PEDIATRIC ONCOLOGY GROUP OF ONTARIO

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).

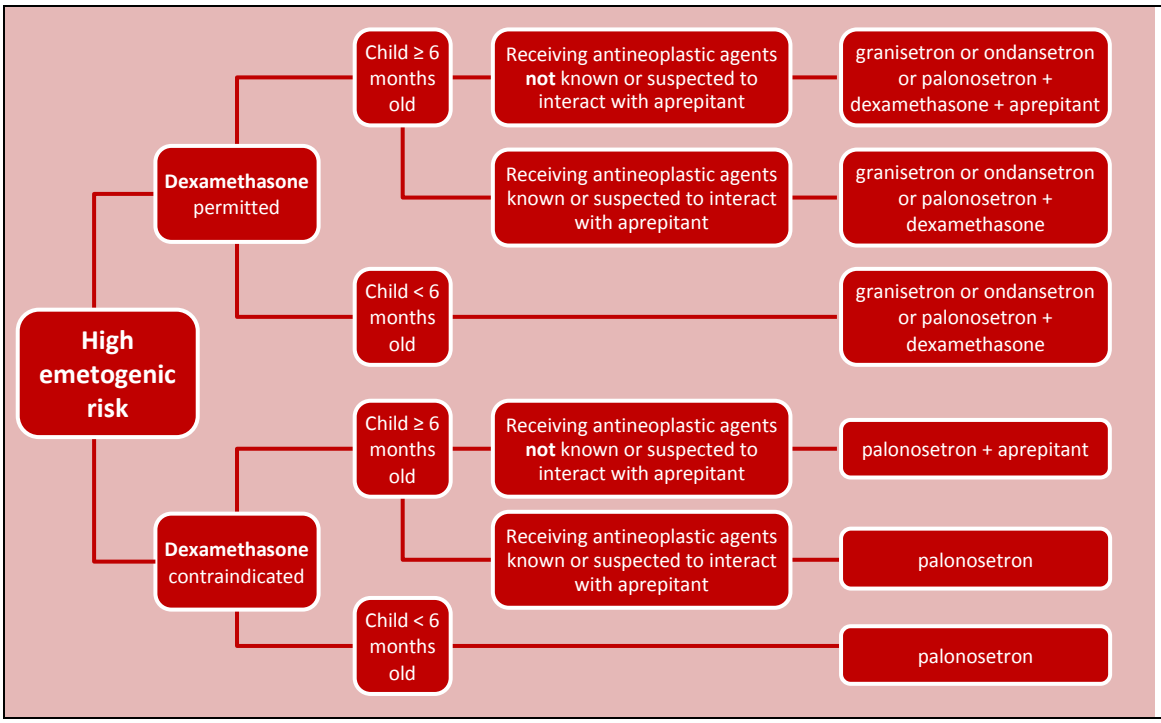
This Quick Review Summary summarizes the recommended pharmacological interventions. It is intended to be used in conjunction with the complete guidelines within the CINV guideline series (available at http://www.pogo.ca/healthcare/practiceguidelines). These guidelines provide a standardized, evidence-based 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.

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 (*Erwinia*) IV ≥ 20 000 IU/m²/dose
Busulfan IV ≥ 0.8 mg/kg/dose
Busulfan PO ≥ 1 mg/kg/dose
Carboplatin IV ≥ 175 mg/m²/dose
Cisplatin IV ≥ 12 mg/m²/dose
Cyclophosphamide IV ≥ 1200 mg/m² /dose
Cytarabine IV ≥ 3 g/m²/day
Dactinomycin IV ≥ 1.35 mg/m²/dose
Doxorubicin IV ≥ 30 mg/m²/dose
Idarubicin PO ≥ 30 mg/m²/dose
Melphalan IV
Methotrexate IV ≥ 12 g/m²/dose
Multiple agent antineoplastic therapy
With the exceptions listed below, emetogenicity is classified based on the most highly emetogenic agent. The following are also classified as high emetic risk: Cyclophosphamide ≥ 600 mg/m²/dose + dactinomycin ≥ 1 mg/m²/dose Cyclophosphamide ≥ 400 mg/m²/dose + doxorubicin ≥ 40 mg/m²/dose Cytarabine ≥ 90 mg/m²/dose IV + methotrexate IV ≥ 150 mg/m²/dose Cytarabine IV + teniposide IV Dacarbazine ≥ 250 mg/m²/dose IV + doxorubicin IV ≥ 60 mg/m²/dose Dactinomycin 900 µg/m²/dose IV + ifosfamide 3 g/m²/dose Etoposide IV ≥ 60 mg/m²/dose + ifosfamide IV ≥ 1.2 g/m²/dose Etoposide IV ≥ 250 mg/m²/dose + thiotepa IV ≥ 300 mg/m²/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/m²/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/m²/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 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

Refer to the complete POGO guidelines, available at http://www.pogo.ca/healthcare/practiceguidelines for further details.

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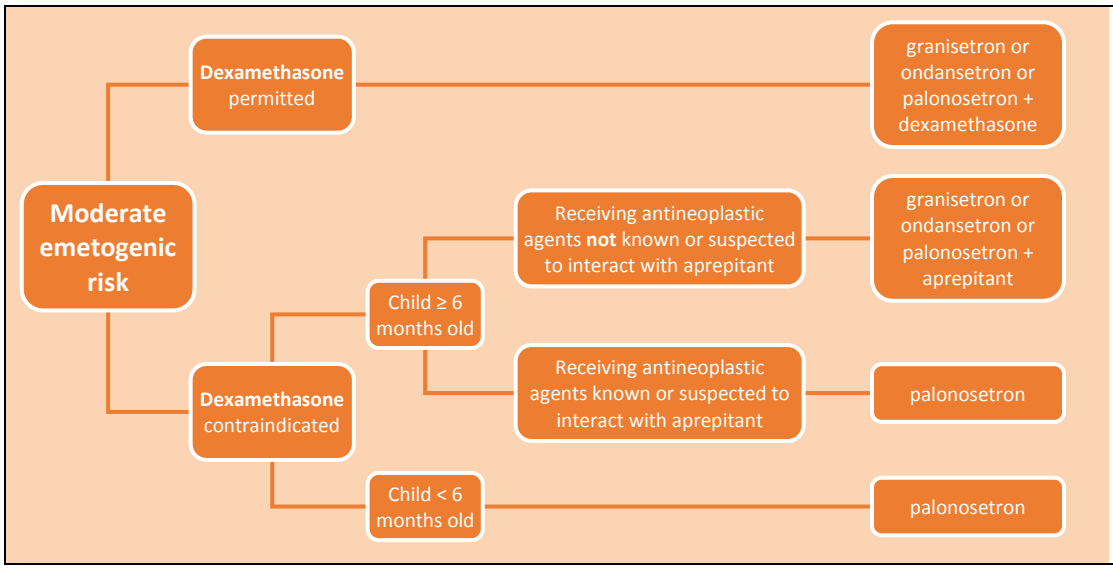

Antineoplastic Agents with MODERATE Emetic Risk 30% to < 90% frequency of emesis in absence of prophylaxis
Single agent antineoplastic therapy
Cyclophosphamide IV 1000 mg/m²/dose
Cytarabine IV 75 mg/m²/dose
Dactinomycin IV 10 µg/kg/dose
Doxorubicin IV 25 mg/m²/dose
Gemtuzumab IV 3-9 mg/m²/dose
Imatinib PO > 260 mg/m²/day
Interferon alpha IV 15-30 million U/m²/day
Ixabepilone IV 3-10 mg/m²/dose
Methotrexate IV 5 g/m²/dose
Methotrexate IT
Topotecan PO 0.4-2.3 mg/m²/day
Multiple agent antineoplastic therapy
With the exceptions listed under high emetic risk, emetogenicity is classified based on the most highly emetogenic agent. Cytarabine IV 100 mg/m²/dose + daunorubicin IV 45 mg/m²/dose + etoposide IV 100 mg/m²/dose + prednisolone PO + thioguanine PO 80 mg/m²/dose Cytarabine 60 or 90 mg/m²/dose + methotrexate 120 mg/m²/dose Liposomal doxorubicin IV 20-50 mg/m²/dose + topotecan PO 0.6 mg/m²/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 MODERATELY 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	**≤ 0.6m²:** 2mg/dose IV/PO q12h **> 0.6m²:** 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 **or** 40 µg/kg/dose PO q12h	**IV:** Strong recommendation Moderate quality evidence **PO:** Weak recommendation Low quality evidence
Ondansetron	5 mg/m²/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 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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Prevention of Acute AINV in Pediatric Cancer Patients

Low emetogenic risk → ondansetron **or** granisetron

Strong recommendation
Moderate quality evidence

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 38-83 mg/m^2/dose IV 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 exceptions 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 or 40 µg/kg/dose PO q12h	**IV:** Strong recommendation Low quality evidence **PO:** Weak recommendation Low quality evidence
Ondansetron	10 mg/m^2/dose (0.3 mg/kg/dose) prechemotherapy x 1 Maximum 16 mg/dose IV 24 mg/dose PO	Strong recommendation Low quality evidence

Minimal emetogenic risk → no routine prophylaxis

Strong recommendation
Very low quality evidence

Antineoplastic Agents with MINIMAL Emetic Risk <10% frequency of emesis in absence of prophylaxis	
Single agent antineoplastic therapy	**Multiple agent antineoplastic therapy**
Asparaginase (*E.coli*) IM ≤ 6000 IU/m^2/dose Asparaginase (*Erwinia*) 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 Mercaptopurine PO ≤ 4.2 mg/kg/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 ≤ 60 mg/m^2/dose intra-arterially + doxorubicin ≤ 30 mg/m^2/dose intra-arterially Cisplatin ≤ 60 mg/m^2/dose intra-arterially + pirarubicin ≤ 30 mg/m^2/dose intra-arterially Mercaptopurine PO ≤ 2.5 mg/kg/dose + methotrexate PO ≤0.1 mg/kg/day

Refer to the complete POGO guidelines, available at http://www.pogo.ca/healthcare/practiceguidelines for further details.