Cancer Care Ontario

June 2019

Summary of 2019 Antiemetic Recommendations

Clinical Question 1
What is the optimal prevention strategy for nausea and vomiting with highly emetogenic chemotherapy (HEC) in adult patients who receive single day intravenous chemotherapy?

Recommendation 1.1: Adults who receive HEC should be offered primary prophylaxis with a four-drug regimen consisting of a neurokinin-1 receptor antagonist (NK_1 RA), serotonin receptor antagonist (5-HT_3 RA), dexamethasone, and olanzapine. For patients at increased risk of sedation, clinical judgement should be used to determine the need for olanzapine, especially in patients at lower risk of CINV.

Recommendation 1.2: Olanzapine
Adults who receive HEC should be offered olanzapine at a dose of 5 mg PO prior to chemotherapy, and 5 mg PO daily (or 2.5 mg PO bid) continued on days 2 to 4. For patients at increased risk of sedation, clinical judgement should be used to determine the need for olanzapine, especially in at lower risk of CINV.

Recommendation 1.3: Palonosetron
Adults who receive HEC may be offered palonosetron as an alternative to other 5-HT_3 RA. One 5-HT_3 RA is not preferred over another based on the available evidence.

Recommendation 1.4: NEPA
For adults who receive HEC, the combination agent, NEPA (NK_1 RA, netupitant/ 5-HT_3 RA, palonosetron) is a reasonable alternative to an NK_1 RA plus a 5-HT_3 RA.

Recommendation 1.5: Dexamethasone with Anthracycline plus Cyclophosphamide (AC)
Adult patients who receive an anthracycline plus cyclophosphamide for a breast cancer indication should receive a four-drug regimen as part of HEC prophylaxis. If palonosetron is the 5-HT_3 RA used, dexamethasone does not need to continue after day 1. If other 5-HT_3 RAs are used for AC, the need for dexamethasone beyond day 1 is uncertain. Clinicians may choose to limit dexamethasone to day 1, especially when intolerance to steroids, or comorbid conditions exist that make minimizing corticosteroid use desirable.

Clinical Question 2
What is the optimal prevention strategy for nausea and vomiting with moderately emetogenic chemotherapy (MEC) in adult patients who receive single day intravenous chemotherapy?

Recommendation 2.1: MEC regimens excluding carboplatin AUC ≥ 5
Adults who receive MEC, excluding carboplatin regimens with an area under the curve (AUC) ≥ 5, should be offered primary prophylaxis with a 5-HT_3 RA and dexamethasone, on day 1. Olanzapine or an NK_1 RA may be added, as prophylaxis, to subsequent cycles if the patient experiences suboptimal control of CINV. Clinicians should continue to assess patient response throughout chemotherapy treatment in order to optimize the use of these agents; consider adding olanzapine if the patient experiences suboptimal control of nausea and NK_1 RA if the patient experiences suboptimal control of emesis.

Recommendation 2.2: Carboplatin AUC ≥ 5
Adults who receive chemotherapy regimens with carboplatin AUC ≥ 5, should be offered primary prophylaxis with an NK_1 RA in addition to a 5-HT_3 RA and dexamethasone. Olanzapine may be added, as prophylaxis, to subsequent cycles if the patient experiences suboptimal control of CINV.

Recommendation 2.3: Palonosetron
Adults who are treated with MEC may receive palonosetron as an alternative to other 5-HT3 RAs. One 5-HT_3 RA is not preferred over another based on the available evidence

Recommendation 2.4: Dexamethasone duration
For adults treated with oxaliplatin- or carboplatin-based regimens, there is insufficient evidence to recommend dexamethasone beyond day 1 for prevention of CINV.

Clinical Question 3
What is the optimal prevention strategy for nausea and vomiting with low (LEC) and minimally emetogenic chemotherapy in adult patients who receive single day intravenous chemotherapy?

Recommendation 3.1: Adults who receive LEC should be offered a single dose of dexamethasone prior to chemotherapy.

Recommendation 3.2: Adults who receive minimally emetogenic chemotherapy should not be routinely offered antiemetic prophylaxis.

Clinical Question 4
What is the optimal prevention strategy for nausea and vomiting in adult patients who receive high-dose chemotherapy for stem cell transplantation (SCT)?

Recommendation 4: Adults who receive high-dose chemotherapy for SCT should be offered a three-drug antiemetic regimen of an NK_1 RA, a 5-HT_3 RA and dexamethasone.

Clinical Question 5
What is the optimal prevention strategy for nausea and vomiting in adult patients who receive multiple-day intravenous chemotherapy?

Recommendation 5.1: Adults who receive multiple-day chemotherapy regimens should be offered the antiemetic agents appropriate for the chemotherapy agent(s) with the highest emetic risk on the day of chemotherapy, and for up to 2 days after completion of chemotherapy.

Recommendation 5.2: Adults who receive 5-day cisplatin regimens should be offered a four-drug antiemetic regimen consisting of aprepitant, a 5-HT_3 RA, dexamethasone, and olanzapine. Aprepitant, dexamethasone, and olanzapine should be continued for up to 2 days after chemotherapy.

Clinical Question 6
What is the role of cannabinoids in the prevention of chemotherapy-induced nausea and vomiting?

Recommendation 6: Due to the lack of high quality clinical trials, no recommendation can be made to incorporate synthetic or non-synthetic cannabinoids as part of standard antiemetic therapy. If a cannabinoid is used, it should be after optimal therapy (including combination therapy with a 5-HT_3 RA, NK_1 RA, dexamethasone and olanzapine) has failed to provide adequate control of nausea and vomiting. If used, patients should be guided to access products with consistent concentrations.

Clinical Question 7
What is the optimal treatment for adult patients who experience nausea and vomiting secondary to chemotherapy, despite optimal prophylaxis (breakthrough)?

Recommendation 7.1: Adult patients who experience CINV despite optimal prophylaxis and did not receive olanzapine prophylactically, should be offered olanzapine 5 mg daily or 2.5 mg bid in addition to the standard antiemetic regimen.

Recommendation 7.2:
Adult patients who experience CINV despite optimal prophylaxis and have already received olanzapine, may be offered olanzapine 5 mg bid (for a total of 10 mg/day) or a drug of a different class in addition to continuing the standard antiemetic regimen.

Clinical Question 8
What is the optimal prevention strategy for nausea and vomiting in adult patients who receive single day oral chemotherapy?

Recommendation 8: There is insufficient evidence to recommend routine antiemetic prophylaxis prior to an oral chemotherapy. In the event that a patient develops significant nausea or vomiting, consider initiating a routine prophylactic antiemetic agent. Clinical judgement should be used for individual cases where primary prophylaxis may be warranted.

Summary Antiemetic Tables

1. Single Day IV Chemotherapy:

1.1 Highly Emetogenic Chemotherapy (HEC)[+]:

Dosing on day of chemotherapy[¥]	Dosing on subsequent days
Choose one NK_1 receptor antagonist: Aprepitant 125 mg PO **OR** Fosaprepitant 150 mg IV **OR** NEPA (netupitant 300 mg + palonosetron 0.5 mg) PO	Aprepitant 80 mg PO daily (days 2 – 3)[a] if started on Day 1
Choose one 5-HT_3 receptor antagonist: Granisetron 2 mg PO or 1 mg IV **OR** Ondansetron 8 mg PO BID or 8 mg IV **OR** Palonosetron 0.25 mg IV or 0.5 mg PO[b]	No 5-HT_3 RA recommended after day of chemotherapy
Dexamethasone[c] 12 mg PO or 10 mg IV	Dexamethasone[c] 8 mg PO or 10 mg IV (days 2 – 3 or 4)
Olanzapine 5 mg PO	Olanzapine 5 mg PO daily (or 2.5 mg BID) days 2 – 4

[+] In breast cancer population receiving a combination of anthracycline and cyclophosphamide (AC), may consider limiting dexamethasone to day 1, when minimizing corticosteroid is desirable. Dexamethasone does not need to be continued after day 1 with the use of palonosetron.
[¥] Antiemetics should be given as a one-time dose (unless otherwise specified) an hour prior to chemotherapy administration, on the day of chemotherapy.
[a] Aprepitant is given on subsequent days only if used on day of chemotherapy. Do not give aprepitant on subsequent days if fosaprepitant or netupitant is given on day of chemotherapy.
[b] Palonosetron 0.5 mg PO is not approved for HEC by Health Canada.
[c] Dexamethasone dose listed is if used with NK_1 receptor antagonist. If NK_1 receptor antagonist is not used, dexamethasone dose is 20 mg on day of chemotherapy and 16 mg on days 2 – 3 (or 4).

1.2 Moderately Emetogenic Chemotherapy (MEC) †:

Dosing on day of chemotherapy¥	Dosing on subsequent days
Choose one 5-HT$_3$ receptor antagonist: Granisetron 2 mg PO or 1 mg IV **OR** Ondansetron 8 mg PO BID or 8 mg IV **OR** Palonosetron 0.25 mg IV or 0.5 mg PO	No 5-HT$_3$ RA recommended after day of chemotherapy
Dexamethasone 8 mg PO or 10 mg IV	No dexamethasone recommended after day of chemotherapy
OPTIONAL ON SUBSEQUENT CYCLES if inadequate control of CINV in previous cycle£:	
Choose one NK$_1$ receptor antagonist: Aprepitant 125 mg PO **OR** Fosaprepitant 150 mg IV **OR** NEPA (netupitant 300 mg + palonosetron 0.5 mg) PO	Aprepitant 80 mg PO daily (days 2 – 3)[a] if started on Day 1
OR Olanzapine 5 mg PO	Olanzapine 5 mg PO daily (or 2.5 mg BID) days 2 – 4

† Patients receiving carboplatin AUC ≥ 5 should receive an NK$_1$ receptor antagonist up front with a 5-HT$_3$ receptor antagonist and dexamethasone.
¥ Antiemetics should be given as a one-time dose (unless otherwise specified) an hour prior to chemotherapy administration, on the day of chemotherapy.
£ Consider olanzapine if patient experiences suboptimal control of nausea and NK$_1$ RA if patient experiences suboptimal control of emesis, after the first cycle.
[a] Aprepitant is given on subsequent days only if used on day of chemotherapy. Do not give aprepitant on subsequent days if fosaprepitant or netupitant is given on day of chemotherapy.

1.3 Low Emetic Risk Chemotherapy (LEC):

Dosing on day of chemotherapy¥	Dosing on subsequent days
Dexamethasone 8 mg PO or 10 mg IV	No dexamethasone recommended after day of chemotherapy

¥ Antiemetics should be given as a one-time dose (unless otherwise specified) an hour prior to chemotherapy administration, on the day of chemotherapy

1.4 Minimal Emetic Risk Chemotherapy:

Dosing on day of chemotherapy	Dosing on subsequent days
No antiemetics recommended	No antiemetics recommended

2. Multiple Day IV Chemotherapy:

2.1 Highly Emetogenic Chemotherapy (HEC):

Dosing on days of chemotherapy[¥]	Dosing on subsequent days
Aprepitant 125 mg PO on Day 1 then 80 mg PO on remaining days of chemotherapy	Aprepitant 80 mg PO daily (up to 2 days after last dose of chemotherapy)
Choose one 5-HT_3 receptor antagonist: Granisetron 2 mg PO or 1 mg IV **OR** Ondansetron 8 mg PO BID or 8 mg IV	No 5-HT_3 RA recommended after day of chemotherapy
Dexamethasone[a] 12 mg PO or 10 mg IV	Dexamethasone[a] 8 mg PO or 10 mg IV (up to 2 days after last dose of chemotherapy)
Olanzapine 5 mg PO	Olanzapine 5 mg PO daily or 2.5mg PO BID (up to 2 days after last dose of chemotherapy)

[¥] Antiemetics should be given as a one-time dose (unless otherwise specified) an hour prior to chemotherapy administration, on the day of chemotherapy.
[a] Dexamethasone dose listed is if used with NK_1 receptor antagonist. If NK_1 receptor antagonist is not used, dexamethasone dose is 20 mg on day of chemotherapy and 16 mg on subsequent days up to 2 days after last dose of chemotherapy.

2.2 Moderately Emetogenic Chemotherapy (MEC):

Dosing on days of chemotherapy[¥]	Dosing on subsequent days
Choose one 5-HT_3 receptor antagonist: Granisetron 2 mg PO or 1 mg IV **OR** Ondansetron 8 mg PO BID or 8 mg IV	No 5-HT_3 RA recommended after day of chemotherapy
Dexamethasone 8 mg PO or 10 mg IV	No dexamethasone recommended after day of chemotherapy
OPTIONAL ON SUBSEQUENT CYCLES if inadequate control of CINV in previous cycle[£]:	
Aprepitant 125 mg PO on Day 1 then 80 mg PO on remaining days of chemotherapy	Aprepitant 80 mg PO daily (up to 2 days after last dose of chemotherapy)
OR Olanzapine 5 mg PO	Olanzapine 5 mg PO daily or 2.5 mg PO BID (up to 2 days after last dose of chemotherapy)

[¥] Antiemetics should be given as a one-time dose (unless otherwise specified) an hour prior to chemotherapy administration, on the day of chemotherapy.
[£] Consider olanzapine if patient experiences suboptimal control of nausea and NK_1 RA if patient experiences suboptimal control of emesis, after the first cycle.

3. High-dose Chemotherapy for Stem Cell Transplantation

Dosing on day of chemotherapy[¥]	Dosing on subsequent days
Choose one NK_1 receptor antagonist: Aprepitant 125 mg PO **OR** Fosaprepitant 150 mg IV **OR** NEPA (netupitant 300 mg + palonosetron 0.5 mg) PO	Aprepitant 80 mg PO daily (days 2 – 3)[a] if started on Day 1
Choose one 5-HT_3 receptor antagonist: Granisetron 2 mg PO or 1 mg IV **OR** Ondansetron 8 mg PO BID or 8 mg IV **OR** Palonosetron 0.25 mg IV or 0.5 mg PO	No 5-HT_3 RA recommended after day of chemotherapy
Dexamethasone 12 mg PO or 10 mg IV	Dexamethasone[b] 8 mg PO or 10 mg IV (days 2 – 3 or 4)

[¥] Antiemetics should be given as a one-time dose (unless otherwise specified) an hour prior to chemotherapy administration, on the day of chemotherapy.
[a] Aprepitant is given on subsequent days only if used on day of chemotherapy. Do not give aprepitant on subsequent days if fosaprepitant or netupitant is given on day of chemotherapy.
[b] Dexamethasone dose listed is if used with aprepitant. If aprepitant not used, dexamethasone dose is 20 mg on day of chemotherapy and 16 mg on days 2 – 3 (or 4).

4. Oral Chemotherapy

Emetic Risk	Management
High to Moderate	Consider prophylaxis daily as per patient experience of CINV * • 5-HT_3 Receptor Antagonist (granisetron 2 mg PO or ondansetron 8 mg PO BID)
Low to Minimal	No routine prophylaxis; PRN recommended • Prochlorperazine 10 mg PO then q4-6h PRN **OR** • Metoclopramide 10-20 mg PO then q4-6h PRN

* Insufficient evidence to recommend routine prophylaxis; Consider if patient develops significant nausea or vomiting and re-assess routinely. Use clinical judgement for individual cases where primary prophylaxis may be warranted.

5. Breakthrough Nausea and/or Vomiting[†]

Examples may include the following [£]:

Drug	Dose
Domperidone	10 mg PO q4-6h PRN nausea and/or vomiting
Haloperidol	0.5-2 mg PO q4-6h PRN nausea and/or vomiting
Metoclopramide	10 mg PO q4-6h PRN nausea and/or vomiting
Olanzapine*	2.5 mg PO BID PRN nausea and/or vomiting
Prochlorperazine	10 mg PO 4-6h PRN nausea and/or vomiting

[†] Use caution when dopamine receptor antagonists (eg. Metoclopramide, haloperidol or prochlorperazine) or medications that cause sedation are given in combination with prophylactic olanzapine.
[£] Not a comprehensive list of agents for breakthrough nausea and vomiting.
* Preferred agent. If olanzapine given prophylactically for HEC or MEC, patients may be offered olanzapine (max daily dose suggested is 10 mg, due to sedation) or an agent of a different class.

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