Pharmacy Medical Necessity Guidelines: Anti-emetic Medications

Effective: November 12, 2024

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	√
Pharmacy (RX) or Medical (MED) Benefit	RX	Department to Review	RXUM
These pharmacy medical necessity guidelines apply to the following: ☒ Tufts Health RITogether – A Rhode Island Medicaid Plan		**Fax Numbers:** RXUM: 617.673.0939	

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

OVERVIEW

FOOD AND DRUG ADMINISTRATION-APPROVED INDICATIONS

Syndros (dronabinol oral solution) is a cannabinoid indicated in adults for the treatment of anorexia associated with weight loss in patients with AIDS. It is also approved for the treatment of nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic therapies. Dronabinol is available as capsules and oral solution. Dronabinol capsules are the preferred formulation for RITogether.

Diclegis (doxylamine/pyridoxine) and Bonjesta (doxylamine/pyridoxine ER) are indicated for the treatment of nausea and vomiting of pregnancy in women who do not respond to conservative management.

Anzemet (dolasetron) tablet is a 5-HT_3 antagonist indicated for the prevention of nausea and vomiting associated with moderately emetogenic chemotherapy in adults and children 2 years of age and older.

Aprepitant capsule is a substance P/neurokinin 1 (NK_1) receptor antagonist 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 chemotherapy (including high-dose cisplatin), and nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy. The capsules are also approved for prevention of postoperative nausea and vomiting (PONV) in adults. Aprepitant capsule is the preferred NK1 receptor antagonist for RITogether and is covered without Prior Authorization.

Emend oral suspension (aprepitant) is indicated in combination with other antiemetic agents, in patients 6 months of age and older, for prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin. It is also approved for the prevention of nausea and vomiting associated with initial and repeat courses of moderately emetogenic chemotherapy.

Akynzeo (netupitant/palonosetron) oral capsule is a fixed combination of an NK_1 receptor antagonist and a serotonin-3 ($5HT_3$) receptor antagonist indicated in combination with dexamethasone 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. Oral palonosetron prevents nausea and vomiting during the acute phase and netupitant prevents nausea and vomiting during both the acute and delayed phase after cancer chemotherapy. Akynzeo capsule is administered approximately one hour prior to the start of chemotherapy.

Sancuso (granisetron) transdermal is a 5-HT_3 receptor antagonist indicated for the prophylaxis of nausea and vomiting associated with moderately or highly emetogenic chemotherapy for up to five consecutive days.

Varubi (rolapitant) tablet is an NK_1 receptor antagonist 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.

The American Society of Clinical Oncology (ASCO) established a grading system to determine the likelihood of emesis following treatment with a chemotherapeutic regimen. Guidelines for the treatment of chemotherapy induced nausea and vomiting (CINV) are based on the emetogenicity of the treatment regimen. The 2020 ASCO antiemesis guidelines recommend the use of an NK_1 receptor antagonist in combination with a 5-HT_3 receptor antagonist, dexamethasone, and olanzapine for adult patients on antineoplastic agents with high-emetic risk. Adult patients being treated with a moderately emetogenic

chemotherapy regimen should be treated with a 5-HT_3 receptor antagonist and dexamethasone. However, patients being treated with carboplatin area under the curve (AUC) ≥ 4 mg/mL/min should be treated with an NK_1 receptor antagonist, a 5-HT_3 receptor antagonist, and dexamethasone. A single dose of a 5-HT_3 receptor antagonist or a single 8-mg dose of dexamethasone prior to chemotherapy is suggested for patients being treated with regimen with low emetogenic potential. The table below lists the level of emetogenicity of intravenous antineoplastic agents in adults. Emetogenicity is based on chemotherapeutic drug and dose. For multi-drug regimens with varying levels of emetogenicity, the overall emetogenicity of the regimen is based on the drug component with the greatest emetic risk.

Level of Emetogenicity	Chemotherapeutic Drug and Dose	
High (>90%)	Anthracycline/cyclophosphamide Carmustine Cisplatin Cyclophosphamide ≥ 1500 mg/m^2	Dacarbazine Mechlorethamine Streptozocin
Moderate (30-90%)	Alemtuzumab Arsenic trioxide Azacitidine Bendamustine Carboplatin† Clofarabine Cyclophosphamide < 1500 mg/m^2 Cytarabine > 1000 mg/m^2 Daunorubicin* Daunorubicin and cytarabine liposome	Doxorubicin* Epirubicin* Idarubicin* Ifosfamide Irinotecan Irinotecan liposomal injection Oxaliplatin Romidepsin Temozolomide Thiotepa Trabectedin
Low (10-30%)	Aflibercept Axicabtagene ciloleucel Belinostat Blinatumomab Bortezomib Brentuximab Cabazitaxel Carfilzomib Catumaxumab Cetuximab Copanlisib Cytarabine ≤ 1000 mg/m^2 Decitabine Docetaxel Eribulin Etoposide Fluorouracil Gemcitabine Gemtuzuab ozogamicin	Inotuzumab ozogamicin Ixabepilone Methotrexate Mitomycin Mitoxantrone Moxetumomab pasudotox Necitumumab Nelarabine Paclitatel and nab-paclitaxel Panitumumab Pegylated liposomal doxorubicin Pemetrexed Pertuzumab Tagraxofusp-erzs Temsirolimus Tisagenlecleucel Topotecan Trastuzumab emtansine Vinflunine
Minimal (<10%)	Atezolizumab Avelumab Bevacizumab Bleomycin Busulfan Cemiplimab 2-Chlorodeoxyadenosine Cladribine Daratumumab Darvalumab Emapalumab Fludarabine Iplimumab	Pembrolizumab Pixantrone Pralatrexate Nivolumab Obinutuzumab Ofatumumab Ramucirumab Rituximab Trastuzumab Vinblastine Vincristine Vinorelbine

*When combined with cyclophosphamide, these agents are designated as having high emetogenic potential.
†Patients treated with carboplatin ≥ 4 AUC should be treated with an NK_1 receptor antagonist, and 5-HT_3 receptor antagonist, and dexamethasone.

COVERAGE GUIDELINES

The plan may authorize coverage of a non-preferred anti-emetic medication for Members when **ALL** the following criteria are met:

Anzemet (dolasetron) tablet

1. The member is being treated with chemotherapy that has moderate or high emetogenic potential

AND

2. The member has had an inadequate response, adverse reaction, or contraindication to a trial with generic ondansetron and generic granisetron

Aprepitant oral solution (Emend)

1. The member is being treated with chemotherapy that has moderate or high emetogenic potential, as defined by American Society of Clinical Oncology (ASCO)

AND

2. The member is unable to administer aprepitant capsules due to swallowing difficulties **OR** the member is 6 months through 11 years of age

Doxylamine/pyridoxine (Diclegis)

1. The Member is diagnosed with nausea and vomiting associated with pregnancy

AND

2. The Member had an inadequate response to concurrent therapy with over-the counter doxylamine and pyridoxine, or the provider indicates clinical inappropriateness of treatment with the concurrent use of over-the counter doxylamine and pyridoxine

Doxylamine/pyridoxine ER (Bonjesta)

1. The Member is diagnosed with nausea and vomiting associated with pregnancy

AND

2. The Member had an inadequate response to concurrent therapy with over-the counter doxylamine and pyridoxine, or the provider indicates clinical inappropriateness of treatment with the concurrent use of over-the counter doxylamine and pyridoxine

AND

3. The Member has had an inadequate response to Diclegis (doxylamine/pyridoxine)

Dronabinol oral solution (Syndros)

1. The Member has one of the following diagnoses:
   a. Anorexia associated with weight loss in patients with AIDS
   b. Nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments

AND

2. Provider indicates a clinical rationale why the Member is unable to administer generic dronabinol oral capsules (e.g., swallowing difficulties)

Granisetron transdermal (Sancuso)

1. The member has had an inadequate response or intolerance to generic ondansetron and generic granisetron

OR

The member is unable to administer or had an inadequate response to generic ondansetron oral dispersible tablet (ODT)

Netupitant/palonosetron (Akynzeo) capsule, Rolapitant (Varubi) tablet

1. The member is being treated with chemotherapy that had moderate or high emetogenic potential, as defined by American Society of Clinical Oncology (ASCO)

AND

2. The member has had an inadequate response, intolerance, or contraindication to a trial of aprepitant oral capsule in combination with a serotonin antagonist (e.g., ondansetron, granisetron) and dexamethasone

LIMITATIONS

1. Akynzeo (netupitant/palonosetron) capsule is limited to one capsule per prescription.
2. Anzemet (dolasetron) 50 mg tablet is limited to 5 tablets per fill.
3. Aprepitant capsule is limited to 6 capsules per fill.
4. Emend (aprepitant) oral solution is limited to 3 units per 7 days.
5. Sancuso (granisetron) is limited to one transdermal patch per 7 days, not to exceed 4 patches per 28 days.
6. Varubi (rolapitant) tablet is limited to 6 tablets every 30 days and 2 tablets per fill.
7. Approval duration of Diclegis (doxylamine/pyridoxine) and Bonjesta is nine months.

CODES

None

REFERENCES

1. Akynzeo (netupitant and palonsetron) [prescribing information]. Iselin, NJ: Helsinn Therapeutics; Decembersanc 2023.
2. Anzemet (dolasetron) [prescribing information]. Parisppany, NJ: Validus Pharmaceuticals LLC; December 2023.
3. Aprepitant capsule [prescribing information]. Basking Ridge, NJ: Torrent Pharma Inc.; September 2022.
4. Bonjesta (doxyamine/pyridoxine ER) [prescribing information]. Princeton, NJ: Duchesnay USA, Inc; July 2023.
5. Diclegis (doxylamine/pyridoxine) [package insert]. Princeton, NJ: Duchesnay USA, Inc.; June 2023.
6. Emend (aprepitant) [package insert]. Rahway, NJ: Merch Sharp & Dohme LLC; July 2024.
7. Hesketh PJ, Kris MG, Basch E, et al. Antiemetics: ASCO guideline update. *J Clin Oncol*. 2020;38(24):2782-2797.
8. Koren G, Clark S, Hankins GDV, et al. Effectiveness of delayed-release doxylamine and pyridoxine for nausea and vomiting of pregnancy: a randomized placebo controlled trial. *Am J Obstet Gynecol*. 2010;203(6):571.e1-7.
9. Sancuso (granisetron) [prescribing information]. Bedminster, NJ: Kywona Kirin, Inc; April 2020..
10. Syndros (dronabinol) [prescribing information]. Chandler, AZ: Insys Therapeutics, Inc; September 2022.
11. Varubi (rolapitant) [prescribing information]. Lake Forest, IL: TerSera Therapeutics LLC; August 2020.

APPROVAL HISTORY

October 11, 2022: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

1. November 14, 2023: Effective December 1, 2023, removed Anzemet 100 mg and nabilone from the MNG due to product discontinuation. Updated previous trial language throughout the MNG. Updated Sancuso criteria to remove required length of chemotherapy treatment. Updated fax number for Pharmacy Utilization Management.
2. November 12, 2024: No changes

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.

Provider Services