUEST

DURATION OF APPROVAL:

Post-Operative nausea/vomiting prophylaxis: one-time authorization

All other indications: Initial authorization: 3 months (or length of chemotherapy or radiation therapy, whichever is shorter)
Continuation of Therapy: 6 months (or length of chemotherapy or radiation, whichever is shorter)

PRESCRIBER REQUIREMENTS:
No requirements

AGE RESTRICTIONS:
Akynzeo (fosnetupitant/palonosteron; netupitant/palonosetron):18 years of age or older
Aloxi (palonosetron): moderately emetogenic cancer chemotherapy (MEC) or postoperative nausea and vomiting (PONV) for up to 24 hours following surgery: 18 years and older
Highly emetogenic cancer chemotherapy (MEC): 1 month of age and older
Emend oral suspension or injection: age ≥ 6 months;
Emend capsules: age ≥ 12 years;
Cinvanti: age ≥ 18 years
Granisetron: 2 years of age and older,
Sustol- 18 years of age and older
Sancuso- ages 18 through 64 years of age
Varubi(rolapitant)- 18 years of age and older

QUANTITY:
Akynzeo (fosnetupitant/palonosteron; netupitant/palonosetron): Maximum 1 day per cycle of chemotherapyAloxi (palonosetron): FOR CHEMOTHERAPY INDUCED NAUSEA/VOMITING PROPHYLAXIS:
(0.25mg/5ml) 1 vials per 7-day supply FOR POST-OPERATIVE NAUSEA/VOMITINGPROPHYLAXIS: 0.075mg approved ONCE per authorization
Emend (aprepitant capsules)- Prevention of Nausea and Vomiting Associated with Cancer Chemotherapy- oral suspension or capsules: Dose does not exceed 125 mg on Day 1, followed by 80mg on Days 2 and 3 per chemotherapy cycle; injection: 150 mg on Day 1; [doses are weight based and should follow FDA label for members 6 months to 12 years of age]
Emend (aprepitant capsules)- Prevention of Postoperative Nausea and Vomiting: Dose does not exceed 40 mg(1 capsule) once.
Cinvanti: 130 mg on Day 1 for HEC and MEC (single-dose regimen), or 100 mg on Day 1 for MEC(3-day regimen).
Granisetron tablets: up to a maximum of 60 tablets/30 days
Sustol(granisetron ER inj.), Sancuso (granisetron patches) and granisetron injection- quantity not to exceedFDA label per indication

Varubi (rolapitant)- maximum quantity of 180 mg on day 1 of chemo every 14 days
Quantities above the program set limit will be approved when ONE of the following is met:

1. *The member has cancer chemotherapy related nausea and vomiting and will be receiving chemotherapy more than 7 days per month*
   OR
2. *The member has delayed emesis in highly emetogenic chemotherapy*
   OR
3. *The member has radiation therapy induced nausea and vomiting and radiation treatment that extends beyond 7 days per month*
   OR
4. *The prescriber has submitted documentation in support of the requested therapeutic use and quantity for the requested medication which has been reviewed and approved by the Clinical Review pharmacist*

PLACE OF ADMINISTRATION:

The recommendation is that oral and transdermal medications in this policy will be for pharmacy benefit coverage and patient self-administered.

The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-inpatient hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral, Intravenous, Transdermal

DRUG CLASS:

Antiemetics

FDA-APPROVED USES:

AKYNZEO **capsules** is indicated:

in combination with dexamethasone in adults 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.

AKYNZEO **for injection** are indicated:

combination with dexamethasone in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy.

Limitations of Use

AKYNZEO for injection and AKYNZEO injection have not been studied for the prevention of nausea and vomiting associated with anthracycline plus cyclophosphamide chemotherapy.

ALOXI (palonosetron)indicated in:

Adults for prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately and highly emetogenic cancer chemotherapy (MEC) or (HEC), postoperative nausea and vomiting (PONV) for up to 24 hours following surgery. *Efficacy beyond 24 hours has not been demonstrated*

Pediatric patients aged 1 month to less than 17 years for prevention of: acute nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including highly emetogenic cancer chemotherapy (HEC)

Sancuso (granisetron) is indicated:

prevention of nausea and vomiting in adults receiving moderately and/or highly emetogenic chemotherapy for up to 5 consecutive days.

SUSTOL (granisetron) ER inj. is indicated :

in combination with other antiemetics in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy (MEC) or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens.

CINVANTI indicated:

in adults, in combination with other antiemetic agents, for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin and nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). *Limitations of Use: CINVANTI has not been studied for treatment of established nausea and vomiting.*

EMEND for **oral suspension** is indicated:

in combination with other antiemetic agents, in patients **6 months of age and olde**r for prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin or moderately emetogenic cancer chemotherapy (MEC)

EMEND **capsules** is indicated: in combination with other antiemetic agents, in patients **12 years of age and older** for prevention of: acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin or moderately emetogenic cancer chemotherapy (MEC)
Limitations of Use: EMEND has not been studied for treatment of established nausea and vomiting. Chronic continuous administration of EMEND is not recommended.

EMEND for **injection** is indicated: in adults, in combination with other antiemetic agents, for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin or moderately emetogenic cancer chemotherapy (MEC)

VARUBI is indicated in combination with other antiemetic agents in adults for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy

GRANISETRON is indicated for:
Prevention of nausea and/or vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin and prevention and treatment of postoperative nausea and vomiting in adults.

COMPENDIAL APPROVED OFF-LABELED USES:
GRANISETRON is indicated for: post-operative nausea/vomiting (PONV) prophylaxis and treatment

APPENDIX

APPENDIX:
Antiemetics: ASCO Guideline Update J Clin Oncol 38:2782-2797. © 2020 by American Society of Clinical Oncology

Emetic Risk of Single Intravenous Antineoplastic Agents in Adults

Risk Level High (>90%)

- Anthracycline/cyclophosphamide combination
- Carmustine
- Cyclophosphamide > 1,500 mg/m2
- Dacarbazine
- Mechlorethamine
- Streptozocin

Moderate (30%-90%)

- Alemtuzumab
- Arsenic trioxide
- Azacitidine
- Bendamustine
- Busulfan
- Carboplatin
- Clofarabine
- Cyclophosphamide, 1,500mg/m2
- Cytarabine 1,000 mg/m2
- Daunorubicin
- Daunorubicin and cytarabineliposome
- Doxorubicin
- Epirubicin
- Fam-trastuzumabderuxtecan-nxki
- Idarubicin
- Ifosfamide
- Irinotecan
- Irinotecan liposomal injection
- Oxaliplatin
- Romidepsin
- Temozolomidea
- Thiotepab
- Trabected

Low (10%-30%)

- Aflibercept
- Axicabtagene ciloleucel
- Belinostat
- Blinatumomab
- Bortezomib
- Brentuximab
- Cabazitaxel
- Carfilzomib
- Catumaxumab
- Cetuximab
- Copanlisib
- Cytarabine # 1,000 mg/m2
- Decitabine
- Docetaxel
- Elotuzumab
- Enfortumab vedotin-ejfv
- Eribulin
- Etoposide
- Fluorouracil
- Gemcitabine
- Gemtuzumab ozogamicin
- Inotuzumab ozogamicin
- Ixabepilone
- Methotrexate
- Mitomycin
- Mitoxantrone
- Moxetumomab
- pasudotox
- Nab-paclitaxel
- Necitumumab
- Nelarabine
- Paclitaxel
- Panitumumab
- Pegylated
- liposomal
- doxorubicin
- Pemetrexed
- Pertuzumab
- Tagraxofusp-erzs
- Temsirolimus
- Tisagenlecleucel
- Topotecan
- Trastuzumab-emtansine
- Vinflunine

Minimal (<10%)

- Atezolizumab
- Avelumab
- Bevacizumab
- Bleomycin
- Cemiplimab
- Chlorodeoxyadenosine
- Cladribine
- Daratumumab
- Durvalumab
- Emapalumab
- Fludarabine
- Ipilimumab
- Nivolumab
- Obinutuzumab
- Ofatumumab
- Pembrolizumab
- Pixantrone
- Polatuzumab vedotin
- Pralatrexate
- Ramucirumab
- Rituximab
- Trastuzumab
- Vinblastine
- Vincristine
- Vinorelbine

Moderate or high (≥ 30%)

- Abemaciclib
- Avapritinib
- Bosutinib
- Cabozantinib
- Ceritinib
- Crizotinib
- Cyclophosphamide
- Enasidenib
- Fedratinib
- Hexamethylmelamine
- Imatinib
- Lenvatinib
- Lomustine
- Midostaurin
- Niraparib
- Procarbazine
- Ribociclib
- Rucaparib
- Selinexor
- TAS-102 (trifluridine-tipiracil)
- Temozolomide
- Vinorelbine

Minimal or low (< 30%)

- 6-Thioguanine
- Acalabrutinib
- Afatinib
- Alectinib
- Alpelisib
- Axitinib
- Bexarotene
- Lapatinib
- Larotrectinib
- Lenalidomide
- Lorlatinib
- Melphalan
- Methotrexate
- Neratinib

Brigatinib
Capecitabine
Chlorambucil
Cobimetinib
Dabrafenib
Dacomitinib
Dasatinib
Duvelisib
Encorafenib
Entrectinib
Erdafitinib
Erlotinib
Estramustine
Etoposide
Everolimus
Fludarabine
Gefitinib
Gilteritinib
Glasdegib
Hydroxyurea
Ibrutinib
Idelalisib
Ivosidenib
Ixazomib
Nilotinib
Olaparib
Osimertinib
Palbociclib
Panobinostat
Pazopanib
Pexidartinib
Pomalidomide
Ponatinib
Regorafenib
Ruxolitinib
Sonidegib
Sorafenib
Sunitinib
Talazoparib
Tazemetostat
Tegafur-Uracil
Thalidomide
Topotecan
Trametinib
Vandetanib
Vemurafenib
Venetoclax
Vismodegib
Vorinostat
Zanubrutinib

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
None

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of antiemetics are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Akynzeo is not indicated for nausea and vomiting not due to cancer chemotherapy, nausea and omitting of pregnancy, hyperemesis gravidarum, prevention and/or treatment of postoperative nausea and vomiting. Aloxi (palonosetron) is contraindicated in patients who have known hypersensitivity topalonosetron or any component of the formulation
Aprepitant; fosaprepitant is contraindicated with pimozide

OTHER SPECIAL CONSIDERATIONS:
Akynzeo (fosnetupitant/palonosetron; netupitatnt/palonosetron): Avoid use in severe hepatic impairment. Avoid use in severe renal impairment or end stage renal disease. Netupitant is a moderate inhibitor of CYP3A4. Use caution with drugs metabolized by CYP3A4

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J1454	Injection, fosnetupitant 235mg/ palonosetron 0.25mg
J8655	Netupitant 300mg/ palonosetron 0.5mg, oral

J2469	Injection, palonosetron, 25mcg
J0185	Injection, aprepitant, 1 mg
J1453	Injection, fosaprepitant, 1 mg

AVAILABLE DOSAGE FORMS:
Sancuso PTCH 3.1MG/24H (granisetron TD Patch 3.1 MG/24HR (Contains 34.3 MG), Sustol PRSY 10MG/0.4ML(granisetron Extended Release Inj Prefilled Syr 10 MG/0.4ML, Granisetron HCl TABS 1MG, Granisetron HCl SOLN 1MG/ML, Ondansetron Orally Disintegrating Tab 4 MG , Aloxi SOLN 0.25MG/5ML, Palonosetron HCl SOLN 0.25MG/5ML, Emend CAPS 40MG, Aprepitant CAPS 40MG, Emend CAPS 80MG, Aprepitant CAPS 80MG, Aprepitant CAPS 125MG, Cinvanti EMUL 130MG/18ML, Emend SUSR 125MG/5ML, Emend Tri-Pack CAPS 80 & 125MG, Aprepitant CAPS 80 & 125MG, Emend SOLR 150MG, Fosaprepitant Dimeglumine SOLR 150MG, Varubi (180 MG Dose) TBPK 2 x 90MG, Akynzeo SOLN 235-0.25MG/20ML, Akynzeo SOLR 235-0.25MG, Akynzeo CAPS 300-0.5MG

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