NCCN Chemotherapy Order Templates
Appendix D

Appendix D: Nausea/Vomiting

1. Antiemetic Therapy
   NCCN Clinical Practice Guidelines in Oncology™ Antiemesis outline antiemetic treatment using four categories of emetogenic potential for intravenous chemotherapeutic agents, which correspond to the Grunberg classification[9]:

   - High emetic risk: ≥90% of patients experience acute emesis
   - Moderate emetic risk: 30%–90% of patients experience acute emesis
   - Low emetic risk: 10%–30% of patients experience acute emesis
   - Minimal emetic risk: ≤10% of patients experience acute emesis

In addition, oral chemotherapeutic agents are categorized as

- Oral High/Moderate
- Oral Low/Minimal

NCCN Guidelines attempt to define antiemetic regimens that cover the entire duration of time a patient is at risk for nausea and vomiting based on the chemotherapy regimen. NCCN treatment algorithms and these templates incorporate a dosing schedule that covers both acute and delayed emesis in a single algorithm. While the emetic risk noted in the NCCN Supportive Care section of the template lists the risk of the specific chemotherapy on the day of administration, the antiemetic regimens in the template consider the emetic risk for the patient over the duration of the regimen based on the emetogenicity of all chemotherapy given in the regimen.

Emetic risk in these templates has been assigned based on NCCN Guidelines.

2. Aprepitant
   Aprepitant is a substrate, moderate inducer, and moderate inhibitor of cytochrome P450 enzyme 3A4 (CYP3A4). Aprepitant also induces CYP2C9. Therefore, aprepitant can alter the metabolism of certain drugs and change their plasma concentrations. These interactions are more significant with oral than with IV drugs because of first-pass metabolism.

Aprepitant has the following drug interactions:

- Administration of aprepitant with pimozide, terfenadine, astemizole, or cisapride is contraindicated.
- Aprepitant has been shown to interact with the nonchemotherapeutic drugs warfarin, dexamethasone, methylprednisolone, and oral contraceptives. Dose reductions are recommended for dexamethasone and methylprednisolone unless these agents are administered as part of anticancer therapy (eg, CHOP regimen). Aprepitant decreases plasma concentrations of oral contraceptives; the package insert should be consulted in this setting.
- Induction of warfarin metabolism by aprepitant may lead to clinically significant reductions in International Normalized Ratio values, particularly for patients on therapeutic (as compared with prophylactic) warfarin regimens. Patient monitoring may be required.
- Certain drugs can affect plasma concentrations of aprepitant. Concomitant administration with CYP3A4 inhibitors (eg, ketoconazole, itraconazole, and erythromycin) may increase aprepitant concentrations, whereas concomitant administration with CYP3A4 inducers (eg, carbamazepine, rifampin, and phenytoin) may lead to decreased aprepitant levels.
- Chemotherapeutic agents known to be metabolized by CYP3A4 include docetaxel, paxlitaxel, etoposide, irinotecan, ifosfamide, imatinib, vinorelbine, vinblastine, and vincristine. In clinical trials, aprepitant was used concurrently with etoposide, vinorelbine, or paclitaxel. Although chemotherapy doses were not adjusted for potential drug interactions in phase 3 trials, caution is urged when using any chemotherapeutic agent that is metabolized by CYP3A4.

3. Fosaprepitant
    - Fosaprepitant is a prodrug of aprepitant. It is rapidly converted to aprepitant when administered intravenously. Therefore, all information regarding drug interactions associated with aprepitant also applies to fosaprepitant (see above).

REFERENCE

1. Grunberg SM, Osoba D, Hesketh PJ, et al. *Support Care Cancer*. 2005;13(2):80-4.

