CHILDREN'S ONCOLOGY GROUP

The world's childhood cancer experts

The following guideline is no longer current and its recommendations may no longer be valid.
This document is provided for historical purposes only.

ARCHIVED: July 2022

Guidelines on Chemotherapy-induced Nausea and Vomiting in Pediatric Cancer Patients

COG Supportive Care Endorsed Guidelines

Click **here** to see all the COG Supportive Care Endorsed Guidelines.

This document summarizes three clinical practice guidelines on the topic of chemotherapy-induced nausea and vomiting:
I. The "Classification of the Acute Emetogenicity of Chemotherapy in Pediatric Patients: A Clinical Practice Guideline" (endorsed by the COG Supportive Care Guideline Committee in August 2019).
II. The "Guideline for the Prevention of Acute Nausea and Vomiting due to Antineoplastic Medication in Pediatric Cancer Patients" (endorsed by the COG Supportive Care Guideline Committee in January 2018) and the "Antiemetics: ASCO Guideline Update" (endorsed by the COG Supportive Care Guideline Committee in December 2020) and
III. The "Prevention and treatment of anticipatory chemotherapy-induced nausea and vomiting in pediatric cancer patients and hematopoietic stem cell recipients: Clinical practice guideline update" (endorsed by the COG Supportive Care Guideline Committee in July 2021).

I. Classification of Chemotherapy Emetogenicity

The "Classification of the Acute Emetogenicity of Chemotherapy in Pediatric Patients: A Clinical Practice Guideline" developed by the Pediatric Oncology Group of Ontario was endorsed by the COG Supportive Care Guideline Committee in August 2019.

The source guideline is published (Paw Cho Sing E, Robinson PD, Flank J et al. Pediatr Blood Cancer. 2019; 66: e27646.) and is available at https://onlinelibrary.wiley.com/doi/epdf/10.1002/pbc.27646. It is an update of an earlier guideline that was published in 2011.

The purpose of this guideline is to provide evidence-based recommendations regarding the acute emetic potential of chemotherapy in pediatric oncology patients aged 1 month to 18 years. The recommendations of the endorsed guideline are presented below.

Summary of Recommendations for the Classification of Chemotherapy Emetogenicity

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
1. Which chemotherapy regimens are highly emetogenic?	
Single-agent regimens: Asparaginase (*Erwinia*) IV ≥ 20,000 IU/m^2/dose Busulfan IV ≥ 0.8mg/kg/dose Busulfan PO ≥ 1mg/kg/dose Carboplatin IV ≥ 175 mg/m^2/dose Cisplatin IV ≥ 12 mg/m^2/dose Cyclophosphamide IV ≥ 1,200 mg/m^2/dose Cytarabine IV ≥ 3g/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	Strong recommendation Very low to high quality of evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
Multiple-agent regimens: Cyclophosphamide ≥ 600 mg/m^2/dose + dactinomycin ≥ 1 mg/m^2/dose Cyclophosphamide ≥ 400 mg/m^2/dose + doxorubicin ≥ 40 mg/m^2/dose Cytarabine IV ≥ 90 mg/m^2/dose + methotrexate IV ≥ 150 mg/m^2/dose Cytarabine IV + teniposide IV Dacarbazine IV ≥ 250 mg/m^2/dose + doxorubicin IV ≥ 60 mg/m^2/dose Dactinomycin IV ≥ 900 µg/m^2/dose + 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	
2. Which single-agent and multiple-agent chemotherapy regimens are moderately emetogenic?	
Single-agent regimens: 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 3–9mg/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 regimens: 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 80mg/m^2/dose Cytarabine 60 or 90 mg/m^2/dose + methotrexate 120 mg/m^2/dose Liposomal doxorubicin IV 20–50 mg/m^2/dose + topotecan PO 0.6mg/m^2/day	Strong recommendation Very low to high quality of evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
3. Which single-agent and multiple-agent chemotherapy regimens are of low emetogenicity?	
Single-agent regimens: Cyclophosphamide IV 500 mg/m^2/dose Cyclophosphamide PO2–3 mg/kg/dose Dasatinib PO 60–120 mg/m^2/dose Erlotinib PO 35–150 mg/m^2/day Everolimus PO 0.8–9mg/m^2/day Gefitinib PO 150–500 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 ≤ 4.2mg/kg/dose Methotrexate 38–83 mg/m^2/dose IV Mitoxantrone IV ≤ 33 mg/m^2/dose Procarbazine PO 50–100 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 regimens: Cytarabine IV 60 mg/m^2/dose + methotrexate IV 90 mg/m^2/dose	Strong recommendation Very low to moderate quality of evidence
4. Which single-agent and multiple-agent chemotherapy regimens are minimally emetogenic?	
Single-agent regimens: Asparaginase (*E. coli*) IM ≤ 6000 IU/m^2/dose Asparaginase (*Erwinia*) IM ≤ 25 000 IU/m^2/dose Chlorambucil ≤ 0.2mg/kg/day PO Doxorubicin IV 10 mg/m^2/dose Liposomal doxorubicin IV ≤ 50 mg/m^2/dose Mercaptopurine PO ≤ 4.2mg/kg/dose Methotrexate PO/SC ≤ 10 mg/m^2/dose Pracinostat PO 25–45 mg/m^2/dose Vincristine IV ≤ 1.5mg/m^2/dose Multiple-agent regimens: 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 ≤ 2.5mg/kg/dose + methotrexate PO ≤ 0.1mg/kg/day	Strong recommendation Very low to low quality of evidence

II. **Prevention of Acute Chemotherapy-induced Nausea and Vomiting**

The "Guideline for the Prevention of Acute Nausea and Vomiting due to Antineoplastic Medication in Pediatric Cancer Patients" developed by the Pediatric Oncology Group of Ontario was endorsed by the COG in January 2018. The "Antiemetics: ASCO Update" developed by the American Society of Clinical Oncology was endorsed by the COG in December 2020.

The source guidelines are published Patel P, Robinson PD, Thackray J, et al. Pediatr Blood Cancer. 2017; 2017; 64: e26542. and Hesketh P, Kris MG, Basch E et al. JCO 2020; 38 (24): 2782-97.) and are available at: http://onlinelibrary.wiley.com/doi/10.1002/pbc.26542/epdf and https://ascopubs.org/doi/10.1200/JCO.20.01296

Implementation tools developed by the guideline developer are available at: https://www.pogo.ca/healthcare/practiceguidelines/chemotherapy-induced-nausea-and-vomiting-cinv/

The purpose of this guideline is to provide evidence-based recommendations for the prevention of acute chemotherapy-induced nausea and vomiting in children. The recommendations of the endorsed guideline are presented below.

Summary of Recommendations for the Prevention of Acute Chemotherapy-induced Nausea and Vomiting (CINV)

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
1. What pharmacological interventions provide optimal control of acute CINV in children receiving highly emetogenic chemotherapy (HEC)?	
We recommend that: • Children ≥ 6 months old receiving HEC which is *not* known or suspected to interact with aprepitant receive: *granisetron, ondansetron or palonosetron + dexamethasone + aprepitant/fosaprepitant* • Children < 6 months old receiving HEC receive: *granisetron, ondansetron or palonosetron + dexamethasone* • Children ≥ 6 months old receiving HEC which is known or suspected to interact with aprepitant/fosaprepitant receive: *granisetron, ondansetron or palonosetron + dexamethasone* • Children ≥ 6 months old receiving HEC which is *not* known or suspected to interact with aprepitant/fosaprepitant and who cannot receive dexamethasone for CINV prophylaxis receive: *palonosetron + aprepitant/fosaprepitant* (POGO 2017 and ASCO 2020)	Strong recommendation Moderate quality evidence Strong recommendation Moderate quality evidence Strong recommendation Moderate quality evidence Strong recommendation Moderate quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
We suggest that: • Children < 6 months old receiving HEC and who *cannot* receive dexamethasone for CINV prophylaxis receive: *palonosetron* • Children receiving HEC which is known or suspected to interact with aprepitant/fosaprepitant and who *cannot* receive dexamethasone for CINV prophylaxis receive: *palonosetron* (POGO 2017 and ASCO 2020)	Weak recommendation Moderate quality evidence Weak recommendation Moderate quality evidence
2. What pharmacological interventions provide optimal control of acute CINV in children receiving moderately emetogenic chemotherapy (MEC)?	
We recommend that: • Children receiving MEC receive: *granisetron, ondansetron or palonosetron + dexamethasone* We suggest that: • Children ≥ 6 months old receiving MEC who *cannot* receive dexamethasone for CINV prophylaxis receive: *granisetron, ondansetron or palonosetron + aprepitant/fosaprepitant* • Children < 6 months old receiving MEC who cannot receive dexamethasone for CINV prophylaxis receive: *palonosetron* • Children receiving MEC which is known or suspected to interact with aprepitant/fosaprepitant and who *cannot* receive dexamethasone for CINV prophylaxis receive: *palonosetron* (POGO 2017 and ASCO 2020)	Strong recommendation Moderate quality evidence Weak recommendation Moderate quality evidence Weak recommendation Moderate quality evidence Weak recommendation Moderate quality evidence
3. What doses of aprepitant and palonosetron are known to be effective in children receiving chemotherapy?	
We suggest the following **aprepitant** dose for children ≥ 6 months old: *Day 1: 3 mg/kg/dose (maximum: 125mg) PO x 1;* *Days 2 and 3: 2 mg/kg/dose (maximum: 80mg) PO once daily* (POGO 2017)	Weak recommendation Moderate quality evidence
We suggest the following **palonosetron** dose for children: *1 month to < 17 years: 0.02 mg/kg/dose (maximum 1.5 mg) IV once pre-therapy* *≥ 17 years: 0.5 mg/dose PO once pre-therapy* (POGO 2017)	Weak recommendation Moderate quality evidence

III. **Prevention and Treatment of Anticipatory Chemotherapy-Induced Nausea and Vomiting**

The "Prevention and treatment of anticipatory chemotherapy-induced nausea and vomiting in pediatric cancer patients and hematopoietic stem cell recipients: Clinical practice guideline update" was endorsed by the COG in July 2021.
The source guideline is published (Patel P, Robinson PD, Devine KA, et al. Pediatr Blood Cancer 2021; e28947.) and is available at: https://onlinelibrary.wiley.com/doi/epdf/10.1002/pbc.28947

The purpose of this guideline is to provide those caring for pediatric oncology or hematopoietic stem cell recipients up to 18 years of age with updated recommendations for the prevention of anticipatory CINV. The recommendations of the endorsed guideline are presented below.

Summary of Recommendations for the Prevention and Treatment of Anticipatory Chemotherapy-induced Nausea and Vomiting (CINV)

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
1. What strategies are recommended for primary prevention of anticipatory CINV in pediatric patients?	
1.1 Optimize acute and delayed CINV control to minimize the risk of anticipatory CINV *Remarks:* This recommendation places high value on the consistent evidence that a history of acute or delayed CINV is a risk factor for anticipatory CINV. This recommendation also considers the other benefits of optimized acute or delayed CINV control including improved quality of life and the low risk of toxicities anticipated with CPG-consistent antiemetics.	Strong recommendation Moderate- quality evidence
2. What strategies are recommended for secondary prevention of anticipatory CINV in pediatric patients?	
2.1: Consider offering cooperative patients one or more of the following nonpharmacological interventions for secondary prevention of anticipatory CINV: hypnosis, systematic desensitization, or relaxation techniques. *Remarks*: This recommendation places a high value on the minimal risks associated with these interventions. A conditional recommendation was made as the supporting evidence was limited to a small number of studies, the direct pediatric experience is scant and reports of the benefits of these interventions are inconsistent.	Conditional recommendation Low-quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
2.2 Consider using lorazepam for secondary prevention of anticipatory CINV. *Remarks*: This recommendation remained unchanged from the 2014 CPG. It places a high value on the limited data demonstrating improved anticipatory CINV control in adults given benzodiazepines. It is a conditional recommendation because there is no direct pediatric evidence among included studies describing the use of benzodiazepines for this purpose.	Conditional recommendation Very low-quality evidence
2.3 We suggest that ginger not be used routinely for secondary prevention of anticipatory CINV. *Remarks:* The panel made a conditional recommendation against the routine use of ginger given inconsistent study results in adult patients and the absence of pediatric data to support the use of ginger for this purpose. The panel also appreciated that the ginger formulations evaluated in included studies may not be comparable because doses of the components thought to be medically active are not uniformly reported.	Conditional recommendation Low-quality evidence
2.4 Do not use clonidine for secondary prevention of anticipatory CINV. *Remarks*: The panel made a strong recommendation against the use of clonidine given its poor safety profile, lack of clear benefit, and lack of direct data for its use in pediatric patients for anticipatory CINV prevention.	Strong recommendation Low-quality evidence
3. What strategies are recommended for acute treatment of anticipatory CINV in pediatric patients?	
No recommendation can be made. *Remarks:* No identified study directly evaluated an intervention aimed at the treatment of anticipatory CINV. The evidence describing primary and secondary anticipatory CINV prevention could not be extrapolated to make a recommendation.	

*See Appendix 1

Appendix 1: GRADE

Strength of Recommendations:

Strong Recommendation	When using GRADE, panels make strong recommendations when they are confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects.
Weak/Conditional Recommendation	Weak recommendations indicate that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is less confident.

Strength of Recommendations Determinants:

Factor	Comment
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted
Costs (resource allocation)	The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted

Quality of Evidence

High Quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate Quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low Quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very Low Quality	Any estimate of effect is very uncertain

Guyatt, G.H., et al., *GRADE: an emerging consensus on rating quality of evidence and strength of recommendations.* BMJ, 2008; 336: 924-926.
Guyatt, G.H., et al., *GRADE: going from evidence to recommendations.* BMJ, 2008; 336: 1049-1051.