Aprepitant (Emend®)
Criteria for Use: Prevention of chemotherapy-induced nausea and vomiting
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VHA Pharmacy Benefits Management Services and Medical Advisory Panel

The following recommendations are based on current medical evidence and expert opinion from clinicians. The content of the document is dynamic and will be revised as new clinical data become available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The clinician should utilize this guidance and interpret it in the clinical context of the individual patient.

EXCLUSION CRITERIA (if ONE is checked, patient is not eligible)

- ☐ Hypersensitivity to aprepitant
- ☐ Patients on concurrent pimozide or cisapride (aprepitant is a weak-moderate dose dependent inhibitor of CYP3A4)
- ☐ Chemotherapy regimens with minimal, low, or moderate potential for incidence of emetogenicity (except the combination of cyclophosphamide plus an anthracycline for breast cancer as noted below)

INCLUSION CRITERIA**

- ☐ Highly emetogenic chemotherapy* (includes multiple moderately emetogenic drugs) in combination with a $5HT_3$ antagonist and dexamethasone
- ☐ Moderately emetogenic chemotherapy* regimens (consisting of cyclophosphamide plus an anthracycline for breast cancer) in combination with a 5 HT_3 antagonist and dexamethasone
- ☐ Patients who fail standard antiemetic therapy with a $5HT_3$ antagonist plus dexamethasone for moderately emetogenic regimens

DOSING RECOMMENDATIONS

Highly Emetogenic Chemotherapy

Drug	Day 1 prior to chemotherapy	Day 2	Day 3	Day 4
Aprepitant	125 mg orally	80 mg orally	80 mg orally	None
Dexamethasone†	12 mg orally Once daily	8 mg orally Once daily	8 mg orally Once daily	8 mg orally Once daily
Ondansetron	8 mg IV (or 0.15mg/kg) or 24mg orally	None	None	None

Moderately Emetogenic Chemotherapy (cyclophosphamide plus an anthracycline)

Drug	Day 1 prior to chemotherapy	Day 2	Day 3
Aprepitant	125 mg orally	80 mg orally	80 mg orally
Dexamethasone†	12 mg orally Once daily	None	None
Ondansetron	8 mg orally twice a day	None	None

MONITORING

- ☐ Aprepitant is a substrate for and inhibitor of CYP3A4. Drug interactions with chemotherapy drugs have not been investigated even though several are metabolized by CYP3A4. In clinical trials, there was an increased incidence of infections, neutropenia, and pulmonary toxicity that may be the result of a drug interaction. Monitor all patients for adverse events when adding aprepitant, especially in patients receiving chemotherapy drugs metabolized by CYP3A4.
- ☐ For patients on chronic warfarin therapy, closely monitor the INR in the 2 weeks following the initiation of the 3 day aprepitant regimen (especially days 7-10) due to the potential for a significant decrease in the INR.

*See Appendix

** Patients at high risk for chemotherapy-induced nausea and vomiting include: patients with poor emesis control on previous chemotherapy, females, age under 50, history of motion sickness, history of hyperemesis gravidarum, history of postoperative nausea and vomiting

† If steroids are part of the chemotherapy regimen, for example in lymphoma and multiple myeloma, dexamethasone is not required as part of the antiemetic regimen. The chemotherapy regimen steroid dose should not be reduced when aprepitant is used.

Appendix

Classifying Emetogenicity

There is no one standard classification for the emetogenic potential of chemotherapy drugs and combinations of drugs. A number of schemas have been proposed, containing 3 to 5 levels of emetogenicity. The following table and guidance on assessing the emetogenic potential for combination chemotherapy is based on limited information from clinical trials plus expert opinion from two widely used sources.[1,2]

Degree of emetogenic risk	Agent
High (>90%)	Carmustine Cisplatin Cyclophosphamide ≥ 1500 mg/m^2 Dacarbazine Hexamethylmelamine orally Mechlorethamine Procarbazine orally Streptozocin
Moderate (30-90%)	Carboplatin Cyclophosphamide < 1500 mg/m^2 Cyclophosphamide orally Cytarabine > 1g/m^2 Daunorubicin Doxorubicin Epirubicin Etoposide orally Idarubicin Ifosfamide Imatinib orally Irinotecan Oxaliplatin Temozolomide orally Vinorelbine orally
Low (10-30%)	5-Flourouracil Bortezomib Capecitabine orally Cetuximab Cytarabine ≤ 100mg/m^2 Docetaxel Etoposide inje Fludarabine orally Gemcitabine Methotrexate Mitomycin Mitoxantrone Paclitaxel Pemetrexed Topotecan Trastuzumab
Minimal (<10%)	6-Thioguanine orally Bevacizumab Bleomycin Busulfan Chlorambucil orally Cladribine Fludarabine Gefitinib orally Hydoxyurea orally Methotrexate orally Vinblastine Vincristine Vinorelbine

General Schema for Predicting Acute Emetogenicity of Combination Chemotherapy

1. Identify the most emetogenic agent in the combination
2. Adding one or more agents with Low potential increases the emetogenicity by 1 category
3. Adding agents with Moderate potential increases the emetogenicity by 1 category per agent
4. Adding an agent with Minimal potential does not contribute to the emetogenicity of the combination

For classification of newer drugs see: http://www.nccn.org/professionals/physician_gls/PDF/antiemesis.pdf

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References

[1] Hesketh PJ, Kris MG, Grunberg SM, Beck T, Hainsworth JD, Harker G, et al. Proposal for classifying the acute emetogenicity of cancer chemotherapy. J Clin Oncol 1997; 15:103-109.
[2] Grunberg SM, Osoba D, Hesketh PJ, Gralla RJ, Borjeson S, Rapoport BL, du Bois A, Tonat M. Evaluation of new antiemetic agents and definition of antineoplastic agent emetogenicity-an update. Supportive Care Cancer 2005; 13:80-84.