Oscar Clinical Guideline: Varubi (rolapitant) (PG178, Ver. 4)

Varubi (rolapitant)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Chemotherapy-Induced Nausea and Vomiting (CINV) is one of the most distressing symptoms of chemotherapy. Nausea and vomiting are one of the most common side effects of chemotherapy, and while this can occur in those receiving cancer-related radiation and surgery, chemotherapy-induced nausea and vomiting (CINV) is potentially the most severe. . There are three distinct types of CINV: acute emesis, occurring within 1-2 hours of chemotherapy; delayed emesis, occurring more than 24 hours after chemotherapy; and, anticipatory emesis, occurring prior to chemotherapy administration as a conditioned response from the individual who has previously experienced nausea and/or vomiting from prior chemotherapy exposures. The goal of managing CINV is preventing it entirely, thus a typical regimen will include several drugs from different classes administered 1-2 days prior to chemotherapy and 1-2 days after the last chemotherapy administration day (e.g., in a multi-day chemotherapy regimen). The classes of drugs most broadly accepted as having the highest therapeutic index for management of CINV include the type-three 5-hydroxytryptamine (5-HT3) receptor antagonists (e.g. ondansetron [Zofran], dolasetron [Anzemet], granisetron [Sancuso], palonosetron [Aloxi]), the neurokinin-1 receptor (NK1R) antagonists (e.g., aprepitant [Emend], fosaprepitant [Focinvez], Varubi [rolapitant]) and glucocorticoids (e.g., dexamethasone).

Varubi (rolapitant) is a substance P/neurokinin 1 (NK1) receptor antagonist indicated in combination with dexamethasone and a 5-HT3 receptor antagonist for the prevention of delayed nausea and vomiting associated with initial and repeat courses of moderately or highly emetogenic cancer chemotherapy in adults.

- Varubi (rolapitant) inhibits the CYP2D6 enzyme and is contraindicated with concomitant use of CYP2D6 substrates with a narrow therapeutic index, such as thioridazine and pimozide, due to an increased risk of QT prolongation.
- The American Society of Clinical Oncology (ASCO) guidelines recommend a 3- or 4-drug combination regimen including a neurokinin 1 (NK1) receptor antagonist for prevention of nausea and vomiting associated with moderate and highly emetogenic chemotherapy.

Definitions

"5-HT3 Receptor Antagonist" is a class of antiemetic agents (e.g. ondansetron, granisetron) that block serotonin binding to 5-HT3 receptors in the gut and central nervous system.

"Chemotherapy-Induced Nausea and Vomiting (CINV)" is nausea and/or vomiting that occurs as a side effect of chemotherapy treatment. It can be acute (within 24 hours of treatment) or delayed (more than 24 hours after treatment).

"Emetogenic Chemotherapy" is chemotherapy that has a high risk of causing nausea and vomiting.

"Moderately or highly emetogenic chemotherapy" is chemotherapy that has 30-90% or >90% frequency of nausea and/or vomiting, respectively (i.e., cisplastin, doxorubicin, carboplatinoxaliplatin, irinotecan, and azacitidine).

"Neurokinin-1 (NK1) Receptor Antagonist" is a class of antiemetic agents (e.g. rolapitant) that block NK1 receptors in the brain and gut to prevent nausea and vomiting signals.

"QT prolongation" refers to a prolonged period of time required for the ventricles of the heart to recharge between heartbeats; it can increase the risk of heart rhythm abnormalities and be life threatening. The QT is an interval measured on an electrocardiogram (ECG). QT prolongation is often drug-induced.

"[s]" indicates state mandates may apply.

Clinical Indications

Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

The Plan considers Varubi (rolapitant) medically necessary when ALL of the following criteria are met:

1. Prescribed by or in consultation with an oncologist or hematologist; *AND*
2. The member is 18 years of age or older; *AND*
3. Varubi (rolapitant) is being prescribed at a dose and frequency that is within FDA approved labeling OR is supported by compendia or evidence-based published dosing guidelines; *AND*
4. The member meets the applicable Medical Necessity Criteria for Initial Clinical Review or Subsequent Clinical Review listed below.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Emetogenic Chemotherapy

The Plan considers Varubi (rolapitant) medically necessary when ALL of the following criteria are met:

5. The member meets the above General Medical Necessity Criteria; *AND*
6. The member has been diagnosed with cancer and is receiving moderately or highly emetogenic chemotherapy OR combinations of anthracycline and cyclophosphamide; *AND*
7. Varubi (rolapitant) is being prescribed in combination with other antiemetic agents as part of a comprehensive treatment plan to prevent nausea and vomiting; *AND*
8. The member meets ONE (1) of the following:
    a. Varubi (rolapitant) is being used to treat stage IV advanced, metastatic cancer [based upon applicable state regulations][s]; *or*
    b. The member is unable to use, or has tried and failed aprepitant (Emend) for prevention of chemotherapy-induced nausea and vomiting[s]; *AND*
9. The member is not taking CYP2D6 substrates with a narrow therapeutic index (e.g., thioridazine and pimozide).

If the above prior authorization criteria are met, the requested product will be approved for the duration of chemotherapy treatment.[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Emetogenic Chemotherapy

The Plan considers Varubi (rolapitant) medically necessary when ALL of the following criteria are met:

1. The member meets the above applicable General Medical Necessity Criteria and/or Initial Clinical Review; *AND*
2. The member continues to receive moderately or highly emetogenic chemotherapy; *AND*
3. The member has demonstrated a positive response to Varubi (rolapitant), as evidenced by ONE of the following:
    a. A decrease in the frequency or severity of nausea/vomiting episodes; *or*
    b. A reduced need for rescue antiemetic medications; *or*
    c. Ability to complete planned chemotherapy cycles without dose reduction or delays due to nausea/vomiting; *or*
    d. Absence of emetic episodes; *or*
    e. No episodes of emesis and absence of nausea that interferes with daily activities; *or*
    f. No use of rescue medication.

If the above reauthorization criteria are met, the requested product will be authorized for up to 6-months.[s]

Experimental / Investigational, or unproven[s]

Varubi (rolapitant) for any other indication or use is considered experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Chemo-radiation Induced Nausea and Vomiting
- In patients receiving antineoplastic regimens with a low or minimal emetogenic risk
- Post Operative Nausea and Vomiting (PONV)

Applicable Billing Codes

Table 1	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
J8670	Rolapitant, oral, 1 mg

Table 2	
ICD-10 codes considered medically necessary with Table 1 (CPT/HCPCS) codes if criteria are met: if criteria are met:	
Code	*Description*
R11.2	Nausea with vomiting, unspecified
Z79.899	Other long term (current) drug therapy
R11.0	Nausea
R11.10	Vomiting, unspecified
R11.11	Vomiting without nausea
R11.12	Projectile vomiting
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs, initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs, subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs, sequela
T45.95XA	Adverse effect of unspecified primarily systemic and hematological agent, initial encounter
T45.95XD	Adverse effect of unspecified primarily systemic and hematological agent, subsequent encounter
T45.95XS	Adverse effect of unspecified primarily systemic and hematological agent, sequela
T50.905A	Adverse effect of unspecified drugs, medicaments and biological substances, initial encounter
T50.905D	Adverse effect of unspecified drugs, medicaments and biological substances, subsequent encounter
T50.905S	Adverse effect of unspecified drugs, medicaments and biological substances, sequela
Z51.11	Encounter for antineoplastic chemotherapy
Z51.12	Encounter for antineoplastic immunotherapy

Appendix A

Chemotherapy-induced nausea and vomiting (CINV) prevention and treatment should be tailored to an individual's specific chemotherapy regimen and emetic risk classification. Emetogenic potential depends on the chemotherapy agent, dose, route, and patient risk factors. The American Society of Clinical Oncology (ASCO) and Multinational Association of Supportive Care in Cancer (MASCC)/European Society for Medical Oncology (ESMO) provide evidence-based guidelines for CINV prophylaxis and treatment.

- Preventive antiemetic therapy is most effective and should be administered prior to chemotherapy based on emetic risk classification. Using multiple agents with different mechanisms improves prevention.
- Olanzapine should be added to preventive regimens for highly emetogenic chemotherapy. NK1 antagonists and dexamethasone effectively prevent delayed CINV.
- Rescue therapy for breakthrough CINV includes dopamine antagonists, 5-HT3 antagonists, olanzapine, benzodiazepines, cannabinoids.
- Refractory CINV may require changing to alternative agents in a different pharmacologic class.
- Anticipatory CINV is best managed with optimal control in initial chemotherapy cycles along with behavioral interventions.

Table 3[*]: Emetogenic Potential of Anticancer Agents and Recommended Preventive Antiemetic Regimens

Emetogenic Potential	Parenteral Agents	Oral Agents	Recommended Preventive Antiemetic Regimen
Highly Emetogenic (Frequency of Emesis: >90%)	❖ Anthracycline + cyclophosphamide (e.g., AC) ❖ ❖ Carmustine ❖ Chlormethine ❖ Cisplatin ❖ Cyclophosphamide ≥ 1,500 mg/m^2 ❖ Dacarbazine ❖ Mechlorethamine ❖ Streptozocin	❖ Abemaciclib ❖ Adagrasib ❖ Altretamine ❖ Avapritinib ❖ AzaCITIDine ❖ Binimetinib ❖ Bosutinib ❖ Busulfan ≥4 mg/day ❖ Cabozantinib ❖ Ceritinib ❖ Crizotinib ❖ Cyclophosphamide ❖ Enasidenib ❖ Fedratinib ❖ Hexamethylmelamine ❖ Imatinib ❖ Lenvatinib ❖ Lomustine ❖ Midostaurin	NK1 antagonist + 5HT3 antagonist + olanzapine + dexamethasone
Moderately Emetogenic (Frequency of Emesis: 30% to 90%)	❖ Alemtuzumab ❖ Amifostine > 300 mg/m^2 ❖ Arsenic trioxide ❖ Azacitidine ❖ Bendamustine		NK1 antagonist + 5HT3 antagonist + dexamethasone

	❖ Busulfan ❖ Carboplatin ❖ Clofarabine ❖ Cyclophosphamide < 1,500 mg/m^2 ❖ Cytarabine > 1,000 mg/m^2 ❖ Cytarabine/daunorubicin liposomal ❖ Daunorubicin ❖ Dinutuximab beta ❖ Doxorubicin ❖ Epirubicin ❖ Idarubicin ❖ Ifosfamide ❖ Irinotecan ❖ Irinotecan peg-liposomal ❖ Lubrinectedin ❖ Methotrexate ≥ 250 mg/m^2 ❖ Natalizumab ❖ Oxaliplatin ❖ Romidepsin ❖ Sactizumab-govitecan ❖ Temozolomide ❖ Thiotepa ❖ Trabectedin ❖ Tastuzumab-deruxtecan	❖ Mitotane ❖ Mobocertinib ❖ Niraparib ❖ Olaparib ❖ Procarbazine ❖ Ribociclib ❖ Rucaparib ❖ Selinexor ❖ Temozolomide ❖ Trifluridine and tipiracil ❖ Vinorelbine	
Low Emetogenic (Frequency of Emesis: 10% to 30%)	❖ Aflibercept ❖ Amivantamab ❖ Axicabtagene-ciloleucel ❖ Belinostat ❖ Blinatumomab ❖ Bortezomib ❖ Brentuximab vedotin ❖ Cabazitaxel ❖ Catumaxomab ❖ Cetuximab ❖ Copanlisib ❖ Cytarabine ≤ 1000 mg/m^2 ❖ Decitabine ❖ Docetaxel ❖ Doxorubicin peg-liposomal ❖ Elotuzumab ❖ Enfortumab-vedotin ❖ Eribulin ❖ Etoposide ❖ 5-Fluorouracil ❖ Gemcitabine	❖ ❖ Acalabrutinib ❖ Afatinib ❖ Alectinib ❖ Alpelisib ❖ Apalutamide ❖ Asciminib ❖ Axitinib ❖ Belzutifan ❖ Bexarotene ❖ Brigatinib ❖ Busulfan <4 mg/day ❖ Capecitabine ❖ Capmatinib ❖ Chlorambucil ❖ Cobimetinib ❖ Dabrafenib ❖ Dacomitinib ❖ Darolutamide ❖ Dasatinib ❖ Decitabine and cedazuridine	5HT3 antagonist OR dexamethasone

	❖ Gemtuzumab-ozogamicin ❖ Inotuzumab-ozogamicin ❖ Isatuximab ❖ Ixabepilone ❖ Loncastuximab-tesirine ❖ Margetuximab ❖ Methotrexate < 250 mg/m^2 ❖ Mirvetuximab-soravtansine ❖ Mitomycin ❖ Mitoxantrone ❖ Moxetumomab-pasudotox ❖ Necitumumab ❖ Nelarabine ❖ ❖ Paclitaxel ❖ Paclitaxel nab-albumin ❖ Pemetrexed ❖ Pertuzumab ❖ Pentostatin ❖ Tafasitamab ❖ Tagraxofusp ❖ Teclistamab ❖ Temsirolimus ❖ Tisagenlecleucel ❖ Tisotumab-vedotin ❖ Topotecan ❖ Trastuzumab-emtansine ❖ Vinflunine	❖ Duvelisib ❖ Elacestrant ❖ Encorafenib ❖ Entrectinib ❖ Erdafitinib ❖ Erlotinib ❖ Estramustine ❖ Etoposide ❖ Everolimus ❖ Futibatinib ❖ Gefitinib ❖ Gilteritinib ❖ Glasdegib ❖ Hydroxyurea ❖ Ibrutinib ❖ Idelalisib ❖ Infigratinib ❖ Ivosidenib ❖ Ixazomib ❖ Lapatinib ❖ Larotrectinib ❖ Lenalidomide ❖ Lorlatinib ❖ Melphalan ❖ Mercaptopurine ❖ Methotrexate ❖ Neratinib ❖ Nilotinib ❖ Nintedanib ❖ Niraparib/abiraterone acetate ❖ Olaparib ❖ Olutasidenib ❖ Osimertinib ❖ Pacritinib ❖ Palbociclib ❖ Panobinostat ❖ PAZOpanib ❖ Pemigatinib ❖ Pexidartinib ❖ Pirtobrutinib ❖ Pomalidomide ❖ PONATinib ❖ Pralsetinib ❖ Quizartinib ❖ Regorafenib ❖ Relugolix ❖ Ripretinib ❖ Ruxolitinib ❖ Selpercatinib ❖ Sonidegib ❖ SORAfenib ❖ Sotorasib	
Minimally Emetogenic (Frequency of Emesis: <10%)	❖ Asparaginase ❖ Atezolizumab ❖ Avelumab ❖ Belantamab-mafodotin ❖ Bevacizumab ❖ Bleomycin ❖ Cemiplimab ❖ Cladribine ❖ Daratumumab ❖ Dostarlimab ❖ Durvalumab ❖ Emapalumab ❖ Fludarabine ❖ Ipilmumab ❖ Mosunetuzumab ❖ Nivolumab ❖ Obinutuzumab ❖ Ofatumumab ❖ Pembrolizumab		No routine prophylaxis

	❖ Pixantrone ❖ Polatuzumab-vedotin ❖ Pralatrexate ❖ Ramucirumab ❖ Rituximab ❖ Trastuzumab ❖ Tremelimumab ❖ Vinblastine ❖ Vincristine ❖ Vinorelbine	❖ SUNItinib ❖ Talazoparib ❖ Tazemetostat ❖ Tegafur/uracil ❖ Tepotinib ❖ Thalidomide ❖ Tioguanin (6-Thioguanine) ❖ Tivozanib ❖ Topotecan ❖ Trametinib ❖ Tretinoin ❖ Trifluridine/tipiracil ❖ Tucatinib ❖ Umbralisib ❖ Vandetanib ❖ Vemurafenib ❖ Venetoclax ❖ Vismodegib ❖ Vorinostat ❖ Zanubrutinib	

[~]*<u>NOTE:</u> This table summarizes the emetogenic potential of parenteral and oral anticancer agents (not all-inclusive) and provides general recommended preventive antiemetic regimens based on guidelines. However, choice of antiemetic therapy should be individualized for each patient based on specific chemotherapy regimen, dosing, and risk factors. Higher doses of chemotherapy are generally more emetogenic. Patient factors like younger age, female gender, and prior CINV increase susceptibility. For combination regimens, the emetic level is based on the most emetic agent in the combination (except in the setting of anthracycline and cyclophosphamide, which are both moderate emetogenic agents but together are highly emetogenic).*

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Clinical Guideline Revision / History Information

Original Date: 9/21/2023

Reviewed/Revised: 9/18/2024, 12/01/2025, 11/02/2026