



Quick Review Summary

Guideline for the Prevention of Acute Chemotherapy-Induced Nausea and Vomiting in Pediatric Cancer Patients

The purpose of this guideline is to provide health care providers with an approach to the prevention of acute chemotherapy-induced nausea and vomiting (CINV) in children who are receiving antineoplastic medication. The scope is limited to the prevention of CINV in the acute phase (within 24 hours of administration of an antineoplastic agent).

The Pediatric Oncology Group of Ontario (POGO) CINV Guideline Development Panel included inter-disciplinary representatives from several POGO institutions as well as content and methodological experts. Using established methods, ADAPTE and CAN-IMPLEMENT, the scope of the guideline was determined and existing guidelines were identified for adaptation to the POGO context. A library scientist-guided literature search was undertaken and the source guidelines were updated and reframed based on a systematic review of pediatric evidence. The quality of evidence was assessed and the strength of each recommendation was determined. The guideline development process included an extensive two-stage external review: first by international experts in adult and pediatric CINV and then by Ontario health care provider stakeholders. A focused update of this guideline was published in 2017.

This guideline represents the second in a series of guidelines to address the need for, and the selection of, antiemetic prophylaxis in children with cancer receiving antineoplastic therapy. The first, *Classification of the acute emetogenicity of chemotherapy in pediatric cancer patients: a clinical practice guideline*, provides evidence-based recommendations on the assessment of a regimen's emetogenicity. Since appropriate antiemetic selection for acute CINV prophylaxis begins with an assessment of the intrinsic emetogenicity of the antineoplastic therapy to be given, this Quick Review Summary will reference both guidelines (including focused update).

This Quick Review Summary summarizes the recommended pharmacological interventions. It is intended to be used in conjunction with the complete guidelines within the CINV guideline series (available at <http://www.pogo.ca/healthcare/practiceguidelines>). These guidelines provide a standardized, evidence-based approach to the prevention of CINV in children receiving antineoplastic agents. They are a platform upon which individual clinicians and institutions may frame local recommendations. Each institution is encouraged to adapt them to their local context.

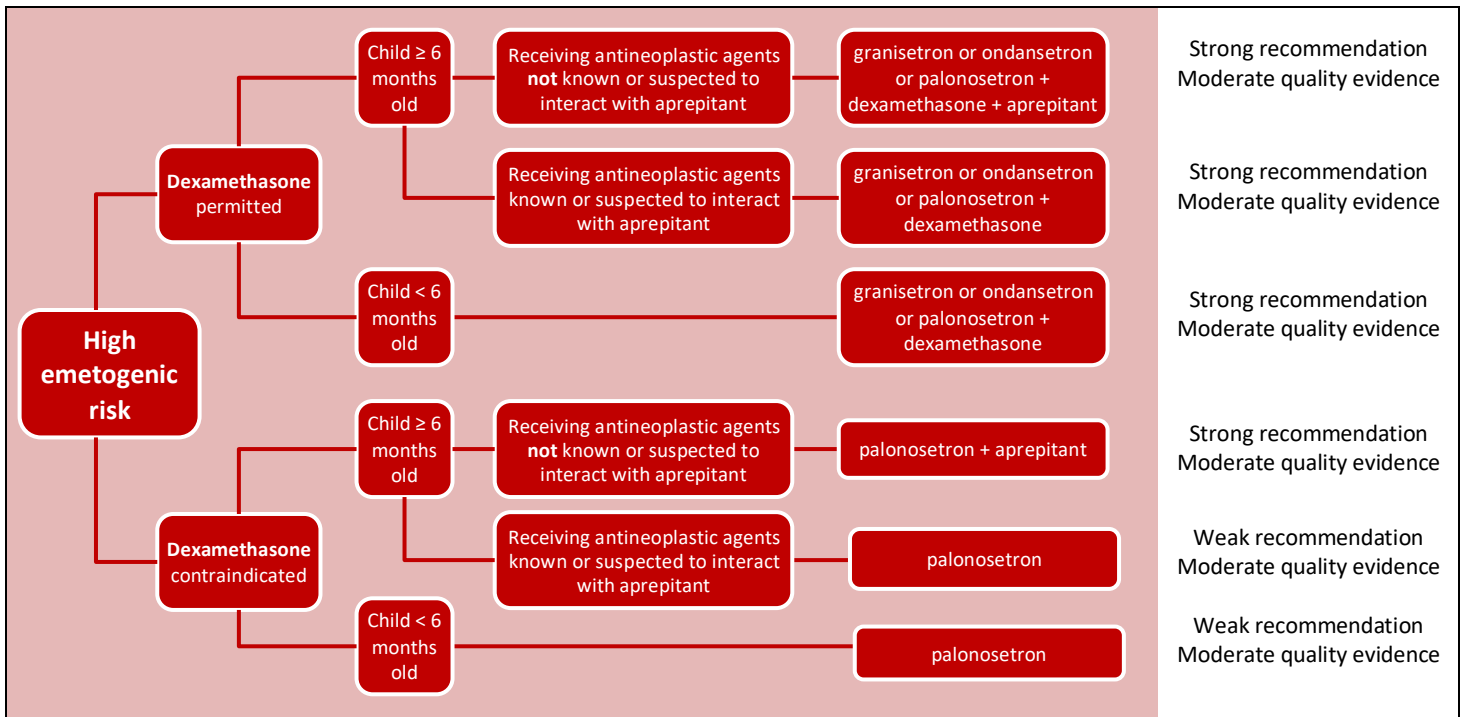
Recommended citations:

Patel P, Robinson PD, Thackray J, Flank J, Holdsworth MT, Gibson P, Orsey A, Portwine C, Freedman J, Madden JR, Phillips R. Guideline for the prevention of acute chemotherapy-induced nausea and vomiting in pediatric cancer patients: a focused update. *Pediatr Blood Cancer*. 2017 Oct;64(10):e26542.

Paw Cho Sing E, Robinson PD, Flank J, Holdsworth M, Thackray J, Freedman J, Gibson P, Orsey AD, Patel P, Phillips R, Portwine C. Classification of the acute emetogenicity of chemotherapy in pediatric patients: A clinical practice guideline. *Pediatr Blood Cancer*. 2019 May;66(5):e27646.

Disclaimer: This summary and the full guideline were developed by health care professionals using evidence-based or best practice references available at the time of its creation. The content of the guideline will change as it will be reviewed and revised on a periodic basis. Care has been taken to ensure accuracy of the information. However, every health care professional using this guideline is responsible for providing care according to their best professional judgement and the policies and standards in place at their institution.

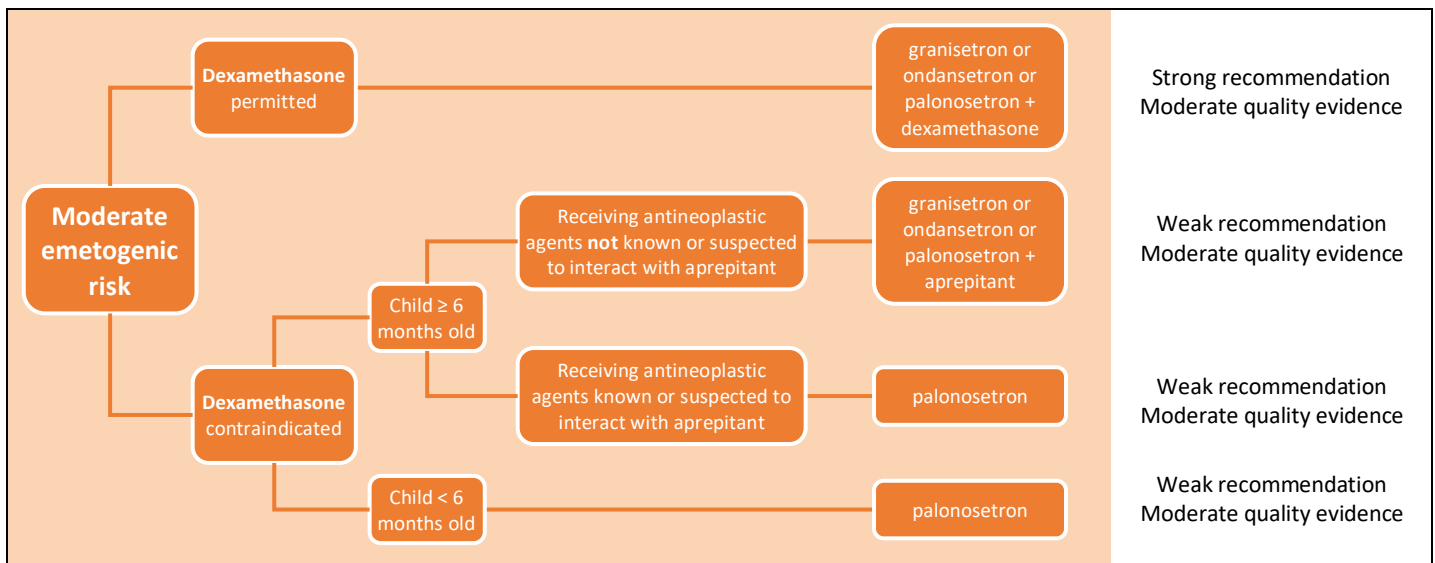
Prevention of Acute AINV in Pediatric Cancer Patients



Antineoplastic Agents with HIGH Emetic Risk > 90% frequency of emesis in absence of prophylaxis
Single agent antineoplastic therapy
Asparaginase (<i>Erwinia</i>) IV ≥ 20 000 IU/m ² /dose Busulfan IV ≥ 0.8 mg/kg/dose Busulfan PO ≥ 1 mg/kg/dose Carboplatin IV ≥ 175 mg/m ² /dose Cisplatin IV ≥ 12 mg/m ² /dose Cyclophosphamide IV ≥ 1200 mg/m ² /dose Cytarabine IV ≥ 3 g/m ² /day Dactinomycin IV ≥ 1.35 mg/m ² /dose Doxorubicin IV ≥ 30 mg/m ² /dose Idarubicin PO ≥ 30 mg/m ² /dose Melphalan IV Methotrexate IV ≥ 12 g/m ² /dose
Multiple agent antineoplastic therapy
With the <u>exceptions</u> listed below, emetogenicity is classified based on the most highly emetogenic agent. The following are <u>also</u> classified as high emetic risk: Cyclophosphamide IV ≥ 600 mg/m ² /dose + dactinomycin IV ≥ 1 mg/m ² /dose Cyclophosphamide IV ≥ 400 mg/m ² /dose + doxorubicin IV ≥ 40 mg/m ² /dose Cytarabine IV ≥ 90 mg/m ² /dose + methotrexate IV ≥ 150 mg/m ² /dose Cytarabine IV + teniposide IV Dacarbazine ≥ 250 mg/m ² /dose IV + doxorubicin IV ≥ 60 mg/m ² /dose Dactinomycin 900 µg/m ² /dose IV + ifosfamide IV 3 g/m ² /dose Etoposide IV ≥ 60 mg/m ² /dose + ifosfamide IV ≥ 1.2 g/m ² /dose Etoposide IV ≥ 250 mg/m ² /dose + thiotepa IV ≥ 300 mg/m ² /dose
Multi-day antineoplastic therapy
Emetogenicity is classified based on the most highly emetogenic agent on each day of therapy.

Antiemetic Dosage Recommendations for Children receiving HIGHLY Emetogenic Antineoplastic Therapy		
Drug	Dose	GRADE
Aprepitant	Day 1: 3 mg/kg PO x 1 (maximum: 125 mg) Days 2 and 3: 2 mg/kg PO once daily (maximum: 80 mg)	Weak recommendation Moderate quality evidence
Dexamethasone	6 mg/m ² /dose IV/PO q6h If given concurrently with aprepitant, reduce dexamethasone dose by half.	Weak recommendation Low quality evidence
Granisetron	40 µg/kg/dose IV as a single daily dose	Strong recommendation Low quality evidence
Ondansetron	5 mg/m ² /dose (0.15 mg/kg/dose) IV/PO prechemotherapy x 1 and then q8h	Strong recommendation Moderate quality evidence
Palonosetron	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	Weak recommendation Moderate quality evidence

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Antineoplastic Agents with <u>MODERATE</u> Emetic Risk 30% to < 90% frequency of emesis in absence of prophylaxis
Single agent antineoplastic therapy
Cyclophosphamide IV 1000 mg/m ² /dose Cytarabine IV 75 mg/m ² /dose Dactinomycin IV 10 µg/kg/dose Doxorubicin IV 25 mg/m ² /dose Gemtuzumab IV 3-9 mg/m ² /dose Imatinib PO > 260 mg/m ² /day Interferon alpha IV 15-30 million U/m ² /day Ixabepilone IV 3-10 mg/m ² /dose Methotrexate IV 5 g/m ² /dose Methotrexate IT Topotecan PO 0.4-2.3 mg/m ² /day
Multiple agent antineoplastic therapy
With the <u>exceptions</u> listed under high emetic risk, emetogenicity is classified based on the most highly emetogenic agent. Cytarabine IV 100 mg/m ² /dose + daunorubicin IV 45 mg/m ² /dose + etoposide IV 100 mg/m ² /dose + prednisolone PO + thioguanine PO 80 mg/m ² /dose Cytarabine IV 60 or 90 mg/m ² /dose + methotrexate IV 120 mg/m ² /dose Liposomal doxorubicin IV 20-50 mg/m ² /dose + topotecan PO 0.6 mg/m ² /day
Multi-day antineoplastic therapy
Emetogenicity is classified based on the most highly emetogenic agent on each day of therapy.

Antiemetic Dosage Recommendations for Children Receiving <u>MODERATELY</u> Emetogenic Antineoplastic Therapy		
Drug	Dose	GRADE
Aprepitant	Day 1: 3 mg/kg PO x 1 (maximum: 125 mg) Days 2 and 3: 2 mg/kg PO once daily (maximum: 80 mg)	Weak recommendation Moderate quality evidence
Dexamethasone	≤ 0.6m ² : 2mg/dose IV/PO q12h > 0.6m ² : 4mg/dose IV/PO q12h If given concurrently with aprepitant, reduce dexamethasone dose by half	Strong recommendation Low quality evidence
Granisetron	40 µg/kg/dose IV as a single daily dose <u>or</u> 40 µg/kg/dose PO q12h	IV: Strong recommendation Moderate quality evidence PO: Weak recommendation Low quality evidence
Ondansetron	5 mg/m ² /dose (0.15 mg/kg/dose; maximum 8 mg/dose) IV/PO prechemotherapy x 1 and then q12h	Strong recommendation Moderate quality evidence
Palonosetron	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	Weak recommendation Moderate quality evidence

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<div style="border: 1px solid black; border-radius: 10px; padding: 5px; display: inline-block;"> Low emetogenic risk </div>	<div style="border: 1px solid black; border-radius: 10px; padding: 5px; display: inline-block;"> ondansetron or granisetron </div>	Strong recommendation Moderate quality evidence
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Antineoplastic Agents with LOW Emetic Risk
10% to <30% frequency of emesis in absence of prophylaxis
Single agent antineoplastic therapy
Cyclophosphamide IV 500 mg/m ² /dose Cyclophosphamide PO 2-3 mg/kg/dose Dasatinib PO 60-120 mg/m ² /dose Erlotinib PO 35-150 mg/m ² /day Everolimus PO 0.8-9 mg/m ² /day Gefitinib PO 150-100 mg/m ² /day Imatinib PO 260 mg/m ² /day Mafosfamide IT 1-6.5 mg/dose Melphalan PO 0.2 mg/kg/dose Mercaptopurine PO ≤ 4.2 mg/kg/dose Methotrexate IV 38-83 mg/m ² /dose Mitoxantrone IV ≤ 33 mg/m ² /dose Procarbazine PO 500-100 mg/m ² /day Ruxolitinib PO 15-21 mg/m ² /dose Selumetinib PO 20-30 mg/m ² /dose Sorafenib PO 150-325 mg/m ² /dose Temozolomide PO 200 mg/m ² /dose
Multiple agent antineoplastic therapy
With the <i>exceptions</i> listed under high emetic risk, emetogenicity is classified based on the most highly emetogenic agent.
Cytarabine IV 60 mg/m ² /dose + methotrexate IV 90 mg/m ² /dose
Multi-day antineoplastic therapy
Emetogenicity is classified based on the most highly emetogenic agent on each day of therapy.

Antiemetic Dosage Recommendations for Children receiving LOW Emetic Risk Antineoplastic Therapy		
Drug	Dose	GRADE
Granisetron	40 µg/kg/dose IV as a single daily dose	IV: Strong recommendation Low quality evidence PO: Weak recommendation Low quality evidence
	or 40 µg/kg/dose PO q12h	
Ondansetron	10 mg/m ² /dose (0.3 mg/kg/dose) prechemotherapy x 1	Strong recommendation Low quality evidence
	<u>Maximum</u>	
	16 mg/dose IV 24 mg/dose PO	

<div style="border: 1px solid black; border-radius: 10px; padding: 5px; display: inline-block;"> Minimal emetogenic risk </div>	<div style="border: 1px solid black; border-radius: 10px; padding: 5px; display: inline-block;"> no routine prophylaxis </div>	Strong recommendation Very low quality evidence
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Antineoplastic Agents with MINIMAL Emetic Risk	
<10% frequency of emesis in absence of prophylaxis	
Single agent antineoplastic therapy	Multiple agent antineoplastic therapy
Asparaginase (<i>E.coli</i>) IM ≤ 6000 IU/m ² /dose Asparaginase (<i>Erwinia</i>) IM ≤ 25 000 IU/m ² /dose Chlorambucil PO ≤ 0.2 mg/kg/day Doxorubicin IV 10 mg/m ² /dose Liposomal doxorubicin IV ≤ 50 mg/m ² /dose Methotrexate PO/SC ≤ 10 mg/m ² /dose Pracinostat 25-45 PO mg/m ² /dose Vincristine IV ≤ 1.5 mg/m ² /dose	Cisplatin intra-arterially ≤ 60 mg/m ² /dose + doxorubicin intra-arterially ≤ 30 mg/m ² /dose Cisplatin intra-arterially ≤ 60 mg/m ² /dose + pirarubicin intra-arterially ≤ 30 mg/m ² /dose Mercaptopurine PO ≤ 2.5 mg/kg/dose + methotrexate PO ≤ 0.1 mg/kg/day