APPENDIX 6 – Dosage Modification for Hematologic and Non-Hematologic Toxicities

Many regimens, especially combination regimens, have specific dose modification recommendations pertinent to that regimen, and dosage should be adjusted accordingly where at all possible.

If no guidelines are available, the following recommendations could be considered. The following are general recommendations and do not replace clinical judgment. Note that these recommendations do not address the potential usage of G-CSF or GM-CSF for specific regimens. Readers are advised to consult the specific regimen monograph, CCO Program in Evidence-Based Care Practice Guideline, "*The Use of Colony-Stimulating Factor (CSF) in Patients Receiving Myelosuppressive Chemotherapy for the Treatment of Cancer*", CED-CCO Special Advice Reports "*The Prophylactic Use of Filgrastim in Patients with Hematological Malignancies*", or "*The Prophylactic Use of Filgrastim in Patients with Breast Cancer*", for further information.

For chemotherapy used for palliative purposes, where dose intensity may not be as important as for curative regimens, dose modification for less severe toxicity may be warranted especially for heavily pretreated patients. In such patients, the use of dose modifications rather than growth factor support for hematologic toxicity is also recommended. In general, for both intermittent (e.g. q3 weekly doxorubicin) and continuous (e.g. capecitabine) schedules, the planned dose of chemotherapy should be **DELAYED** until neutrophil and platelet counts have recovered to adequate levels such as:

- Platelet count has recovered to ≥ 100 x 10^9/L
- Neutrophil (ANC) count has recovered to ≥ 1.5 x 10^9/L

In addition, dose modifications should be considered for subsequent doses if severe hematologic toxicity has occurred in the prior cycle/dosing period.

Dose Modification for Hematologic Toxicity:

Toxicity Grade			**Dose next cycle[a]**
ANC (x 10^9/L)		*Platelets (x 10^9/L)*	
<0.5 for 5-7 days or Febrile neutropenia	and /or	<25 or bleeding	↓ by 25%[b]

a. Do not retreat until platelets ≥ 100 x 10^9/L and ANC ≥ 1.5 x 10^9/L. If clinically indicated to retreat with lower counts, consider significant (25-50%) dose modification and close monitoring

b. If chemotherapy is given with curative intent, consider growth factor support if ↓ in ANC only.

APPENDIX 6 – Dosage Modification for Hematologic and Non-Hematologic Toxicities (continued)

Dose Modification for Non-hematologic toxicity (suggested):[1]

Toxicity Grade[1]	Action	Dose (% previous dose)
1	Continue treatment; manage symptoms appropriately.	No change
2	Continue treatment; manage symptoms appropriately.	No change or dose reduce according to regimen
3	Hold[2]; manage symptoms appropriately	75% or according to regimen
4	Discontinue or Hold[3]; manage symptoms appropriately	If resume, resume dose according to regimen

[1]Generally limited to organ toxicity; excludes alopecia and suboptimally treated nausea and vomiting.
[2]In general, treatment should be held for grade 3 non-hematological toxicities until recovery to ≤ grade 2, unless stated otherwise.
[3]Depending on the regimen, may resume treatment at a reduced dose once toxicity has resolved, after risk-benefit assessment.