Oscar Clinical Guideline: Varubi (rolapitant) (PG178, Ver. 2)

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 a common and distressing side effect of cancer treatments. It can occur immediately after treatment (acute CINV), or it can be delayed, occurring more than 24 hours after treatment (delayed CINV). The severity and risk of CINV depend on the specific chemotherapy agents used, with some agents being highly emetogenic, meaning they have a high risk of causing nausea and vomiting.

Varubi (rolapitant) is a substance P/neurokinin 1 (NK1) receptor antagonist indicated for use in adults 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.

- 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.

"**Highly Emetogenic Chemotherapy**" is chemotherapy agents that cause vomiting in >90% of patients receiving them. Examples include cisplatin, carboplatin, cyclophosphamide, and doxorubicin.

"**Moderately Emetogenic Chemotherapy**" is chemotherapy agents that cause vomiting in 30-90% of patients receiving them. Examples include oxaliplatin, 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.

Medical Necessity Criteria for Initial Authorization

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. The member has been diagnosed with cancer and is undergoing moderately or highly emetogenic chemotherapy; ***AND***
4. Varubi (rolapitant) is being prescribed in combination with other antiemetic agents as part of a comprehensive treatment plan to prevent nausea and vomiting; ***AND***
5. The member is unable to use, or has tried and failed aprepitant (Emend) for prevention of chemotherapy-induced nausea and vomiting; ***AND***

6. The member is not taking CYP2D6 substrates with a narrow therapeutic index such as thioridazine and pimozide; ***AND***
7. 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.

If the above prior authorization criteria are met, Varubi (rolapitant) will be approved for the duration of chemotherapy treatment.

Medical Necessity Criteria for Reauthorization

Reauthorization for up to 6 months will be granted if the member has recent (within the last 3 months) clinical chart documentation demonstrating ALL of the following criteria:

1. The member still meets the applicable **Initial Authorization** criteria; ***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 ANY 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.

Experimental or Investigational / Not Medically Necessary

Varubi (rolapitant) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be 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 (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
J2797	Injection, rolapitant, 0.5 mg
J8670	Rolapitant, oral, 1 mg
ICD-10 codes considered medically necessary 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

Chemotherapy-induced nausea and vomiting (CINV) prevention and treatment should be tailored to patients' 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 1[7]: Emetogenic Potential of Anticancer Agents and Recommended Preventive Antiemetic Regimens

Emetogenic Potential	Parenteral Agents	Oral Agents	Recommended Preventive Antiemetic Regimen
Highly Emetogenic	❖ Anthracycline + cyclophosphamide (e.g.,	❖ Adagrasib	NK1 antagonist + 5HT3 antagonist +

(Frequency of Emesis: >90%)	AC) ❖ Carboplatin AUC ≥ 4 mg/mL/min ❖ Cisplatin ❖ Cyclophosphamide ≥ 1,500 mg/m^2 ❖ Dacarbazine ❖ Doxorubicin ≥ 60 mg/m^2 ❖ Epirubicin ≥ 90 mg/m^2 ❖ Ifosfamide ≥ 2 g/m^2 ❖ Mechlorethamine ❖ Streptozocin	❖ Altretamine ❖ Avapritinib ❖ AzaCITIDine ❖ Binimetinib ❖ Bosutinib ❖ Busulfan ≥4 mg/day ❖ Cabozantinib ❖ Ceritinib ❖ Crizotinib ❖ Cyclophosphamide ❖ Enasidenib ❖ Fedratinib ❖ Imatinib ❖ Lenvatinib ❖ Lomustine ❖ Midostaurin ❖ Mitotane ❖ Mobocertinib ❖ Niraparib ❖ Procarbazine ❖ Ribociclib ❖ Rucaparib ❖ Selinexor ❖ Temozolomide ❖ Trifluridine and tipiracil	olanzapine + dexamethasone
Moderately Emetogenic (Frequency of Emesis: 30% to 90%)	❖ Amifostine > 300 mg/m^2 ❖ Arsenic trioxide ❖ Azacitidine ❖ Bendamustine ❖ Carboplatin AUC < 4 mg/mL/min ❖ Clofarabine ❖ Cyclophosphamide < 1,500 mg/m^2 ❖ Cytarabine > 1,000 mg/m^2 ❖ Daunorubicin ❖ Doxorubicin < 60 mg/m^2 ❖ Epirubicin < 90 mg/m^2 ❖ Idarubicin ❖ Ifosfamide < 2 g/m^2 ❖ Irinotecan ❖ Methotrexate ≥ 250 mg/m^2 ❖ Oxaliplatin ❖ Temozolomide		NK1 antagonist + 5HT3 antagonist + dexamethasone
Low Emetogenic (Frequency of Emesis: 10% to 30%)	❖ Brentuximab vedotin ❖ Docetaxel ❖ Etoposide ❖ 5-Fluorouracil ❖ Gemcitabine ❖ Liposomal doxorubicin ❖ Paclitaxel ❖ Pemetrexed ❖ Pentostatin	❖ Abemaciclib ❖ Acalabrutinib ❖ Afatinib ❖ Alectinib ❖ Alpelisib ❖ Asciminib ❖ Axitinib ❖ Belzutifan ❖ Bexarotene	5HT3 antagonist OR dexamethasone

	❖ Topotecan ❖ Trastuzumab	❖ Brigatinib ❖ Busulfan <4 mg/day ❖ Capecitabine ❖ Capmatinib ❖ Chlorambucil ❖ Cobimetinib ❖ Dabrafenib ❖ Dacomitinib ❖ Dasatinib ❖ Decitabine and cedazuridine ❖ Duvelisib ❖ Elacestrant ❖ Encorafenib ❖ Entrectinib ❖ Erdafitinib ❖ Erlotinib ❖ Estramustine ❖ Etoposide ❖ Everolimus ❖ Futibatinib ❖ Gefitinib ❖ Gilteritinib ❖ Glasdegib ❖ Hydroxyurea ❖ Ibrutinib ❖ Idelalisib ❖ Ivosidenib ❖ Ixazomib ❖ Lapatinib ❖ Larotrectinib ❖ Lenalidomide ❖ Lorlatinib ❖ Melphalan ❖ Mercaptopurine ❖ Methotrexate ❖ Neratinib ❖ Nilotinib ❖ Niraparib/abiraterone acetate ❖ Olaparib ❖ Olutasidenib ❖ Osimertinib	
Minimally Emetogenic (Frequency of Emesis: <10%)	❖ Bevacizumab ❖ Bleomycin ❖ Busulfan ❖ Fludarabine ❖ Rituximab ❖ Vinblastine ❖ Vincristine		No routine prophylaxis

		❖ Pacritinib ❖ Palbociclib ❖ Panobinostat ❖ PAZOpanib ❖ Pemigatinib ❖ Pexidartinib ❖ Pirtobrutinib ❖ Pomalidomide ❖ PONATinib ❖ Pralsetinib ❖ Quizartinib ❖ Regorafenib ❖ Ripretinib ❖ Ruxolitinib ❖ Selpercatinib ❖ Sonidegib ❖ SORAfenib ❖ Sotorasib ❖ SUNItinib ❖ Talazoparib ❖ Tazemetostat ❖ Tepotinib ❖ Thalidomide ❖ Thioguanine ❖ Tivozanib ❖ Topotecan ❖ Trametinib ❖ Tretinoin ❖ Tucatinib ❖ Vandetanib ❖ Vemurafenib ❖ Venetoclax ❖ Vismodegib ❖ Vorinostat ❖ Zanubrutinib	

[1] ***NOTE:*** *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.*

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Clinical Guideline Revision / History Information

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