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Endorsement of the 2017 American Society of Clinical Oncology's Guideline for Antiemetics

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Alberta Health Services
CancerControl Alberta

Clinical Practice Guideline SUPP-011 – Version 1
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Background

Chemotherapy- and radiation-induced nausea and vomiting (CINV/RINV) is a common side effect of patients undergoing cancer treatment. Without appropriate antiemetic therapy, 70% to 80% of cancer patients undergoing chemotherapy develop CINV.[1] Similarly, upward of 50% to 80% of patients treated with radiation therapy (RT) develop RINV.[2] CINV/RINV can lead to morbidity, poor performance status and decreased quality of life in patients.[1,3]

CINV. The common patient-related factors for CINV include younger age (<50 years), female gender, history of motion sickness and/or pregnancy-related nausea and vomiting, anxiety and non-habitual alcohol intake.[4-6] However, the main risk factor for CINV is the type of chemotherapy agents being administered. Chemotherapy agents are classified according to their relative emetogenic risk potential:[7-11]

- High emetogenic chemotherapy (HEC) – affects > 90% of patients;
- Moderate emetogenic chemotherapy (MEC) – affects 30-90% of patients;
- Low emetogenic chemotherapy (LEC) – affects 10-30% of patients; and,
- Minimal emetogenic chemotherapy – affects <10% of patients.

CINV can also be classified according to its onset relative to the start of chemotherapy and the patients' previous responses to antiemetic prophylaxis:[8,12]

- Acute – occurs within 24 hours after chemotherapy;
- Delayed – occurs more than 24 hours after chemotherapy;
- Breakthrough – occurs within 5 days of chemotherapy after the use of appropriate prophylactic antiemetic agents;
- Anticipatory – a conditioned response that occurs in patients who experienced CINV during previous cycles of chemotherapy; and,
- Refractory – occurs in subsequent cycles of chemotherapy, after the use of appropriate prophylactic antiemetic agents have failed in earlier cycles.

Neurotransmitters including dopamine, serotonin, and substance P are thought to be important mediators of CINV (Hesketh 2008). Chemotherapy agents can cause nausea and vomiting by activating neurotransmitter receptors present in the area postrema of the brain (central pathway) and the enterochromaffin cells of the gastrointestinal tract (peripheral pathway).[13]
Effective antiemetic agents provide control of vomiting by blocking neurotransmitter receptors and thus inhibiting stimulation of the chemoreceptor trigger zone.
RINV. Only previous treatment with chemotherapy has been identified as a patient-related risk factor for RINV.[14,15] The risk of emesis from RT is categorized according to the radiation field:[9,10,16]

- High emetogenic RT – total body irradiation

- Moderate emetogenic RT – upper abdomen, craniospinal
- Low emetogenic RT – brain, head and neck, thorax, pelvis
- Minimal emetogenic RT – extremities, breast

The risk levels listed above do not take into account radiation dose, fractionation, or technique and are mainly based on incidence of emesis in clinical studies and expert opinions.[16] While little is known about the pathophysiology of RINV, the causal factors underlying RINV and CINV are believed to be related.[17]

The goal of antiemetic therapy is to prevent CINV/RINV, and while significant progress has been made to develop a number of effective and well-tolerated antiemetic treatments, CINV/RINV remains a serious side effect of cancer treatment. The objective of this guideline is to provide clinicians with recommendations for the prevention and management of CINV/RINV. This document describes Alberta Health Services (AHS) endorsement of the 2017 American Society of Clinical Oncology (ASCO) clinical practice guideline for antiemetics.[9]

Note: Some chemotherapy agents recommended by ASCO do not appear in this document because they are not currently available in Alberta (see Appendix A). Similarly, some drug delivery systems (e.g. oral dissolving films, transdermal patches) have been omitted because they are not available from the cancer center pharmacies.

Guideline Questions

1. What are the most effective strategies for preventing and managing nausea and vomiting caused by chemotherapy and radiotherapy?

Search Strategy

The PubMed database was searched for relevant studies, guidelines and consensus documents published between January 1 2007 and April 9 2019. For CINV, the search terms were: (chemotherapy induced nausea vomiting) AND (prevention OR treatment OR therapy OR Anti-Anxiety Agents [MeSH Terms] OR acupuncture therapy [MeSH Terms] OR Psychological Techniques [MeSH Terms] OR antiemetics [MeSH Terms]). Results were limited to humans, English language studies, and studies of adult patients aged 19 years and older. Case reports and retrospective studies were excluded, as well as studies with under 100 patients and meta-analyses with under 300 patients. A total of 398 articles resulted from the literature review, of which 42 were included in final evidence table. For RINV, the search terms were: (radiotherapy induced nausea vomiting) AND (prevention OR treatment OR therapy OR Anti-Anxiety Agents [MeSH Terms] OR acupuncture therapy [MeSH Terms] OR Psychological Techniques [MeSH Terms] OR antiemetics [MeSH Terms]). Results were limited to humans, English language studies, and studies of adult patients aged 19 years and older. Case reports and retrospective studies were excluded, as well as studies

with under 30 patients. A total of 90 articles resulted from the literature review, of which 19 were included in final evidence table.

Online resources from oncology-based health organizations and guideline developers were also systematically searched, and relevant guidelines published between January 1 2015 and April 9 2019 from the following organizations were considered in the development of this document: American Society of Clinical Oncology (ASCO), BC Cancer (BCC), BC Guidelines, Cancer Care Ontario (CCO), ECRI Guideline Trust®, European Society for Medical Oncology (ESMO), Multinational Association of Supportive Care in Cancer (MASCC), National Comprehensive Cancer Network (NCCN), and UptoDate.

The recommendations in the present guideline have been adapted from the evidence-based clinical guideline Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. Beyond this, the working group updated the guideline by including supplementary supporting research and evidence-based recommendations from the literature searches.

Evidence tables are available upon request from GURU@ahs.ca.

Target Population

Adult patients receiving potentially emetogenic chemotherapy and/or radiotherapy for cancer.

Recommendations

1. Combination Chemotherapy. ENDORSED

Patients who are treated with combination chemotherapy should be offered antiemetics that are appropriate for the agent with the highest emetogenic level. Please refer to Appendix B and Appendix C to identify the risk level of single oral and IV antineoplastic agents in adults, respectively.

2. Highly Emetogenic Chemotherapy (>90% frequency of emesis). ENDORSED WITH ADAPTATIONS

a) Patients who are treated with ***cisplatin and other highly emetogenic single agents*** should be offered a four-drug combination of a neurokinin 1 (NK_1) receptor antagonist (RA), a serotonin (5-HT_3) RA, dexamethasone, and olanzapine. Dexamethasone and olanzapine should be continued on days 2 to 4.

Drug	Dose on Day of Chemotherapy	Dose on Subsequent Days
NK_1 RA*		
• Aprepitant	125 mg PO	80 mg PO days 2, 3
5-HT_3 RA†		

Drug	Dose on Day of Chemotherapy	Dose on Subsequent Days
• Ondansetron, or • Granisetron	• 8 mg PO bid or 8 mg ODT bid or 8 mg IV • 2 mg PO or 1 mg IV	
Dexamethasone[ŧ]	12 mg PO/IV	8 mg PO daily; days 2-4
Olanzapine[§]	5-10 mg PO	5-10 mg PO days 2-4 before bed

[*]Netupitant-palonosetron (NEPA) 300 mg/0.5 mg is a fixed dose oral combination not listed on the AHS Drug Formulary, but that may be offered once per-cycle treatment before chemotherapy. If NEPA is used, no additional 5-HT_3 RA is needed.
[†]Single agent palonosetron 0.5 mg PO or 0.25 mg IV may also be used, but is not listed on the AHS Drug Formulary.
[ŧ]The dexamethasone dose is for patients who are receiving the recommended four-drug regimen for highly emetic chemotherapy. If patients do not receive an NK_1 RA, the dexamethasone dose should be adjusted to 20 mg on day 1 and to 16 mg on days 2-4.
[§]The decision to include a lower olanzapine dose differs from the ASCO recommendations and is based on data showing comparable efficacy between 10 mg and 5 mg and the risk of increased sedation.[18-20] Olanzapine may be used on a scheduled or PRN basis. If you choose to use olanzapine, we recommend against using metoclopramide, prochlorperazine, or haloperidol because of an increased risk of extrapyramidal symptoms.

b) Patients who are treated with an ***anthracycline combined with cyclophosphamide*** should be offered a four-drug combination of an NK_1 RA, a 5-HT_3 RA, dexamethasone, and olanzapine. Olanzapine should be continued on days 2 to 4.

Drug	Dose on Day of Chemotherapy	Dose on Subsequent Days
NK_1 RA[*] • Aprepitant	125 mg PO	80 mg PO days 2, 3
5-HT_3 RA[†] • Ondansetron, or • Granisetron	• 8 mg PO bid or 8 mg ODT bid or 8 mg IV • 2 mg PO or 1 mg IV	
Dexamethasone[ŧ]	12 mg PO/IV	**21
Olanzapine[β]	5-10 mg PO	5-10 mg PO days 2-4 before bed

[*]NEPA may be offered once per-cycle treatment before chemotherapy. If NEPA is used, no additional 5-HT_3 RA is needed.
[†]Single agent palonosetron 0.5 mg PO or 0.25 mg IV may also be used, but is not listed on the AHS Drug Formulary.
[ŧ]The dexamethasone dose is for patients who are receiving the recommended four-drug regimen for highly emetic chemotherapy. If patients do not receive an NK_1 RA, the dexamethasone dose should be adjusted to 20 mg on day 1 and to 16 mg on days 2-4.
[**]If palonosetron is the 5-HT3 RA used, dexamethasone does not need to continue after day 1. If other 5-HT3 RAs are used, the need for dexamethasone beyond day 1 is uncertain.
[β]The decision to include a lower olanzapine dose differs from the ASCO recommendations and is based on data showing comparable efficacy between 10 mg and 5 mg and the risk of increased sedation.[18-20] Olanzapine may be used on a scheduled or PRN basis. If you choose to use olanzapine, we recommend against using metoclopramide, prochlorperazine, or haloperidol because of an increased risk of extrapyramidal symptoms.

3. Moderately Emetogenic Chemotherapy (30–90% frequency of emesis). ENDORSED WITH ADAPTATIONS

a) Patients who are treated with ***carboplatin-based regimens AUC ≥ 4*** should be offered a three-drug combination of a NK_1 RA, a 5-HT_3 RA, and dexamethasone.

Drug	Dose on Day of Chemotherapy	Dose on Subsequent Days
NK_1 RA[*] • Aprepitant	 125 mg PO	 80 mg PO days 2, 3
5-HT_3 RA[†] • Ondansetron, or • Granisetron	 • 8 mg PO bid or 8 mg ODT bid or 8 mg IV • 2 mg PO or 1 mg IV	
Dexamethasone	12 mg PO/IV	± 8 mg PO (or 4 mg bid) days 2, 3[t]

[*]NEPA may be offered. If NEPA is used, no additional 5-HT_3 RA is needed.
[†]Single agent palonosetron 0.5 mg PO or 0.25 mg IV may also be used, but is not listed on the AHS Drug Formulary.
[t]The decision to add dexamethasone on subsequent days differs from the ASCO recommendations. The Working Group agreed with NCCN guidance that dexamethasone may be offered to patients at high risk for emesis or those with poorly controlled CINV on days 2 and 3.[11] Lower doses, given for shorter durations may be acceptable based on patient characteristics. If dexamethasone is eliminated on subsequent days for delayed nausea and emesis prevention, consider other alternative antiemetics (e.g. olanzapine).

b) Patients who are treated with ***carboplatin-based regimens AUC <4 or non-carboplatin-based regimens*** should be offered a two-drug combination of a 5-HT_3 RA (day 1) and dexamethasone (day 1).

Drug	Dose on Day of Chemotherapy	Dose on Subsequent Days
5-HT_3 RA[†] • Ondansetron, or • Granisetron	 • 8 mg PO bid or 8 mg ODT bid or 8 mg IV • 2 mg PO or 1 mg IV	
Dexamethasone	8 mg PO/IV	Patients receiving agents with known risk for delayed nausea and vomiting (e.g. cyclophosphamide*, doxorubicin, oxaliplatin) may be offered 8 mg PO days 2, 3

[†]Single agent palonosetron 0.5 mg PO or 0.25 mg IV may also be used, but is not listed on the AHS Drug Formulary.
*Treat according to high emetogenic risk if dose ≥1500 mg/m^2 and moderate emetogenic risk if dose <1500 mg/m^2.

4. Low Emetogenic Chemotherapy (10–30% frequency of emesis). ENDORSED WITH ADAPTATIONS

Patients who are treated with low-emetic-risk chemotherapy agents should be offered a single dose of a 5-HT_3 RA or dexamethasone before chemotherapy treatment.

Drug	Dose on Day of Chemotherapy
5-HT_3 RA[†] • Ondansetron, or • Granisetron Or, • Dexamethasone*[§]	 • 8 mg PO bid or 8 mg ODT bid or 8 mg IV • 2 mg PO or 1 mg IV 8 mg PO/IV

[†]Single agent palonosetron 0.5 mg PO or 0.25 mg IV may also be used, but is not listed on the AHS Drug Formulary.
*The Working Group agreed with NCCN guidance that a single dose of a dopamine antagonist, e.g. metoclopramide (10 mg PO/IV) or prochlorperazine (10 mg PO/IV), is a reasonable alternative to dexamethasone.[11]

Drug	Dose on Day of Chemotherapy
[§]When dexamethasone is required as premedication for drugs with higher risk of hypersensitivity reactions (e.g. docetaxel, paclitaxel, etc.), or other reasons (e.g. pemetrexed), the dose and dosing schedule as a premedication may be different than antiemetic doses. The dexamethasone dose should be considered in the calculation of the required antiemetic dosage.	

5. Minimal Emetogenic Chemotherapy (<10%). REJECTED AND REVISED

ASCO recommends that patients who are treated with minimal-emetic-risk chemotherapy agents should not be offered routine antiemetic prophylaxis. However, the Working Group agreed that prophylactic antiemetics may be administered to patients who have had emesis with prior low-risk regimens, or on an as needed basis. Examples include, dexamethasone (4 to 8 mg PO/IV), prochlorperazine (10 mg PO/IV), or metoclopramide (10 mg PO/IV).

6. Adjunctive Drugs. ENDORSED WITH ADAPTATIONS

Lorazepam is not recommended as a single-agent antiemetic, but is a useful adjunct to antiemetic drugs because it reduces anxiety and anticipatory nausea and/or vomiting. The Working Group agreed with NCCN guidance that a proton pump inhibitor (e.g. omeprazole 20 mg PO daily) or H2 blocker (e.g. ranitidine 150 mg PO bid) may also be considered to prevent or manage dyspepsia.[11]

7. Cannabinoids. ENDORSED WITH ADAPTATIONS

In agreement with ASCO and Canadian-developed guidelines[22] for prescribing medical cannabinoids, the Working Group agreed that medical cannabis (inhaled, oils, or edibles), as well as nabiximols are not recommended for CINV/RINV. In addition, the Working Group agreed against the use of medical cannabinoids as first- or second-line therapy for CINV/RINV due to a lack of randomized clinical trial data. However, medical cannabinoids may be considered for treatment of refractory CINV/RINV assuming that patients have had a reasonable therapeutic trial of standard therapies, and they are used as adjuncts to other prescribed therapies.[11,21-23] Nabilone (1 to 2 mg PO bid) is recommended.[11,22,23] Dose reduction may be required when prescribing for medically frail patients. Clinicians should discuss the risks and benefits of medical cannabinoids for CINV/RINV with patients before prescribing.[22,24-26]

8. Complementary and Alternative Therapies. ENDORSED

Evidence is insufficient to make a recommendation for or against the use of ginger, acupuncture /acupressure, and other complementary or alternative therapies for the prevention of NV in patients with cancer.[9]

9. High-Dose Chemotherapy with Stem Cell or Bone Marrow Transplantation. ENDORSED WITH ADAPTATIONS

The Working Group agreed with ASCO that patients who are treated with high-dose chemotherapy and stem cell or bone marrow transplantation should be offered a three-drug combination of an NK_1 RA, a 5-HT_3 RA, and dexamethasone before chemotherapy. However, the use of steroids is not recommended with cellular therapies, including preparative lymphodepleting chemotherapy regimens because the risk of inactivating the immune response is very high with even small doses of steroids.[27,28] NCCN recommends avoiding the use of corticosteroid antiemetic premedication for 3-5 days prior to and 90 days after CAR T-cell therapies.[11] However, because prednisone, methylprednisone and dexamethasone have half-lives of only several hours, the Working Group agreed that corticosteroids may be used as late as on day -1.

10. Immune Checkpoint Inhibitors

There is currently inconclusive data regarding interactions between concurrent corticosteroid use and immune checkpoint inhibitors.[11] The Working Group recommends a corticosteroid-sparing approach to antiemetic prophylaxis where feasible and on a case-by-case basis of individual regimens when immune checkpoint inhibitors are administered with chemotherapy.

11. Multiday Chemotherapy. ENDORSED WITH ADAPTATIONS

a) Patients who are treated with multiday highly emetogenic chemotherapy (e.g. 3 or 5-day cisplatin regimens) should be offered a three-drug combination of an NK_1 RA, a 5-HT_3 RA, and dexamethasone administered on each day of chemotherapy and for up to 2 days after chemotherapy is completed.[9]

b) Patients who are treated with multiday moderately or low emetogenic chemotherapy should be offered antiemetics before treatment that are appropriate for the emetic risk of the chemotherapy agent administered on each day of the chemotherapy treatment, and for up to 2 days after the completion of the chemotherapy regimen.[9]

12. Breakthrough Nausea and Vomiting. ENDORSED WITH ADAPTATIONS

a) Clinicians should re-evaluate emetic risk to ascertain that the best regimen is being administered, as well as re-evaluate disease status, concurrent illnesses and medications to assess for possible other mechanisms of nausea and vomiting. Isolated vomiting without substantial nausea is usually related to motility problems.

b) Patients who experience nausea or vomiting despite optimal prophylaxis, and who did not receive olanzapine prophylactically should be offered olanzapine (2.5 to 5 mg PO daily as a starting dose to a maximum of 10 mg PO daily)[21] in addition to continuing the standard antiemetic regimen. Alternatively, clinicians may choose metoclopramide 10 to 20 mg PO every 4-6 hours or prochlorperazine 10 mg PO every 6 hours.[11]

c) In addition to continuing the standard antiemetic regimen, patients who experience nausea or vomiting despite optimal prophylaxis, and who have already received olanzapine, may be offered a drug of a different class including one or more of the following (not a comprehensive list):[11,21,23]

- Proton pump inhibitor (e.g. omeprazole 20 mg PO daily) or H2 blocker (e.g. ranitidine 150 mg PO bid)
- Dimenhydrinate 50 mg PO every 4-6 h
- Scopolamine patch
- Nabilone 1 to 2 mg PO bid
- Dopamine antagonists may be used at low doses with close monitoring for extrapyramidal and/or central nervous system depression. Options include: prochlorperazine 5 mg PO every 6 h, haloperidol 0.5 mg PO bid

Note: If the clinician chooses to use olanzapine, we recommend against using metoclopramide due to an increased risk of extrapyramidal symptoms or neuroleptic malignant syndrome.

13. Anticipatory Nausea and Vomiting. ENDORSED WITH ADAPTATIONS

For the prevention of anticipatory nausea and vomiting, all patients should receive optimal antiemetic therapy beginning with the initial cycles of chemotherapy as opposed to assessing the patient's emetic response to a less effective antiemetic treatment. The most common cause of anticipatory nausea and vomiting is anxiety. Therefore, for patients who do develop anticipatory nausea and vomiting, benzodiazepines and behavioral therapy are recommended (e.g. relaxation/systematic desensitization, hypnosis, relaxation exercises, yoga).[11,23]

14. Highly Emetogenic Radiation Therapy. ENDORSED

Patients who are treated with highly emetogenic RT (total body) should be offered a two-drug combination of a 5-HT_3 RA and dexamethasone before each fraction and on the day after each fraction if RT is not planned for that day.[9]

Drug	Dose	Schedule
5-HT_3 RA • Ondansetron, or	• 8 mg PO or 8 mg ODT or 8 mg IV	

Drug	Dose	Schedule
• Granisetron	• 2 mg (or 1 mg bid) PO or 1 mg IV	Use as prophylactic therapy – once to twice daily on days of RT with the first dose administered before RT, and on the day after RT Use as prophylactic therapy – daily on days of RT, with the first dose administered before RT, and on the day after RT
Dexamethasone	4 mg PO/IV	Use as prophylactic therapy – daily on days of RT, before RT, and on the day after RT

15. Moderately Emetogenic Radiation Therapy. ENDORSED

Patients who are treated with moderately emetogenic RT (upper abdomen, craniospinal) should be offered a 5-HT_3 RA before each fraction, with or without dexamethasone before the first five fractions.[9]

Drug	Dose	Schedule
5-HT_3 RA • Ondansetron, or	• 8 mg PO or 8 mg ODT or 8 mg IV	Use as prophylactic therapy – once to twice daily on days of RT with the first dose administered before RT
• Granisetron	• 2 mg (or 1 mg bid) PO or 1 mg IV	Use as prophylactic therapy – daily on days of RT before RT
Dexamethasone	4 mg PO/IV	Use as prophylactic therapy – daily on the days of the first five RT fractions before RT

16. Low Emetogenic Radiation Therapy. ENDORSED

a) Patients who are treated with RT to the brain should be offered rescue dexamethasone therapy.[9]

b) Patients who are treated with RT to the head and neck, thorax, or pelvis should be offered rescue therapy, which could include one or more of a 5-HT_3 RA, dexamethasone, or a dopamine RA.[9]

Drug	Dose	Schedule
5-HT_3 RA • Ondansetron, or	• 8 mg PO or 8 mg ODT or 8 mg IV	Use as rescue therapy[†]
• Granisetron	• 2 mg (or 1 mg bid) PO or 1 mg IV	Use as rescue therapy[†]
Dexamethasone	For brain, if not already taking corticosteroid, 4 mg PO/IV; for other anatomic regions, 4 mg PO/IV	Use as rescue therapy – titrate up as needed to a maximum of 16 mg PO/IV daily[†]

Drug	Dose	Schedule
Dopamine RA • Metoclopramide	• 10 mg PO/IV	Use as rescue therapy – titrate up as needed to maximum of 3-4 administrations daily[†]
• Prochlorperazine	• 10 mg PO/IV	Use as rescue therapy – titrate up as needed to maximum of 3-4 administrations daily[†]
[†]Depending on the severity of symptoms and the remaining duration of RT, patients can receive subsequent rescue therapy as needed or begin receiving prophylactic therapy for the remainder of RT.		

17. Minimal Emetogenic Radiation Therapy. ENDORSED

Patients who are treated with minimal-emetic-risk RT (extremities, breast) should be offered rescue therapy with a 5-HT_3 RA, dexamethasone, or a dopamine RA.

Drug	Dose	Schedule
5-HT_3 RA • Ondansetron, or • Granisetron	 • 8 mg PO or 8 mg ODT or 8 mg IV • 2 mg (or 1 mg bid) PO or 1 mg IV	 Use as rescue therapy[†] Use as rescue therapy[†]
Dexamethasone	4 mg PO/IV	Use as rescue therapy[†]
Dopamine RA • Metoclopramide • Prochlorperazine	 • 10 mg PO/IV • 10 mg PO/IV	 Use as rescue therapy[†] Use as rescue therapy[†]
[†]Patients can receive rescue therapy as needed. Alternative explanations for symptoms should be investigated to avoid the need for prophylactic therapy for the remainder of RT.		

18. Concurrent Chemotherapy and Radiation Therapy. ENDORSED

Patients who are treated with concurrent chemotherapy and RT should receive antiemetic therapy that is appropriate for the emetic risk level of chemotherapy agents, unless the risk level of the RT is higher. During periods when prophylactic antiemetic therapy for chemotherapy agents has ended and ongoing RT would normally be managed with its own prophylactic therapy, patients should receive prophylactic therapy that is appropriate for the emetic risk of the RT until the next period of chemotherapy, rather than receiving rescue therapy for chemotherapy agents as needed.

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Appendix A: Drugs Not on AHS Formulary

Drug	Trade Name	Status
Dolasetron	Anzemet	Health Canada NOC (IV formulation withdrawn) Not on AHS Formulary
Dronabinol	Marinol	Not being manufactured for sale in Canada
Fosaprepitant	Emend	Health Canada NOC Not on AHS Formulary
Granisetron	Kytril	Health Canada NOC On AHS Formulary but restricted
Netupitant/Palonosetron (NEPA)	Akynzeo	Health Canada NOC Not on AHS Formulary
Palonosetron	Aloxi	Health Canada NOC Not on AHS formulary
Ramosetron	Nasea	No Health Canada NOC
Rolapitant	Varubi	No Health Canada NOC
Tropisetron	Navoban	No Health Canada NOC

Appendix B: Emetic Risk of Single Oral Antineoplastic Agents in Adults

Risk Level	Agent
High (>90%)	Procarbazine
Moderate (30%-90%)	Bosutinib Cabozantinib Ceritinib Crizotinib Cyclophosphamide Imatinib Lenvatinib Lomustine* Mitotane* Temozolomide Trifluridine-tipiracil
Low (10%-30%)	Afatinib Alectinib Axitinib Capecitabine Cobimetinib Dabrafenib Dasatinib Everolimus Etoposide Fludarabine Ibrutinib Idelalisib Ixazomib Lapatinib Lenalidomide Midostaurin* Nilotinib Olaparib Osimertinib Palbociclib Pazopanib Ponatinib Regorafenib Sunitinib Thalidomide Trametinib Vandetanib Venetoclax Vorinostat
Minimal (<10%)	Axitinib* Busulfan Chlorambucil Erlotinib Gefitinib Hydroxyurea

Risk Level	Agent
	Melphalan Mercaptopurine* Methotrexate Pomalidomide Ribociclib* Ruxolitinib Sorafenib Thioguanine Tretinoin* Vemurafenib Vismodegib

Note. Adapted from "Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Updated," by Hesketh et al., 2017, *J Clin Oncol*., 35(28), p. 3247.

*Drugs added from "Emetic Risk of Single Oral Agents in Adults," by Cancer Care Ontario, June 2019.[29]

Appendix C: Emetic Risk of Single Intravenous Antineoplastic Agents in Adults

Risk Level	Agent
High (>90%)	Anthracycline/cyclophosphamide combination Carmustine Cisplatin Cyclophosphamide ≥ 1,500 mg/m^2 Dacarbazine Streptozocin
Moderate (30%-90%)	Aldesleukin >12-15 MU/m^{2*} Alemtuzumab Arsenic trioxide* Azacitidine Bendamustine Busulfan Carboplatin Clofarabine Cyclophosphamide < 1,500 mg/m^2 Cytarabine > 1,000 mg/m^2 Dactinomycin* Daunorubicin Doxorubicin Epirubicin Idarubicin Ifosfamide Irinotecan Irinotecan liposomal Oxaliplatin Romidepsin Thiotepa† Trabectedin
Low (10%-30%)	Aldesleukin ≤12 MU/m^{2*} Atezolizumab Belinostat Blinatumomab Bortezomib Brentuximab Cabazitaxel Carfilzomib Cetuximab Cytarabine ≤ 1,000 mg/m^2 Docetaxel Elotuzumab Eribulin Etoposide Fluorouracil Gemcitabine Ipilimumab Melphalan*

Risk Level	Agent
	Methotrexate Mitomycin Mitoxantrone Nab-paclitaxel Necitumumab Paclitaxel Panitumumab Pemetrexed Pegylated liposomal doxorubicin Pertuzumab Raltitrexed* Temsirolimus Teniposide* Topotecan Trastuzumab-emtansine (Kadcyla®)
Minimal (<10%)	Aldesleukin intralesional* Avelumab* L-asparaginase* Bevacizumab Bleomycin Cladribine Daratumumab Dexrazoxane* Fludarabine Interferon alfa-2b* Nelarabine* Nivolumab Obinutuzumab Ofatumumab Pembrolizumab Pralatrexate Ramucirumab Rituximab Trastuzumab Vinblastine Vincristine Vinorelbine

Note. Adapted from "Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Updated," by Hesketh et al., 2017, *J Clin Oncol*., 35(28), p. 3246.
*Drugs added from "Emetic Risk of Single Intravenous Agents in Adults," by Cancer Care Ontario, June 2019.[30]
†Classification refers to individual evidence from pediatric trials.

Development and Revision History

This guideline was reviewed and endorsed by members of the Alberta Provincial Tumour Teams. Members include medical oncologists, radiation oncologists, hematologists, pharmacists, and allied health. Evidence was selected and reviewed by a small working group of clinicians and the Guideline Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the Guideline Resource Unit Handbook.

This guideline was originally developed in 2019.

Maintenance

A formal review of the guideline will be conducted in 2022. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

Abbreviations

AUC, area under the curve; BID, twice a day; HEC, highly emetogenic chemotherapy; IV, intravenous therapy; LEC, low emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy; NEPA, netupitant and palonosetron; NK_1, neurokinin 1; NOC, Notice of Compliance; NV, nausea and vomiting; PO, orally; ODT, oral disintegrating tablet; RT, radiation therapy; 5-HT3, 5-hydroxytryptamine-3

Disclaimer

The recommendations contained in this guideline are a consensus of members of the Alberta Provincial Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

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Conflict of Interest Statements

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