Guidelines for the Management of Nausea and Vomiting in Cancer Patients
Management of chemotherapy-induced nausea and vomiting includes treatment strategies for both acute (within 24 hours of chemotherapy administration) and delayed (>24 hours after chemotherapy) emesis.

To plan the initial antiemetic treatment for adult cancer patients, the clinician should assess the chemotherapy regimen to be given (Assessment tools- Page 2). Based on the chemotherapy agent with the highest potential to cause nausea and vomiting (emetogenic potential), appropriate antiemetic agents are selected to manage the acute emesis and delayed emesis (see Page 4 for Adults or Page 6 for Pediatric Patients). These are prescribed along with the chemotherapy. Some new agents pending approval in Canada, with superior antiemetic management outcomes, are included in the options for consideration.

Some agents may be ordered as take-home prescriptions, for dispensing by the patient's community pharmacy. Clinicians must keep in mind the costs of these prescription medications and the patient's ability to pay for these drugs (including co-payments of prescription insurance and uninsured patients.)

With each cycle of chemotherapy, nausea and vomiting are assessed, using the Common Toxicity Criteria (or the Graphic Rating Scale) for screening and outcome assessment (see Page 8). Attention must focus on both the present circumstances (i.e. how the patient feels right now) and the historic experience since the last chemotherapy treatment (i.e. worst feelings or emesis after the last treatment). If a patient has experienced an unacceptable level of nausea (≥2) or vomiting (≥1), and this experience has not been influenced by some other causal factor, the antiemetic prevention strategy should be reconsidered, and, if necessary, altered (see Ongoing Antiemetic Treatment for adults- page 5).

Effective management of acute and delayed nausea and vomiting is crucial to prevention of anticipatory nausea and vomiting. In addition to pharmacologic antiemetic agents, other drugs (such as benzodiazepines) and non-pharmacologic methods (such as muscle relaxation, distraction or music therapy) can modify the patient experience and reduce morbidity and anxiety from nausea and vomiting experiences(s).

Cancer patients may also experience chronic nausea or vomiting not related to treatment. Careful assessment for reversible underlying causes, and a simple regimen of gastric promotility agents are reasonable steps to deal with this common problem. A step-wise approach is outlined on page 8.

Practice guidelines are intended to assist health care professionals with decisions throughout the spectrum of the cancer experience. Guidelines should never replace specific decisions for individual patients, and do not substitute for the shared decisions between any patient and doctor (or other health professional) which are unique to each circumstance. However, guidelines do provide evidence-based background information, consensus-based recommendations for similar problems, and a context for each individual decision. A full-text version of this guideline is also available. Both versions of this guideline will be revised, from time to time, as new evidence becomes available. Current versions of this guideline are available on the Cancer Care Nova Scotia website (www.cancercare.ns.ca).

### Assessment of Nausea and Vomiting

#### Assessment Recommendations for Nausea and Vomiting

<table>
<thead>
<tr>
<th>Phase</th>
<th>Assessment Recommendations</th>
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</table>
| Chemotherapy treatment phase               | - CTC at each treatment visit, or weekly for continuous treatment; include subjective comments on patient experience  
- Inpatients: assess with CTC before each chemotherapy administration or daily for continuous treatment; repeat CTC 24 hours after treatment and continue q24h for delayed or chronic N&V  
- If symptomatic, assess q4h until symptoms resolve |
| Radiotherapy treatment phase               | - CTC weekly or at review clinic visit                                                                                                                                                                                   |
| Follow-up after active treatment phase     | - CTC at scheduled follow-up visits immediately after active treatment phase, if nausea or vomiting were problematic during active treatment; follow until symptoms resolved |
| Symptom of cancer (usually advanced)       | - CTC at each visit if symptomatic with nausea or vomiting; may assess and follow as required by severity of symptoms  
- Detailed physical history and physical examination at start and repeated at each visit  
- If patient admitted to hospital, assess with CTC daily until symptoms resolved  
- If patient cannot use CTC, consider using Graphic Rating Scale |

#### Common Toxicity Criteria (CTC)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Nausea</th>
<th>Vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>1</td>
<td>loss of appetite without alteration in eating habits</td>
<td>1 episode in 24 hours; IV fluids indicated &lt;24 hrs</td>
</tr>
<tr>
<td>2</td>
<td>oral intake decreased without significant weight loss, dehydration or malnutrition; IV fluids indicated &lt;24 hrs</td>
<td>2-5 episodes in 24 hours</td>
</tr>
<tr>
<td>3</td>
<td>inadequate oral caloric or fluid intake; IV fluids, tube feedings, or TPN indicated ≥ 24 hrs</td>
<td>≥6 episodes in 24 hours; IV fluids, or TPN indicated ≥24 hrs</td>
</tr>
<tr>
<td>4</td>
<td>Life-threatening consequences</td>
<td>Life-threatening consequences</td>
</tr>
</tbody>
</table>

#### Graphic Rating Scale for Nausea

- 10 Worst Nausea
- 9
- 8
- 7
- 6
- 5 Moderate
- 4
- 3
- 2
- 1
- 0 No Nausea

- For the Full Version of this guideline, see the Cancer Care Nova Scotia website at www.cancercare.ns.ca
### Antiemetic Agents for Management of Treatment-Induced Nausea and Vomiting

#### Pre-Chemotherapy Drugs & Doses - High-Risk Chemotherapy

<table>
<thead>
<tr>
<th><strong>Serotonin (5HT3) Receptor Antagonist</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Ondansetron (Zofran) 8 PO or 8mg IV</td>
</tr>
<tr>
<td>• Granisetron (Kytril) 2mg PO or 1mg IV</td>
</tr>
</tbody>
</table>
| • Dolasetron (Anzemet) 100-200mg PO or 100mg IV  
PLUS |

#### Corticosteroid
- Dexamethasone (Decadron) 8-20mg PO or IV  
(Higher doses for highly emetogenic chemo)
- All doses given 15-30 minutes prior to chemotherapy

#### Intermediate-Risk Chemotherapy

<table>
<thead>
<tr>
<th><strong>Corticosteroid</strong></th>
</tr>
</thead>
</table>
| Dexamethasone 4-8mg PO, once before chemotherapy  
AND/OR  
**Dopamine Receptor Antagonist** |
| Metoclopramide (Maxeran) 10-20mg PO before chemotherapy  
OR  
Prochlorperazine (Stemetil) 10mg PO before chemotherapy |

#### Post-Chemotherapy Drugs & Doses - High-Risk Chemotherapy

<table>
<thead>
<tr>
<th><strong>Corticosteroid</strong></th>
</tr>
</thead>
</table>
| Dexamethasone 8mg PO once or twice daily for 2 to 3 days (3-4 days with cisplatin)  
PLUS |

<table>
<thead>
<tr>
<th><strong>Serotonin Receptor Antagonist or Dopamine Receptor Antagonist</strong></th>
</tr>
</thead>
</table>
| Ondansetron 8mg PO q12h for 3 doses  
(Granisetron or Dolasetron effective with only pre-chemo dose, but may be given q24h for one dose)  
OR  
Metoclopramide 10-20mg PO two to four times per day for 2 to 3 days (3-4 days with cisplatin)  
May add Diphenhydramine (Benadryl) 25-50mg PO, to prevent extrapyramidal reactions  
OR  
Prochlorperazine 10mg PO q4-6h PRN |

#### Intermediate-Risk Chemotherapy

| **Prochlorperazine** 10mg PO q4-6h PRN  
Metoclopramide 10mg PO q4h PRN |

#### Other Drugs and Doses to Consider - Neurokinin-1 (NK1) Receptor Antagonist

| Aprepitant (Emend) 125mg PO pre-chemo  
Aprepitant (Emend) 80mg PO once daily on Days 2 & 3 |

#### Adjuvant Drugs and Doses

(May add to other antiemetic regimens)

- Lorazepam (Ativan) 1-2mg PO or SL before chemotherapy  
Dronabinol (Marinol) 2.5-10mg q4-12h OR Nabilone (Cesamet) 1-2mg PO BID- for selected patients only

**Notes:**
- Not currently available in Canada  
- If NK1 Receptor antagonist given, Serotonin RA or Dopamine RA would not be needed for delayed emesis prevention
Initial Antiemetic Treatment for Adult Chemotherapy Patients

Assess Emetogenic Risk of Chemotherapy
- highest risk agent in regimen

HIGH Risk: Cisplatin
- High Risk: Non-cisplatin
  - dacarbazine
  - cyclophosphamide IV
  - lomustine
  - daunorubicin
  - doxorubicin
  - epirubicin
  - idarubicin
  - cytarabine

INTERMEDIATE Risk
- mitoxantrone
- paclitaxel
- docetaxel
- irinotecan
- dactinomycin
- carmustine
- mechlorethamine
- melphalan IV
- streptozotocin
- hexamethylmelamine
- carboplatin

LOW Risk
- vincristine
- busulphan
- chlorambucil
- melphalan PO
- hydroxyurea
- fludarabine
- cladribine
- tamoxifen

Pre-Chemotherapy:
- Serotonin Receptor Antagonist plus a Corticosteroid (IV for higher doses or PO for lower doses)
  - Consider "NK1 Receptor Antagonist"

Post-Chemotherapy:
- Oral corticosteroid q24h for 4 days plus oral serotonin receptor antagonist for 48 hours
  - Consider addition of Lorazepam if patient anxious
  - Consider "NK1 Receptor Antagonist"

Pre-Chemotherapy:
- Oral corticosteroid q24h for 3 days plus oral serotonin receptor antagonist for 24-48 hours
  - Consider addition of Lorazepam

Or
- Oral dopamine receptor antagonist for 2-4 days OR
  - Consider individual patient needs and risk factors- may choose alternate antiemetics as clinically indicated

Consider "NK1 Receptor Antagonist"
Ongoing Antiemetic Treatment for Adult Chemotherapy Patients

Initial treatment for acute and delayed emesis

Measurement of nausea & vomiting since last treatment (see Assessment)

Control of emesis

Good

Complete Control (Acute & Delayed)

Continue with same antiemetic treatment

Poor

Acute emetic episode(s) (within 24 hours of last chemotherapy treatment)

Careful evaluation of antiemetic risk to rule out other causes and to determine that the optimal antiemetic regimen is given

Consider adding an antianxiety agent (e.g. Lorazepam) to the regimen

Consider adding a dopamine receptor antagonist (e.g. Metoclopramide) to the serotonin receptor antagonist

Consider substituting high-dose Metoclopramide (with Diphenhydramine) for the serotonin receptor antagonist

Consider substituting alternate agents from within pharmacologic class:
  e.g. Granisetron or Dolasetron for Ondansetron
  e.g. Domperidone for Metoclopramide

Consider addition of "NK1 Receptor Antagonist" (e.g. Aprepitant) to the regimen- when available in Canada

Consider adding additional agents to delayed antiemetics:
  e.g. Add PRN dopamine receptor antagonist (e.g. Prochlorperazine)
  e.g. Add antianxiety agent (e.g. Lorazepam)

Consider adding non-pharmacologic treatment to drug therapy:
  e.g. muscle relaxation, distraction, music therapy

Consider substituting alternate agents from within pharmacologic class:
  e.g. Granisetron or Dolasetron for Ondansetron
  e.g. Domperidone for Metoclopramide

Consider substituting serotonin receptor antagonist for dopamine receptor antagonist
  e.g. Ondansetron for Metoclopramide (re-assess antiemetic effectiveness with each cycle before re-ordering)

Consider addition of "NK1 Receptor Antagonist" (e.g. Aprepitant) to the regimen- when available in Canada

Delayed emetic episodes (>24 hours after last chemotherapy treatment)

Footnote:
* When available in Canada
Management of Nausea & Vomiting - Pediatric Cancer Patients

Management of chemotherapy-induced nausea and vomiting in children differs from adults. Children are much more sensitive to acute dystonic reactions from dopamine receptor antagonists and are more likely to develop anticipatory nausea and vomiting. The system to rank emetogenicity of drugs and regimens includes additional gradations, to identify patients who are in greater need of higher dose antiemetics and dopamine receptor antagonists. The emetogenicity ranking of full regimens is outlined on this page, and the pediatric dosing is on the following page. Antiemetic agents for children with cancer may be given in the hospital or filled at a community pharmacy. Specific directions for antiemetic treatment will be given by the pediatric oncology program.

**REGIMEN EMETOGENICITY RANK**

1. Start with the highest ranked individual drug
2. For every other drug to be given at the same time, and with a rank >0, add 1 rank per drug to equal the drug rank for the total regimen. (maximum rank of 5)

- **VERY HIGH** Rank: 4
  - carmustine >250 mg/m<sup>2</sup>
  - cisplatin > 50 mg/m<sup>2</sup> *
  - cyclophosphamide > 1500 mg/m<sup>2</sup> *
  - dacarbazine
  - mechlorethamine

- **HIGH** Rank: 3
  - carboplatin *
  - carmustine ≤ 250 mg/m<sup>2</sup>
  - cisplatin < 50 mg/m<sup>2</sup> *
  - cyclophosphamide *
    - > 750 mg/m<sup>2</sup> and ≤ 1500 mg/m<sup>2</sup>
  - cytarabine > 1000 mg/m<sup>2</sup>
  - dactinomycin
  - daunorubicin > 60 mg/m<sup>2</sup>
  - doxorubicin > 60 mg/m<sup>2</sup>
  - methotrexate > 1000 mg/m<sup>2</sup>

- **MODERATE** Rank: 2
  - cyclophosphamide ≤ 750 mg/m<sup>2</sup> *
  - daunorubicin < 60 mg/m<sup>2</sup>
  - doxorubicin < 60 mg/m<sup>2</sup>
  - epirubicin < 90 mg/m<sup>2</sup>
  - etoposide > 60 mg/m<sup>2</sup>
  - idarubicin
  - ifosfamide
  - methotrexate = 250-1000 mg/m<sup>2</sup>
  - mitoxantrone < 15 mg/m<sup>2</sup>
  - Radiotherapy to abdomen, mantle, cranium, cranial spine

- **MILD** Rank: 1
  - etoposide < 60 mg/m<sup>2</sup>
  - methotrexate 51-249 mg/m<sup>2</sup>
  - procarbazine
  - teniposide

- **NONE** Rank: 0
  - asparaginase
  - bleomycin
  - busulfan
  - chlorambucil
  - cytarabine < 1000 mg/m<sup>2</sup>
  - hydroxyurea
  - lomustine
  - mercaptopurine
  - methotrexate ≤ 50 mg/m<sup>2</sup>
  - thioguanine
  - vinblastine
  - vincristine

* may also cause delayed or prolonged nausea and vomiting

- For the Full Version of this guideline, see the Cancer Care Nova Scotia website at www.cancercare.ns.ca
**Antiemetic Treatment for Pediatric Cancer Patients**

**REGIMEN**

**EMETOGENICITY RANK**

**Very High**

- **Rank ≥ 4**
  - Dimenhydrinate 1 mg/kg (max 50 mg) IV/PO q4h PRN b
  - Dexamethasone 8 mg/m2 (max 20 mg/dose) IV q12-24h starting 24 hours post chemo PRN if nausea/vomiting uncontrolled c
  - **PLUS** (as needed)
    - Dimenhydrinate 1 mg/kg (max 50 mg) IV/PO q4h PRN
    - Dexamethasone 8 mg/m2 (max 20 mg/dose) IV q12-24h starting 24 hours post chemo PRN if nausea/vomiting uncontrolled

**High**

- **Rank = 3**
  - Ondansetron 0.15 mg/kg (max 8 mg) IV/PO pre-chemo and q8h b
  - **PLUS** (as needed)
    - Ondansetron 0.15 mg/kg (max 8 mg) IV/PO pre-chemo and q6h

**Moderate**

- **Rank = 2**
  - Ondansetron 0.15 mg/kg (max 8 mg) IV/PO pre-chemo and q12h b

**Mild**

- **Rank = 1**
  - Ondansetron 0.1 mg/kg (max 8 mg) IV/PO x 1 dose pre-chemo b

**None**

- **Rank = 0**
  - No routine treatment

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**Anticipatory Nausea/Vomiting**

- Lorazepam (5-10 yrs: 0.5 mg/dose; > 10 yrs: 1 mg/dose) PO/SL qHS the night before chemo and/or the morning of chemo

**AND**

- Modify antiemetic regimen for next cycle of chemotherapy (i.e. increase to next rank up for regimens < rank 4)

- Ipratropium 0.025 mg/kg/dose (max 4 mg/dose) IV/PO/SL q6h PRN

**OR**

- Dimenhydrinate 1 mg/kg/dose IV/PO q4h PRN

**AND**

- Increase ondansetron dosing frequency (e.g. from q8h to q6h)

**AND**

- Add dexamethasone, if appropriate

**AND**

- Modify antiemetic regimen for next cycle of chemotherapy (i.e. increase to next rank up for regimens < rank 4)

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a. Regular antiemetics given 'round-the-clock' for twice the number of chemotherapy days, up to a duration of +3 days after chemotherapy. PRN antiemetics may be continued beyond this time.

b. Antiemetics given orally when appropriate. Oral Ondansetron rounded to nearest dose of 4mg or 8mg tablet or appropriate dose of liquid

c. Dexamethasone as an antiemetic may be contraindicated in some protocols or in patients receiving treatment for brain tumours.

d. Breakthrough occurs when the patient experiences > 2 vomits or retches within a 24 hour period, or experiences > 3 hours of significant nausea per day, affecting the level of patient activity.

e. If patient fails on 2 consecutive cycles with ondansetron, substitute granisetron for ondansetron.
Antiemetic Treatment for Chronic Nausea

**Initial Treatment**

- **Step 1.** Metoclopramide 10mg PO/SC q4h + 10mg PO/SC for rescue

  **Step 2.**
  - Same dose of Metoclopramide PLUS
  - Dexamethasone 10mg PO/SC BID

  **Side effects**
  - Bowel obstruction
  - Contraindications

  **Poor response**

- **Step 3.**
  - Metoclopramide CSCI 60-120mg/24h PLUS
  - Dexamethasone 10mg PO/SC BID

  **Poor response**

- **Step 4.** Consider Other Antiemetics:
  - Haloperidol
  - Antihistamines (e.g. Dimenhydrinate)

  **Poor response**

- **Step 5.** Consider Serotonin Receptor Antagonist

  **Other Steps Failed**

**NOTES:**
- Poor response: Continued nausea AND >2 rescue doses/day
- CSCI - Continuous Subcutaneous Infusion
- Metoclopramide may cause extrapyramidal reactions, which may require co-administration of an anticholinergic agent, such as benztropine (Cogentin)

Antiemetic Treatment for Radiotherapy Patients

Radiotherapy is available only at a cancer centre. Antiemetic treatment will usually be determined by a radiation oncologist.

**Assess Emetogenic Risk of Radiotherapy:**
- risk by field size, location and dosage

**ANTIEMETIC DRUGS AND DOSES**

- **Serotonin Receptor Antagonists**
  - Ondansetron 8mg PO (may use ODT formulation) Q12H OR
  - Granisetron 2mg PO OR
  - Dolasetron 100-200mg PO
- **Dopamine Receptor Antagonists**
  - Prochlorperazine 10mg PO OR
  - Metoclopramide 10-20mg PO
- **Corticosteroid**
  - Dexamethasone 4mg PO QD

**HIGH Risk**
- Total Body Irradiation

**INTERMEDIATE Risk**
- Hemibody Irradiation
- Upper abdomen
- Abdominal-Pelvic
- Mantle
- Nasopharynx
- Cranium (radiosurgery)
- Craniospinal

**LOW Risk**
- Cranium only
- Breast
- Head and neck (other than nasopharynx)
- Extremities
- Pelvis
- Thorax

**Daily before first fraction and 12 hours later (i.e. twice daily):**
- Serotonin receptor antagonist PLUS corticosteroid
- Dopamine receptor antagonist PRN only

**Before each fraction and 12 hours later (i.e. twice daily):**
- Serotonin receptor antagonist PLUS corticosteroid (and dopamine receptor antagonist PRN only); or
- Dopamine receptor antagonist +/- corticosteroid

**As-needed basis:**
- Dopamine receptor antagonist, or
- Corticosteroid, or
- Serotonin receptor antagonist

- For the Full Version of this guideline, see the Cancer Care Nova Scotia website at www.cancercare.ns.ca