CHILDREN'S ONCOLOGY GROUP

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

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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 source guideline and its focused update are published (Dupuis LL, Boodhan S, Holdsworth M, et al. Pediatr Blood Cancer. 2013; 60: 1073-82. and Patel P, Robinson PD, Thackray J, et al. Pediatr Blood Cancer. 2017; 2017; 64: e26542.) and are available at:
http://onlinelibrary.wiley.com/doi/10.1002/pbc.24508/pdf and
http://onlinelibrary.wiley.com/doi/10.1002/pbc.26542/epdf

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. How is optimal control of acute CINV defined?	
We recommend that optimal control of acute CINV be defined as no vomiting, no retching, no nausea, no use of antiemetic agents other than those given for CINV prevention and no nausea-related change in the child's usual appetite and diet. This level of CINV control is to be achieved on each day that antineoplastic therapy is administered and for 24 hours after administration of the last antineoplastic agent of the antineoplastic therapy block	Strong recommendation Very low quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
2a. 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*	Strong recommendation Moderate quality evidence
• Children < 6 months old receiving HEC receive: *granisetron, ondansetron or palonosetron + dexamethasone*	Strong recommendation Moderate quality evidence
• Children ≥ 6 months old receiving HEC which is known or suspected to interact with aprepitant receive: *granisetron, ondansetron or palonosetron + dexamethasone*	Strong recommendation Moderate quality evidence
• Children ≥ 6 months old receiving HEC which is *not* known or suspected to interact with aprepitant and who cannot receive dexamethasone for CINV prophylaxis receive: *palonosetron + aprepitant*	Strong recommendation Moderate quality evidence
We suggest that:	
• Children < 6 months old receiving HEC and who *cannot* receive dexamethasone for CINV prophylaxis receive: *palonosetron*	Weak recommendation Moderate quality evidence
• Children receiving HEC which is known or suspected to interact with aprepitant and who *cannot* receive dexamethasone for CINV prophylaxis receive: *palonosetron*	Weak recommendation Moderate quality evidence
2b. 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*	Strong recommendation Moderate quality evidence
We suggest that:	
• Children ≥ 6 months old receiving MEC who *cannot* receive dexamethasone for CINV prophylaxis receive: *granisetron, ondansetron or palonosetron + aprepitant*	Weak recommendation Moderate quality evidence
• Children < 6 months old receiving MEC who cannot receive dexamethasone for CINV prophylaxis receive: *palonosetron*	Weak recommendation Moderate quality evidence
• Children receiving MEC which is known or suspected to interact with aprepitant and who *cannot* receive dexamethasone for CINV prophylaxis receive: *palonosetron*	Weak recommendation Moderate quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
2c. What pharmacological interventions provide optimal control of acute CINV in children receiving antineoplastic agents of low emetic risk?	
We recommend that children receiving antineoplastic agents of low emetic risk receive: *ondansetron or granisetron*	Strong recommendation Moderate quality evidence
2d. What pharmacological interventions provide optimal control of acute CINV in children receiving antineoplastic agents of minimal emetic risk?	
We recommend that children receiving antineoplastic agents of minimal emetic risk receive: *no routine prophylaxis*	Strong recommendation Very low quality evidence
3. What adjunctive non-pharmacological interventions provide control of acute CINV in children receiving antineoplastic agents of any emetic risk?	
We suggest that acupuncture, acupressure, guided imagery, music therapy, progressive muscle relaxation and psycho-educational support and information may be effective in children receiving antineoplastic agents. Virtual reality may convey benefit. We suggest that the following dietary interventions may be effective: • eat smaller, more frequent meals; • reduce food aromas and other stimuli with strong odors; • avoid foods that are spicy, fatty or highly salty; • take antiemetics prior to meals so that the effect is present during and after meals; and • measures and foods (e.g. "comfort foods") that helped to minimize nausea in the past.	Weak recommendation Very low quality evidence
4. What doses of antiemetic agents are known to be effective in children receiving antineoplastic agents?	
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*	Weak recommendation Moderate quality evidence
We suggest the following **dexamethasone** dose for children receiving highly emetogenic antineoplastic therapy: *6 mg/m^2/dose IV/PO q6h* If given concurrently with aprepitant, reduce dexamethasone dose by half. We recommend the following **dexamethasone** for children receiving moderately emetogenic antineoplastic therapy: *≤ 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	Weak recommendation Low quality evidence Strong recommendation Low quality evidence

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence
We recommend the following **IV granisetron** dose for children receiving highly emetogenic antineoplastic therapy: *40 mcg/kg/dose IV as a single daily dose*	Strong recommendation Low quality evidence
We recommend the following **IV granisetron** dose for children receiving moderately emetogenic antineoplastic therapy: *40 mcg/kg/dose IV as a single daily dose*	Strong recommendation Moderate quality evidence
We suggest the following **oral granisetron** dose for children receiving moderately emetogenic antineoplastic therapy: *40 mcg/kg/dose PO q12h*	Weak recommendation Low quality evidence
We recommend the following **IV granisetron** dose for children receiving antineoplastic therapy of low emetogenicity: *40 mcg/kg/dose IV as a single daily dose*	Strong recommendation Low quality evidence
We suggest the following **oral granisetron** dose for children receiving antineoplastic therapy of low emetogenicity: *40 mcg/kg/dose PO q12h*	Weak recommendation Low quality evidence
We recommend the following **ondansetron** dose for children receiving highly emetogenic antineoplastic therapy: *5 mg/m^2/dose (0.15 mg/kg/dose) IV/PO pre-therapy x 1 and then q8h*	Strong recommendation Moderate quality evidence
We recommend the following **ondansetron** dose for children receiving moderately emetogenic antineoplastic therapy: *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
We recommend the following **ondansetron** dose for children receiving therapy of low emetogenicity: *10 mg/m^2/dose (0.3 mg/kg/dose; maximum 16 mg/dose IV or 24 mg/dose PO) pre-therapy x 1*	Strong recommendation Low 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*	Weak recommendation Moderate quality evidence

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 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.