

**NCCN Standard Chemotherapy Order Templates
Appendices to the Order Templates**

Appendix A: Calculations, Assumptions, Clearances

BSA

Author	BSA formula
Mosteller ¹	BSA (m ²) = [Ht(cm) * Wt(kg)/3600] ^{1/2} or BSA (m ²) = [Ht(in) * Wt(lbs)/3131] ^{1/2}
Du Bois and Du Bois ²	BSA (m ²) = Wt(kg) ^{0.425} * Ht(cm) ^{0.725} * 0.007184
Haycock et al ³	BSA (m ²) = Wt(kg) ^{0.5378} * Ht(cm) ^{0.3964} * 0.024265
Gehan and George ⁴	BSA (m ²) = Wt(kg) ^{0.51456} * Ht(cm) ^{0.42246} * 0.02350
Boyd ⁵	BSA (m ²) = Wt(kg) ^{0.4838} * Ht(cm) ^{0.3} * 0.017827

Cockcroft-Gault Equation⁶

- Substitute GFR with creatinine clearance that is calculated via Cockcroft-Gault equation

CrCl Calculation (Cockcroft-Gault Formula):

$$\text{CrCl (men; mL/min)} = (140 - \text{age}) \times (\text{weight in kg}) \div (\text{serum creatinine [mg/dL]} \times 72)$$

$$\text{CrCl (women; mL/min)} = 0.85 \times \text{CrCl (men)}$$

Appendix B: Calvert Equation

Calvert Equation⁷

- Calvert equation: Dose (mg) = Target AUC x (glomerular filtration rate [GFR]* + 25)

*GFR estimated by calculated creatinine clearance.

Appendix C: Growth Factors

Patient evaluation should be performed every cycle to determine the risk categorization and treatment intent. The following risk factors are associated with dose-limiting neutropenia and should be considered:

- Neutropenic events:
 - FN, particularly 1st cycle
 - Severe neutropenia, particularly 1st cycle
- Patient Factors:
 - Age
 - Ethnicity
 - Education
 - Compliance
- Comorbidities:
 - Cardiovascular disease
 - Renal disease
 - Obesity or BMI >2 m²
 - Poor functional or nutritional status
 - Connective tissue disease
- Disease factors:
 - Stage
 - Prior treatment
 - Marrow involvement
- Treatment variables:
 - Prior treatment
 - Chemotherapy regimen
 - Treatment intent, dose and schedule
 - Physician/ practice variables
 - Practice setting
 - Practice site
 - Training/experience

High Risk

Prophylactic colony stimulating factor (CSF) support is recommended for a patient considered at high risk, regardless of whether the treatment is intended to be curative, to prolong survival, or to manage symptoms. Refer to NCCN Clinical Practice Guidelines in Oncology™ Myeloid Growth Factors for more information.

Intermediate Risk

The use of prophylactic CSF support should be based on physician-patient discussion of the risk-benefit ratio of the likelihood of developing FN, the potential consequences of a neutropenic event, and the implications of reduced chemotherapy dose delivery. Treatment goals (ie, curative/adjuvant, prolong survival, or symptom management) should be considered. Refer to NCCN Guidelines for more information.

Low Risk

For patients at low risk, use of CSFs is not considered cost effective. Refer to NCCN Guidelines for more information.

Febrile neutropenia risk of each template is assigned based on NCCN Guidelines. If the specific regimen was not mentioned in NCCN Guidelines, the health care provider is referred to NCCN Guidelines for more information.

Appendix D: Nausea/Vomiting

1. Antiemetic Therapy

NCCN Clinical Practice Guidelines in Oncology™ Antiemesis outline antiemetic treatment using four categories of emetogenic potential, which correspond to the Grunberg classification⁸ as follows:

- High emetic risk: $\geq 90\%$ 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: $\leq 10\%$ of patients experience acute emesis

In addition, NCCN Guidelines attempt to define antiemetic regimens for particular chemotherapy drugs that cover the entire duration of time a patient is at risk for nausea and vomiting. NCCN treatment algorithms and these templates incorporate a dosing schedule that covers both acute and delayed emesis into a single algorithm.

Emetic risk and therapy 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).

Appendix E: Regimen References

Each reference will be given a classification according to the following:

- a. Reference/template is consistent with NCCN reference.
- b. If NCCN did not reference the regimen, an alternative reference is included which the template follows.
- c. NCCN did reference the regimen but an alternative reference is included which more closely follows current practices and which the template follows.
- d. The template does not exactly follow the stated reference because of changes in the standard of practice.

REFERENCES

1. Mosteller RD. *N Engl J Med*. 1987;317(17):1098.
2. DuBois D, DuBois EF. *Arch Int Med*. 1916;17:863-71.
3. Haycock GB, Schwartz GJ, Wisotsky DH. *J Pediatr*. 1978;93(1):62-6.
4. Gehan EA, George SL. *Cancer Chemother Rep*. 1970;54(4):225-35.
5. Boyd E. The growth of the surface area of the human body. Minneapolis: University of Minnesota Press, 1935.
6. Cockcroft DW, Gault MH. *Nephron*. 1976;16(1):31-41.
7. Calvert AH, Newell DR, Gumbrell LA, et al. *J Clin Oncol*. 1989;7(11):1748-56
8. Grunberg SM, Osoba D, Hesketh PJ, et al. *Support Care Cancer*. 2005;13(2):80-4.