Guidelines for Prevention and Treatment of Chemotherapy-Induced Nausea and Vomiting in Adults

**Protocol Code**
SCNAUSEA

**Tumour group**
SUPPORTIVE CARE

**Physician Contact**
Dr. Paul Hoskins

**ELIGIBILITY**
- Adults receiving chemotherapy.
- Drug acquisition: Antiemetics are considered supportive treatment. These agents are not BCCA benefit drugs and are not covered by any BCCA program. Patients being treated with these agents should have prescriptions filled at a community pharmacy and must arrange their own payment for the drugs.

**EXCLUSION CRITERIA**
- Pediatric patients.
- Radiation-induced nausea and vomiting.

**APPROACH TO TREATMENT**
- The goal is NO nausea or vomiting.\(^{1-3}\)
- It is far easier to prevent nausea and vomiting than to treat it.\(^{1,2}\)
- Anticipatory nausea and vomiting is a conditioned response, and can only happen after a negative past experience.\(^{1,2}\)
- Ensure optimal antiemetic therapy for every cycle of chemotherapy.
- Use of guidelines: This is a general reference and is not intended to replace the clinical judgment of individual practitioners caring for individual patients.
**PROPHYLACTIC ANTIEMETIC REGIMENS**

- For multiple days of chemotherapy, repeat antiemetics before each treatment.

<table>
<thead>
<tr>
<th>EMETOGENICITY</th>
<th>PRE-CHEMOTHERAPY</th>
<th>POST-CHEMOTHERAPY</th>
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</table>
| High          | **ONE 5-HT₃ ANTAGONIST:**  
- ondansetron 8 mg po  
- granisetron 1 mg po  
PLUS:**  
dexamethasone 8-12 mg po¹-³  
PLUS:  
aprepitant* 125 mg po⁷-⁹  | aprepitant 80 mg po daily x 2 days²,⁵,⁹  
PLUS:**  
dexamethasone 4 mg po evening of chemo,³ then 4 mg po BID x 2-5 days²,³  
AND ONE ANTIEMETIC “AS-NEEDED”:  
- prochlorperazine 10 mg po every 4-6 hours PRN x 3-4 days³,⁵ OR  
- metoclopramide 10-40 mg po every 4-6 hours PRN x 3-4 days¹,⁴ |
| High-moderate | **ONE 5-HT₃ ANTAGONIST:**  
- ondansetron 8 mg po  
- granisetron 1 mg po  
PLUS:  
dexamethasone 8-20 mg po¹-³  | dexamethasone 4 mg po evening of chemo,³ then 4 mg po BID x 2-3 days²,³  
AND ONE ANTIEMETIC “AS-NEEDED”:  
- prochlorperazine 10 mg po every 4-6 hours PRN x 3-4 days³,⁵ OR  
- metoclopramide 10-40 mg po every 4-6 hours PRN x 3-4 days¹,⁴ |
| Low           | **PREFERRED:**  
dexamethasone 4-12 mg po¹,²  
ALTERNATE:  
prochlorperazine 10 mg po OR metoclopramide 20-40 mg po²  | dexamethasone 4 mg BID for up to 2-3 days¹,³ OR  
- prochlorperazine 10 mg po every 4-6 hours PRN x 3-4 days³,⁵ OR  
- metoclopramide 10-40 mg po every 4-6 hours PRN x 3-4 days¹,⁴ |
| Rare          | Prophylactic treatment not normally required.  | prochlorperazine 10 mg po every 4-6 hours PRN x 3-4 days³,⁵ OR  
- metoclopramide 10-40 mg po every 4-6 hours PRN x 3-4 days¹,⁴ |

For prophylaxis after prior treatment failures, refer to Figure 1.

*For inpatients unable to swallow:  
- consider replacing pre-chemotherapy aprepitant with fosaprepitant IV 150 mg  
- post-chemotherapy fosaprepitant NOT needed,²,⁹,¹⁰ dose of 5-HT₃ antagonist and dexamethasone remain the same (fosaprepitant 150 mg confers comparable serum level to aprepitant 125 mg¹¹ which seems sufficient to cover days 2 and ³¹²)  
**If patients do not receive aprepitant /fosaprepitant, may increase dexamethasone to 20 mg day 1 and 16 mg BID days 2 to 4¹  

**TREATMENT NOTES**

- Oral and IV formulations of 5-HT₃ antagonists are equally effective. If IV administration is clinically indicated, use same doses.³  
- Single doses of 5-HT₃ antagonists are as effective as multiple doses.³,⁵  
- Currently available 5-HT₃ antagonists (ondansetron, granisetron) are equally effective. Choose based on availability and cost.¹-³,⁵  
  1. Ondansetron may increase the risk of arrhythmia and Torsade de Pointes in patients:  
     - with congenital long QT syndrome  
     - with pre-existing hypokalemia or hypomagnesemia, or
• using medications that prolong QT interval. ECG monitoring is recommended in patients with electrolyte abnormalities, congestive heart failure, bradycardia, or taking concomitant medications that prolong the QT interval. Results from an ongoing FDA safety review are expected in early 2012.

2. Dolasetron is not recommended due to increased risk of QT prolongation and Torsades de Pointes.

• Except for highly emetogenic chemotherapy, a corticosteroid alone is the cornerstone of therapy for prevention of delayed nausea and vomiting. There is no role for the routine use of 5-HT₃ antagonists more than 24 hours after chemotherapy.

**DETERMINING EMETOGENICITY OF CHEMOTHERAPY**

**Emetogenicity:** percentage of patients who will experience emesis if not treated.
- high greater than 90%
- high-moderate = 60% to 90%
- low-moderate = 30% to less than 60%
- low = 10% to less than 30%
- rare less than 10%

**Single agent chemotherapy:** consult Cancer Drug Manual.

**Combination chemotherapy:**
- Consult chemotherapy protocol.
- If emetogenicity is not specified, consult Cancer Drug Manual.
- Treat for the most emetogenic agent OR use Hesketh Algorithm.

**HESKETH ALGORITHM**

- Identify the most highly emetogenic agent in the combination, then add the contribution of other agents using the following rules:
  - high, high-moderate, low-moderate: increase the emetogenicity of the combination by one level per agent.
  - low: increase the emetogenicity of the combination by one level, regardless of how many such agents are added.
  - rare: do not contribute.

**TREATMENT FAILURES**

- If a patient experiences nausea or vomiting despite optimal prophylactic therapy, complete steps 1, 2, and 3 as follows:

1. Rule out or treat other causes of nausea and vomiting:
   - intestinal obstruction, gastroparesis, gastritis
   - medications (pain meds, bronchodilators)
   - brain metastases
   - vestibular dysfunction
   - electrolyte imbalance, uremia
   - infection

2. Control this episode of nausea and vomiting.

**Approach to treatment:**
- give additional antiemetic agent from a different class
- use rectal or iv route of administration if patient is vomiting
- consider around-the-clock dosing rather than prn
- monitor hydration and electrolytes
- may need to use multiple agents in alternating schedules

**Consider admission to hospital.**

**Possible antiemetic regimens include:**
- dexamethasone 12 mg po/iv daily, if not previously given
- prochlorperazine 25 mg pr q12h or 10 mg po/iv q4-6h
- metoclopramide 20-40 mg po q4-6h or 1-2 mg/kg iv q3-4h ± diphenhydramine 25-50 mg po/iv q4-6h
- lorazepam 0.5-2 mg po or sl q4-6h
- haloperidol 1-2 mg po q4-6h or 1-3 mg iv q4-6h
- dimenhydrinate 100mg po q12h alternating with prochlorperazine 10 mg po q12h (for a q6h regimen)

3. **Plan prophylactic regimen for next cycle using Figure 1.**
Figure 1. SUBSEQUENT ANTIEMETIC REGIMENS AFTER TREATMENT FAILURE

Did patient have ANY nausea or vomiting last cycle? no continue current management

Anxiety or signs of anticipatory nausea and vomiting? yes continue optimal prophylactic regimen and add one or more of:
• lorazepam 0.5-2 mg PO/SL q12h, start the night before chemo\textsuperscript{2,3}
• behavioural therapy (e.g., relaxation, hypnosis, music therapy)\textsuperscript{1,3}

Vomited within 24 h of chemo? yes acute nausea and vomiting:
Is patient on highest pre-chemo antiemetic regimen?

Vomited > 24 h after chemo? no increase to a higher risk regimen pre-chemo\textsuperscript{1,3}

Vomited > 24 h after chemo? no delayed nausea and vomiting:
treat for duration of emesis + 1 day\textsuperscript{3}

Is patient on highest post-chemo antiemetic regimen? yes may increase or change 5-HT\textsubscript{3} antagonist (anecdotal evidence)\textsuperscript{2}

Is patient on highest post-chemo antiemetic regimen? no increase to a higher risk regimen post-chemo\textsuperscript{1,3}

may add one or more of:
• metoclopramide 20-40 mg PO q4-6h\textsuperscript{1-3}
• lorazepam 0.5-2 mg PO/SL bid-qid\textsuperscript{1-3}
• haloperidol 1-2 mg q4-6h\textsuperscript{2}
• dimenhydrinate 100 mg PO q12h, alternate with
  • prochlorperazine 10 mg PO q12h (i.e., q6h regimen)\textsuperscript{3}
  • olanzapine 2.5 – 5 mg PO BID\textsuperscript{2}
  • scopolamine 1 patch q72h\textsuperscript{2}

consider one or more of:\textsuperscript{5 - HT\textsubscript{3} antagonist (anecdotal evidence)\textsuperscript{2}}
• nabilone 1 mg PO q12h
• behavioural modification
• inpatient chemo (monitoring, hydration and electrolyte replacement prn)

may change chemo regimen\textsuperscript{2,3}

controlled continue current management

controlled
Call Dr. Paul Hoskins or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: 4 May 1999

Dated revised: 1 Mar 2012 (addition of fosaprepitant IV, ondansetron QT, olanzapine, scopolamine, references)

REFERENCES