POGO
PEDIATRIC ONCOLOGY GROUP OF ONTARIO

COLLABORATING FOR KIDS WITH CANCER SINCE 1983

Quick Review Summary

Guideline for the Prevention of Acute Nausea and Vomiting due to Antineoplastic Medication in Pediatric Cancer Patients

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

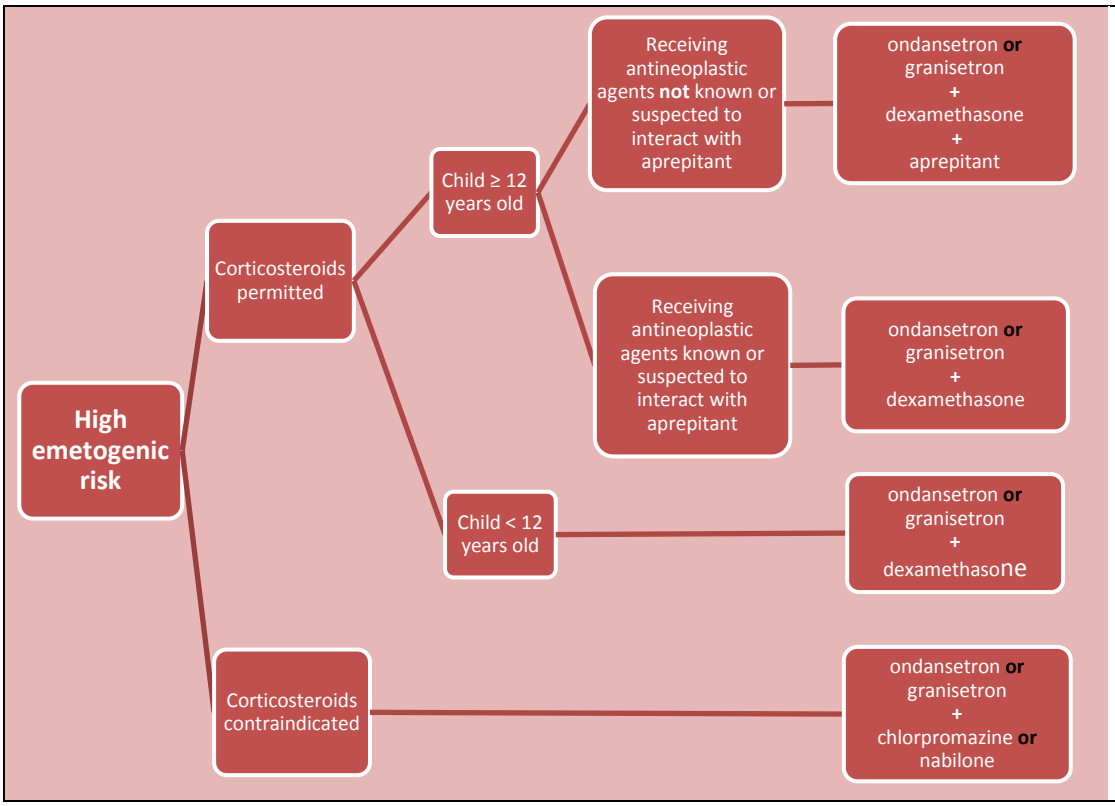
The Pediatric Oncology Group of Ontario (POGO) AINV Guideline Development Panel included inter-disciplinary representation from several POGO institutions as well as content and methodological expertise. Using established methods, ADAPTE and CAN-IMPLEMENT, the scope of the guideline was determined and 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 AINV and then by Ontario health care provider stakeholders.

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, the *POGO Guideline for the Classification of the Acute Emetogenic Potential of Antineoplastic Medication in Pediatric Cancer Patients,* provides evidence-based recommendations on the assessment of a regimen's emetogenicity. Since appropriate antiemetic selection for acute AINV prophylaxis begins with an assessment of the intrinsic emetogenicity of the antineoplastic therapy to be given, this Quick Review Summary will reference both guidelines.

The focus of this Quick Review Summary is on providing a summary of the recommended pharmacological interventions. It is intended to be used in conjunction with the complete guidelines which are available at http://www.pogo.ca/healthcare/practiceguidelines. These guidelines provide a standardized, evidence-based approach to the prevention of AINV in children receiving antineoplastic agents. They offer a platform upon which individual clinicians and institutions may frame local recommendations. Each institution is encouraged to adapt them to their local context.

Recommended citation: Dupuis LL, Boodhan S, Holdsworth M, Robinson PD, Hain R, Portwine C, O'Shaughnessy E and Sung L. *Guideline for the Prevention of Acute Nausea and Vomiting due to Antineoplastic Medication in Pediatric Cancer Patients*. Pediatric Oncology Group of Ontario; Toronto. 2012.

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

Altretamine	Dactinomycin
Carboplatin	Mechlorethamine
Carmustine > 250 mg/m^2	Methotrexate ≥ 12 g/m^2
Cisplatin	Procarbazine (oral)
Cyclophosphamide ≥1 g/m^2	Streptozocin
Cytarabine 3 g/m^2/dose	Thiotepa ≥ 300 mg/m^2
Dacarbazine	

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 + anthracycline
- Cyclophosphamide + doxorubicin
- Cyclophosphamide + epirubicin

Cyclophosphamide + etoposide
Cytarabine 150-200 mg/m^2 + daunorubicin
Cytarabine 300 mg/m^2 + etoposide
Cytarabine 300 mg/m^2 + teniposide
Doxorubicin + ifosfamide
Doxorubicin + methotrexate 5 g/m^2
Etoposide + ifosfamide

Multi-day antineoplastic therapy

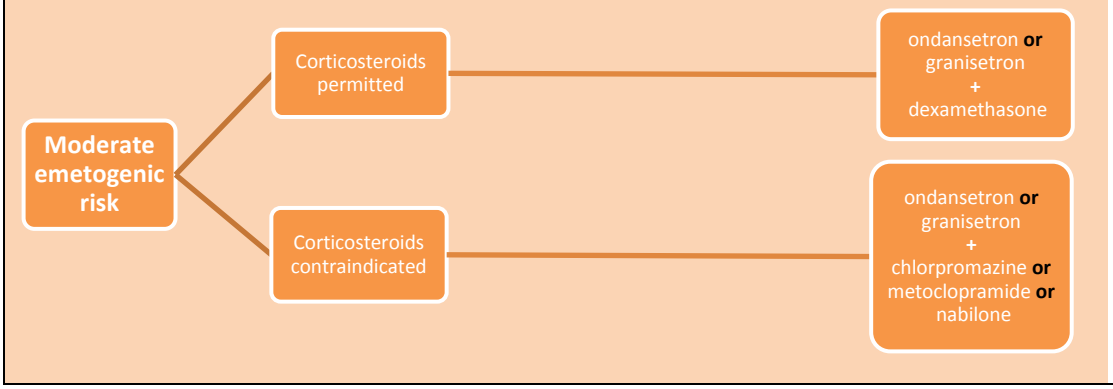
Emetogenicity is classified based on the most highly emetogenic agent on each day of therapy.

Antiemetic Dosage Recommendations for Children receiving HIGHLY Emetogenic Antineoplastic Therapy		GRADE
Drug	**Dose**	
Aprepitant	Day 1: 125 mg PO x 1 Days 2 and 3: 80mg PO once daily	Strong 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 mcg/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 pre-therapy x 1 and then q8h	Strong recommendation Moderate quality evidence
Chlorpromazine	0.5mg/kg/dose IV q6h	Strong recommendation Low quality evidence
Nabilone	< 18 kg: 0.5 mg/dose PO twice daily 18 to 30 kg: 1 mg/dose PO twice daily > 30 kg: 1 mg/dose PO three times daily Maximum: 0.06 mg/kg/day	Weak recommendation Low quality evidence

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

- Guideline for the Prevention of Acute Nausea and Vomiting due to Antineoplastic Medication in Pediatric Cancer Patients. See page 36 and Appendix I for information regarding maximum antiemetic doses.
- Guideline for the Classification of the Acute Emetogenic Potential of Antineoplastic Medication in Pediatric Cancer Patients

Prevention of Acute AINV in Pediatric Cancer Patients



Antineoplastic Agents with <u>MODERATE</u> Emetic Risk 30-90% frequency of emesis in absence of prophylaxis
Single agent antineoplastic therapy
Aldesleukin > 12 to 15 million units/m^2
Amifostine > 300 mg/m^2
Arsenic trioxide
Azacitidine
Bendamustine
Busulfan
Carmustine ≤ 250 mg/m^2
Clofarabine
Cyclophosphamide < 1 g/m^2
Cyclophosphamide (oral)
Cytarabine > 200 mg to < 3 g/m^2
Daunorubicin
Doxorubicin
Epirubicin
Etoposide (oral)
Idarubicin
Ifosfamide
Imatinib (oral)
Intrathecal therapy (methotrexate, hydrocortisone & cytarabine)
Irinotecan
Lomustine
Melphalan > 50 mg/m^2
Methotrexate ≥ 250 mg to < 12 g/m^2
Oxaliplatin > 75 mg/m^2
Temozolomide (oral)
Vinorelbine (oral)
Multiple agent antineoplastic therapy
With the <u>exceptions</u> listed under high emetic risk, emetogenicity is classified based on the most highly emetogenic agent.
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		**GRADE**
Drug	**Dose**	
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 mcg/kg/dose IV as a single daily dose **<u>or</u>** 40 mcg/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 pre-therapy x 1 and then q12h	Strong recommendation Moderate quality evidence
Chlorpromazine	0.5mg/kg/dose IV q6h	Strong recommendation Low quality evidence
Metoclopramide	1 mg/kg/dose IV pre-therapy x 1 then 0.0375 mg/kg/dose PO q6h Give diphenhydramine or benztropine concurrently.	Strong recommendation Low quality evidence
Nabilone	< 18 kg: 0.5 mg/dose PO twice daily 18 to 30 kg: 1 mg/dose PO twice daily > 30 kg: 1 mg/dose PO three times daily <u>Maximum</u>: 0.06 mg/kg/day	Weak recommendation Low quality evidence

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

- Guideline for the Prevention of Acute Nausea and Vomiting due to Antineoplastic Medication in Pediatric Cancer Patients. See page 36 and Appendix I for information regarding maximum antiemetic doses.
- Guideline for the Classification of the Acute Emetogenic Potential of Antineoplastic Medication in Pediatric Cancer Patients

Prevention of Acute AINV in Pediatric Cancer Patients

Low emetogenic risk → ondansetron **or** granisetron

Strong recommendation
Moderate quality evidence

Antineoplastic Agents with <u>LOW</u> Emetic Risk 10% to <30% frequency of emesis in absence of prophylaxis	
Single agent antineoplastic therapy	
Amifostine ≤300 mg/m^2	Methotrexate >50 mg/m^2 to <250mg/m^2
Amsacrine	Mitomycin
Bexarotene	Mitoxantrone
Busulfan (oral)	Nilotinib
Capecitabine	Paclitaxel
Cytarabine ≤200 mg/m^2	Paclitaxel-albumin
Docetaxel	Pemetrexed
Doxorubicin (liposomal)	Teniposide
Etoposide	Thiotepa <300 mg/m^2
Fludarabine (oral)	Topotecan
5-Fluorouracil	Vorinostat
Gemcitabine	
Ixabepilone	
Multiple agent antineoplastic therapy	
With the <u>exceptions</u> listed under high emetic risk, emetogenicity is classified based on the most highly emetogenic agent.	
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>LOW</u> Emetic Risk Antineoplastic Therapy		**GRADE**
Drug	**Dose**	
Granisetron	40 mcg/kg/dose IV as a single daily dose <u>or</u> 40 mcg/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; <u>Maximum</u> 16 mg/dose IV 24 mg/dose PO pre-therapy x 1	Strong recommendation Low quality evidence

Refer to the complete POGO guidelines for further details:

- Guideline for the Prevention of Acute Nausea and Vomiting due to Antineoplastic Medication in Pediatric Cancer Patients
- Guideline for the Classification of the Acute Emetogenic Potential of Antineoplastic Medication in Pediatric Cancer Patients

Available at http://www.pogo.ca/healthcare/practiceguidelines

Minimal emetogenic risk → no routine prophylaxis

Strong recommendation
Very low quality evidence

Antineoplastic Agents with <u>MINIMAL</u> Emetic Risk <10% frequency of emesis in absence of prophylaxis		
Single agent antineoplastic therapy		
Alemtuzumab	Erlotinib	Rituximab
Alpha interferon	Fludarabine	Sorafenib
Aspagarinase (IM or IV)	Gefitinib	Sunitinib
Bevacizumab	Gemtuzumab ozogamicin	Temsirolimus
Bleomycin	Hydroxyurea (oral)	Thalidomide
Bortezomib	Lapatinib	Thioguanine (oral)
Cetuximab	Lenalidomide	Trastuzumab
Chlorambucil (oral)	Melphalan (oral low-dose)	Valrubicin
Cladribine (2-chlorodeoxyadenosine)	Mercaptopurine (oral)	Vinblastine
Dasatinib	Methotrexate ≤ 50 mg/m^2	Vincristine
Decitabine	Nelarabine	Vindesine
Denileukin diftitox	Panitumumab	Vinorelbine
Dexrazoxane	Pentostatin	
For multiple agent and multi-day antineoplastic therapy – Please refer to recommendations in Low emetic risk table.		