4.3 Antiemetics

Chemotherapy Induced Nausea and Vomiting

Nausea and vomiting are a common complication of chemotherapy that significantly impacts the quality of life of patients and their caregivers. With careful planning, nausea and vomiting can be prevented or reduced in severity.

The recommendations provided in this chapter are adapted from POGO's Chemotherapy-induced nausea and vomiting (CINV) guideline series.

Acute CINV

The acute phase begins with the first dose of chemotherapy in a block and continues for 24 hours following the last dose of chemotherapy in the block. A chemotherapy block is defined as consecutive days of chemotherapy within a treatment plan. In order to provide proper prophylaxis for patients, the emetogenicity of the chemotherapy regimen must first be assessed.

Assessing Emetogenicity

When evaluating the emetogenicity of a particular regimen one must first consider the emetogenicity of each agent and identify the most emetogenic agent. Some multiple-agent regimens are also classified on their emetic risk as a whole vs. the emetogenicity of the individual chemotherapy agents. The following is a list of emetogenicity of single-agent and multiple-agent chemotherapy regimens commonly administered in POGO Satellite Clinics.

High Level of Emetic Risk (> 90% frequency of emesis in absence of prophylaxis)	
• Asparaginase (Erwinia) IV ≥20 000 IU/m^2/dose • Carboplatin IV ≥175 mg/m^2/dose • Cisplatin IV ≥ 12 mg/m^2/dose • Cyclophosphamide IV ≥ 1200 mg/m^2/dose • Dactinomycin IV ≥1.35 mg/m^2/dose	• Dacarbazine IV ≥ 250 mg/m^2/dose IV + doxorubicin ≥60 mg/m^2/dose • Dactinomycin 900 μg/m^2/dose IV + ifosfamide 3 g/m^2/dose • Etoposide IV ≥ 60 mg/m^2/dose + ifosfamide IV ≥ 1.2 g/m^2/dose
Moderate Level of Emetic Risk (30-90% frequency of emesis in absence of prophylaxis)	
• Cyclophosphamide IV 1000 mg/m^2/dose • Cytarabine IV 75 mg/m^2/dose • Cytarabine 60 or 90 mg/m^2/dose + methotrexate 120 mg/m^2/dose	• Doxorubicin IV 25 mg/ m^2/dose • Irinotecan[a] • Methotrexate IV 5 g/m^2/dose • Topotecan PO 0.4-2.3 mg/m^2/day
Low Level of Emetic Risk (10- < 30% frequency of emesis in absence of prophylaxis)	
• Cyclophosphamide PO 2-3 mg/kg/dose • Cytarabine IV 60 mg/m^2/dose + methotrexate IV 90 mg/m^2/dose • Cytarabine ≤ 200 mg/m^2	• Etoposide[a] • Methotrexate IV 38-83 mg/m^2/dose • Procarbazine PO 50-100 mg/m^2/day • Temozolomide PO 200 mg/m^2/dose
Minimal (<10% frequency of emesis in absence of prophylaxis)	
• Mercaptopurine PO ≤4.2 mg/kg/dose • Methotrexate PO/SC ≤ 10 mg/m^2/dose	• Thioguanine[a] • Vinblastine[a] • Vincristine ≤1.5 mg/m^2/dose

[a]as per 2017 ASCO guidelines

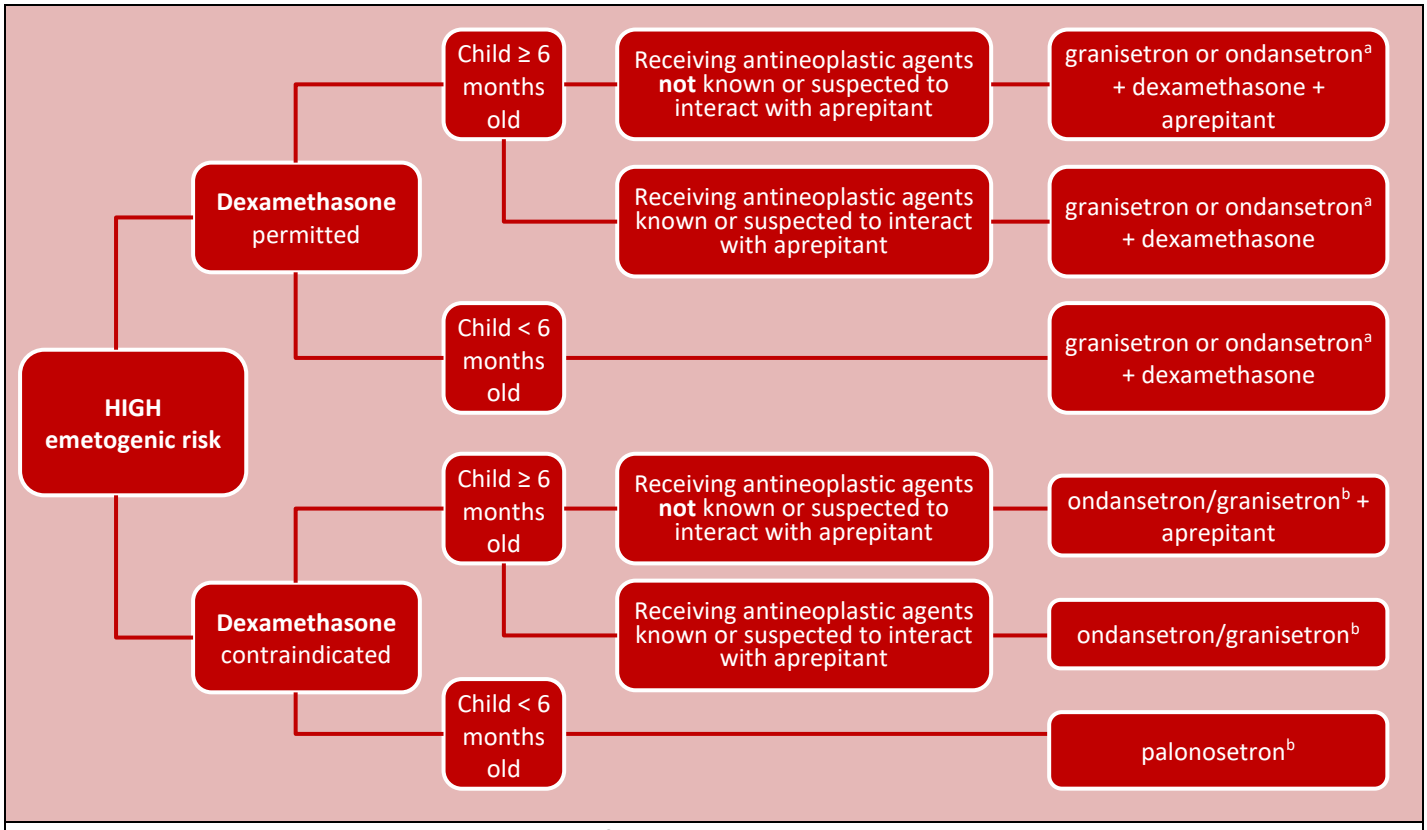
Note: This is an abbreviated list; for a complete list of agents and emetogenicity, including chemotherapy specific combinations of agents with increased emetic risk (not commonly given in satellites) visit: https://onlinelibrary.wiley.com/doi/epdf/10.1002/pbc.27646

Choosing Acute AINV Prophylaxis Regimen

Once the agent with the highest emetic risk has been recognized, prophylaxis can be selected as below. Note that a patient's eligibility for using dexamethasone and aprepitant should be clarified with the referring tertiary centre if unknown.

Note on Palonosetron

The current version of the clinical practice guideline for the prevention of acute chemotherapy-induced nausea and vomiting suggests palonosetron as an alternative 5-HT3 receptor antagonist for patients receiving HEC or MEC. In addition, in situations where dexamethasone or aprepitant are contraindicated, or there is a history of poor CINV control despite other therapy, palonosetron may be offered as the 5-HT3 receptor antagonist of choice. While palonosetron may be administered in satellites, given its significant cost, it is neither expected nor required that satellite pharmacies provide it as an option. In select cases, the oral form may be filled by patients in an outpatient pharmacy prior to their infusion appointment.

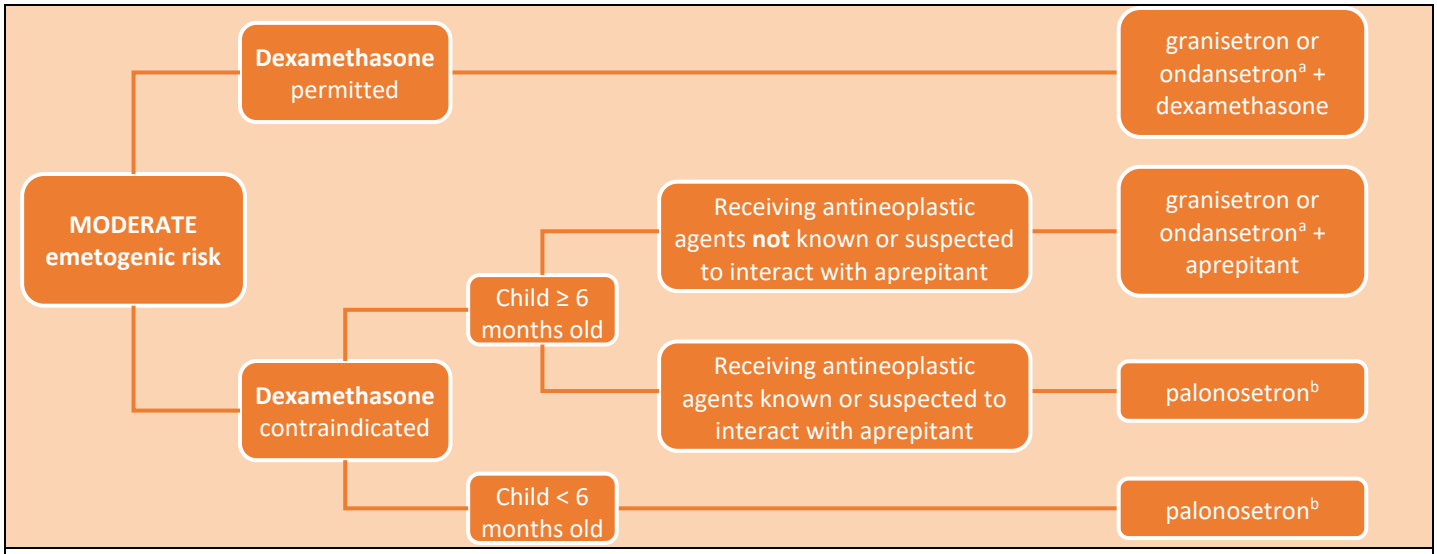


Antiemetic Dosage Recommendations for Children receiving HIGHLY Emetogenic Chemotherapy

Drug	Dose
Aprepitant	Day 1: 3 mg/kg PO x 1 (maximum: 125 mg/dose) Days 2 and 3: 2 mg/kg PO once daily (maximum: 80 mg/dose)
Dexamethasone	6 mg/m^2/dose IV/PO q6h If given concurrently with aprepitant, reduce dexamethasone dose by half.
Granisetron	40 µg/kg/dose IV as a single daily dose
Ondansetron	5 mg/m^2/dose (0.15 mg/kg/dose) IV/PO prechemotherapy x 1 and then q8h
Palonosetron[a]	1 month to <17 years: 0.02 mg/kg IV once prechemotherapy (maximum: 1.5 mg/dose) ≥17 years: 0.25 mg/dose IV or 0.5 mg PO once prechemotherapy

[a]Palonosetron is also a 5-HT_3 receptor antagonist that may be considered depending on availability at the satellite centre and their respective financial implications

[b]While palonosetron is the only 5-HT_3 receptor antagonist recommended by the current version of the clinical practice guideline, ondansetron or granisetron may be considered recognizing limitations to the availability or cost of palonosetron at satellite centres



Antiemetic Dosage Recommendations for Children receiving MODERATELY Emetogenic Chemotherapy

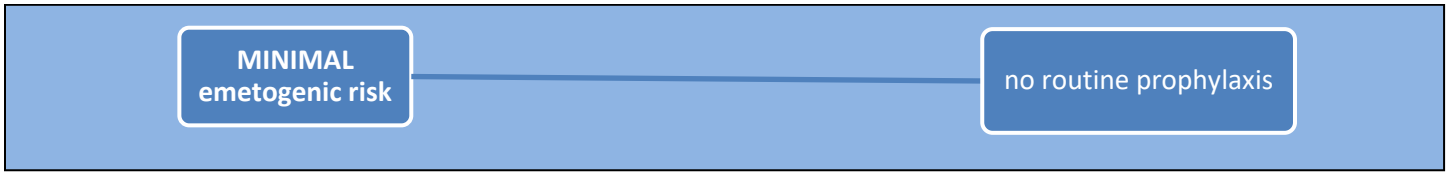
Drug	Dose
Aprepitant	Day 1: 3 mg/kg PO x 1 (maximum: 125 mg/dose) Days 2 and 3: 2 mg/kg PO once daily (maximum: 80 mg/dose)
Dexamethasone	**≤ 0.6m²:** 2mg/dose IV/PO q12h **> 0.6m²:** 4mg/dose IV/PO q12h If given concurrently with aprepitant, reduce dexamethasone dose by half.
Granisetron	40 µg/kg/dose IV as a single daily dose **or** 40 µg/kg/dose PO q12h
Ondansetron	5 mg/m²/dose (0.15 mg/kg/dose) IV/PO prechemotherapy x 1 and then q12h (maximum: 8 mg/dose)
Palonosetron	1 month to <17 years: 0.02 mg IV once prechemotherapy (maximum: 1.5 mg/dose) ≥17 years: 0.25 mg/dose IV or 0.5 mg PO once prechemotherapy

[a]Palonosetron is also a 5-HT_3 receptor antagonist that may be considered depending on availability at the satellite centre and their respective financial implications

[b]While palonosetron is the only 5-HT_3 receptor antagonist recommended by the current version of the clinical practice guideline, ondansetron or granisetron may be considered recognizing limitations to the availability or cost of palonosetron at satellite centres

Antiemetic Dosage Recommendations for Children receiving LOW Emetogenic Chemotherapy

Drug	Dose
Granisetron	40 µg/kg/dose IV as a single daily dose or 40 µg/kg/dose PO q12h
Ondansetron	10 mg/m²/dose (0.3 mg/kg/dose) prechemotherapy x 1 (maximum: 16 mg/dose IV or 24 mg/dose PO)



Breakthrough CINV

Breakthrough CINV is defined as nausea or vomiting that is attributable to chemotherapy that occurs during the acute or delayed phase despite CINV prophylaxis.

For patients receiving minimally, low or moderately emetogenic chemotherapy:
Recommend upgrading acute CINV prophylaxis to that recommended for the next higher level of emetogenic risk. For example, if a patient is receiving moderately emetogenic chemotherapy and experiences breakthrough CINV, they should receive acute CINV prophylaxis consistent with the guideline recommendations for highly emetogenic chemotherapy.

For patients receiving highly emetogenic chemotherapy, olanzapine should be added to the guideline-consistent CINV prophylaxis. Where olanzapine is contraindicated, methotrimeprazine (also known as levomepromazine) or metoclopramide (in children older than 1 year) may be tried. The risks and benefits of extrapyramidal symptoms should be considered and the family educated if therapy is to proceed.

The evidence base to support these recommendations is summarized in the full version of the guideline available at:
https://onlinelibrary.wiley.com/doi/epdf/10.1002/pbc.25955

Refractory CINV

Refractory CINV is defined as nausea or vomiting that is attributable to chemotherapy which occurs during the acute or delayed phase despite CINV prophylaxis in patients who had breakthrough CINV in a previous chemotherapy block.

For patients receiving minimally, low or moderately emetogenic chemotherapy:
Recommend upgrading acute CINV prophylaxis to that recommended for the next higher level of emetogenic risk. For example, if a patient is receiving moderately emetogenic chemotherapy and experiences breakthrough CINV, they should receive acute CINV prophylaxis consistent with the guideline recommendations for highly emetogenic chemotherapy.

For children receiving acute CINV prophylaxis recommended for highly emetogenic chemotherapy, the 5-HT3 receptor antagonist should be changed from ondansetron or granisetron to palonosetron. If palonosetron is unavailable, ondansetron may be switched to granisetron.

If these recommendations are attempted and a child continues to experience refractory CINV and was unable to receive aprepitant due to a drug interaction, we suggest that the addition of aprepitant be considered.

If these recommendations fail, one of the following interventions may be tried: interventions that were successfully employed for breakthrough CINV (metoclopramide or olanzapine) or stimulation of Nei Gaun (P6) by means of acupressure or electroacupuncture.

The evidence base to support these recommendations is summarized in the full version of the guideline available at:
https://onlinelibrary.wiley.com/doi/epdf/10.1002/pbc.25955

Anticipatory CINV

Anticipatory CINV is defined as nausea and vomiting that occurs in the 24 hour period prior to chemotherapy in response to having poorly controlled nausea and vomiting in previous chemotherapy blocks.

Control of acute and delayed CINV should be optimized in order to minimize the risk of a patient developing CINV.

For patients that do develop anticipatory CINV, psychological interventions such as hypnosis or systematic desensitization may be helpful. Lorazepam is a pharmacological alternative that may be given (0.04-0.08 mg/kg/dose, max: 2 mg/dose) the night before chemotherapy and the next day prior to chemotherapy administration.

The evidence base to support these recommendations is summarized in the full version of the guideline available at: https://onlinelibrary.wiley.com/doi/abs/10.1002/pbc.25063

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Record of Updates

Version Number	Date of Effect	Summary of Revisions
1	12/16/2022	• Original version posted.