



**Atlantic Provinces Pediatric Hematology/Oncology Network
Réseau d'Oncologie et Hématologie Pédiatrique des Provinces Atlantiques**

**5850/5980 University Avenue, PO Box 9700, Halifax, NS B3K 6R8
1.902.470.7429 1.888.470.5888**

*Reviewed and approved by specialists at the IWK Health Centre, Halifax NS, and the
Janeway Children's Health and Rehabilitation Centre, NL*

**Guidelines for the Management of Chemotherapy Induced
Nausea and Vomiting in Children with Cancer**

APPHON/ROHPPA supportive care guidelines have been developed by appropriate Atlantic Provinces health professional specialists (physicians, pharmacists, nurses and other health professionals) using evidence-based or best practice references. Format and content of the guidelines will change as they are reviewed and revised on a periodic basis. Care has been taken to ensure accuracy of the information. However, any physician or health professional using these guidelines will be responsible for verifying doses and administering medications and care according to their own institutional formularies and policies and acceptable standards of care.

Unofficial document if printed. To ensure that this printed is the latest version, please check website <http://www.apphon-rohppa.com>.

The recommendations in this guideline are adapted to the local context from the C17 endorsed Pediatric Oncology Group of Ontario (POGO) Guideline for the Prevention of Acute Nausea and Vomiting due to Antineoplastic Medication in Pediatric Cancer Patients, the POGO Guideline for Classification of the Acute Emetogenic Potential of Antineoplastic Medication in Pediatric Cancer Patients, and the POGO Guideline for the Prevention and Treatment of Anticipatory Nausea and Vomiting due to Chemotherapy in Pediatric Cancer Patients recommendations were adopted into this guideline. The full versions of the guidelines which include the systematic reviews are available at: <http://www.pogo.ca/healthcare/practiceguidelines>

The APPHON/ROHPPA guideline utilized the POGO systematic reviews and adapted the information for use in the Atlantic Provinces. The APPHON/ROHPPA guideline provides recommendations on the management of nausea and vomiting in children being treated for cancer or chemotherapy induced nausea and vomiting (CINV). The Pediatric Oncology Group of Ontario (POGO) has classified chemotherapy agents based on their emetogenic potential and this APPHON guideline will follow the POGO classifications. This guideline will not include a review of alternative methods of nausea control, nor will it make recommendations as it is felt the evidence in this area is not sufficient. The guideline will include the management of acute, delayed, anticipatory, breakthrough and refractory CINV in one document to aid health care providers in the management of CINV in the Atlantic Provinces.

The reason for the APPHON adaptation of the POGO guideline for the prevention of acute nausea and vomiting and not adoption of the guideline was the dosing of dexamethasone and metoclopramide (Appendix 9). The target audience of this guideline is the healthcare providers involved in the care of children with cancer in the Atlantic Provinces.

This document is a general reference and is not intended to replace good clinical judgment.

TABLE OF CONTENTS

Definitions	4
Nausea and Vomiting Assessment	4
Non-Pharmacologic Management	6
Pharmacologic Management	7
Antiemetic Management of Chemotherapy Induced Nausea and Vomiting	7
Route of Administration for Antiemetic Agents	7
Duration of Antiemetic Administration	8
Management of Antiemetic Failure	8
Development and Review	10
References.....	11
Appendix 1: APPHON/ROHPPA Prevention and Management of CINV in Pediatric Cancer Patients-Minimal and Low Emetogenic Risk.....	12
Appendix 2: APPHON/ROHPPA - Prevention and Management of CINV in Pediatric Cancer Patients-Moderate Emetogenic Risk	13
Appendix 3: APPHON/ROHPPA - Prevention and Management of CINV in Pediatric Cancer Patients-High Emetogenic Risk	15
Appendix 4: Algorithm 1: Management of breakthrough nausea and vomiting.....	17
Appendix 5: Algorithm 2: Management of refractory nausea and vomiting.....	18
Appendix 6: Algorithm 3: Management of delayed nausea and vomiting	19
Appendix 7: Algorithm 4: Management of anticipatory nausea and vomiting	20
Appendix 8: Table 1: Dosing of Antiemetics	21
Appendix 9: Differences in the APPHON recommendations and the POGO Guideline for the Prevention of Acute Nausea and Vomiting due to Antineoplastic Medication in Pediatric Cancer Patients	22

DEFINITIONS

Types of nausea and vomiting (which includes retching) will be discussed in this guideline:

- ACUTE : most commonly begins within 1-2 hours of chemotherapy and peaks around 4-6 hours and resolves within 24 hours.
- DELAYED: occurs after 24 hours and usually within 7 days after chemotherapy.
- ANTICIPATORY: occurs before the patient receives chemotherapy and is thought to be associated with previously poorly controlled nausea and vomiting.
- BREAKTHROUGH: occurs when prophylactic antiemetics are not effective, and the patient requires use of additional rescue medications.
- REFRACTORY: occurs when antiemetics no longer work to control nausea and vomiting. This usually happens after a few or even several chemotherapy treatments.

The four categories of emetogenic potential:

1. High: CINV in greater than 90% of patients.
2. Moderate: CINV in 30-90% of patients.
3. Low: CINV in 10-30% of patients.
4. Minimal: CINV in less than 10% of patients.

NAUSEA AND VOMITING ASSESSMENT

The health care provider or parent must document vomiting daily and record frequency and volume, if possible.

Nausea can be assessed using the PeNAT tool (Figure 1 & Figure 2). This is a validated tool of faces in children 4 years and older. It is a scale of 1-4 where 1 is no nausea, and 4 is severe nausea. The tool also incorporates a few questions (Figure 2) to determine the language that each family uses to describe nausea and vomiting.

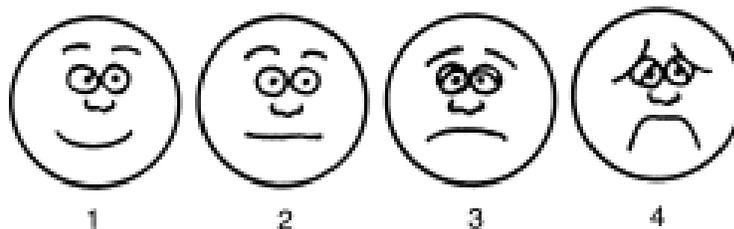


Figure 1.0 Faces used for administration of the Pediatric Nausea Assessment Tool to children older than 8 years. Children aged 8 years or younger were shown the same faces in pairs, without the numbers. These children were first shown faces 1 and 2. Children who chose the second face to describe their nausea intensity were then asked to consider faces 3 and 4. Face numbers range from 1 (no nausea) to 4 (worst nausea) (Faces adapted from Pharmacotherapy 26 (9):1223, 2006).

Determine terms used by the family when referring to nausea and vomiting.

To the child aged 4-8 years:

Have you ever thrown up (use family term) before?

If yes, how did your tummy feel just before you threw up (use family term)? _____

We call that feeling nausea or being nauseous. In your family you call that feeling _____.

If no, have you ever felt like you were going to throw up (use family term) but didn't?

If yes, how did your tummy feel then? _____

We call that feeling nausea or being nauseous. In your family you call that feeling _____.

Some children who get chemo feel nauseous (use family term) and some don't.

Right now, which kind of child is more like you?

If child says no nausea, show faces 1 and 2.

Some children who get chemo feel no nausea (use family term) at all, like this face, and some feel a little bit nauseous (use family term), like this face.

Point to each face at the appropriate time and use hands to emphasize "no nausea" and "a little bit".

Which child is more like you right now?

If child says some nausea, show faces 3 and 4.

Some children who get chemo feel some nausea (use family term), like this face, and some feel a lot of nausea (use family term), like this face.

Point to each face at the appropriate time and use hands to emphasize "some nausea" and "a lot".

Which child is more like you right now?

To the child older than 8 years:

Have you ever thrown up (use family term) before?

If yes, how did your tummy/stomach feel just before you threw up (use family term)? _____

We call that feeling nausea or being nauseous. In your family you call that feeling _____.

If no, have you ever felt like you were going to throw up (use family term) but didn't?

If yes, how did your tummy/stomach feel then? _____

We call that feeling nausea or being nauseous. In your family you call that feeling _____.

Some children who get chemo feel nauseous (use family term) and some don't.

These faces show children who feel no nausea at all, who feel a little bit nauseous, who feel even more nauseous, and who feel nauseous a whole lot.

Point to each face at the appropriate time.

Which face is more like you right now?

Figure 2.0 Scripts according to age for the Pediatric Nausea Assessment Tool administered to children who are receiving antineoplastic agents (adapted from Pharmacotherapy 26 (9):1224, 2006)

Based on the results of the PeNAT tool, the multidisciplinary team should evaluate and make recommendations if necessary on optimizing antiemetic therapy.

I. NON-PHARMACOLOGIC MANAGEMENT

Despite the advances in pharmacological management, standard pharmacological regimens may not fully alleviate symptoms of CINV in pediatric oncology patients. Investigating the adjuvant role of non-pharmacological interventions is an important consideration of antiemetic therapy.

Non-pharmacological measures should be implemented in conjunction with pharmacological regimens to allow for the effective management of CINV. The use of non-pharmacological measures may not be appropriate for each patient; interventions should be implemented according to the individual patient's needs and circumstances.

Some suggested non-pharmacological interventions may include; *music therapy, cognitive distraction, guided imagery, massage, acupuncture and dietary concerns*. These non-pharmacologic interventions are beyond the scope of this guideline and will not be discussed except for dietary concerns which are discussed below.

Dietary Concerns:

- Advise the child not to eat for at least thirty minutes before chemotherapy starts
- Several small meals a day are better tolerated than three large meals
- Try to keep cooking smells or foods with strong odors away from the child
- Offering food while it is cold may help as cold food smells less
- Give plenty of fluids such as clear soups, flat pop, tea, jello or non-citrus fruit juice after episodes of vomiting
- Avoid fried, fatty or spicy foods
- Bland foods such as toast, crackers, potatoes, vegetables and easily digested meats (chicken) are often well tolerated
- Make mealtime as pleasant as possible for the child, for example serve food in an attractive way
- It may be beneficial to keep the child in a comfortable, relaxed, sitting position for at least 2 hours after eating
- Fresh air often helps reduce nausea
- After vomiting, allow time for child to recover, brush teeth and rinse mouth, before offering any food
- When nausea/vomiting is severe, do not pressure the child to eat, they may acquire a learned aversion to certain foods
- Encourage napping times when nausea is expected

II. PHARMACOLOGIC MANAGEMENT:

Guiding principles of nausea and vomiting prevention and management:

- A. Prevention of nausea and vomiting is very important and every effort should be directed to making sure appropriate antiemetics are prescribed prior to the first cycle of chemotherapy. Evidence, both anecdotal and from the literature, indicates that if the patient receives suboptimal antiemetic management with the first cycle of chemotherapy subsequent cycles of chemotherapy become distressing based on this bad experience and possibly more difficult to control.
- B. The success of antiemetic management is in optimizing therapy for every cycle of chemotherapy. Successful management of nausea and vomiting in this document is defined as no nausea and vomiting. If an antiemetic regimen was not completely effective with a cycle of chemotherapy then changes need to be made for subsequent cycles. This may include increasing doses of current agents or adding new agents or using a different regimen.
- C. The emetogenic potential of the chemotherapy cycle is based on the emetogenic potential of the most emetogenic agent and management should be directed to that agent.

1. Antiemetic Management of Chemotherapy Induced Nausea and Vomiting

A. Initial Antiemetic Regimen (Chemo-naive patients)

Follow algorithms (see Appendices 1-7).

***Note:** For patients who are receiving multiple drugs known to prolong QT or who have a significant clinical history of QT prolongation: It is suggested that these patients receive baseline and continued ECG monitoring at the discretion of the treating physician. They should also receive oral ondansetron rather than intravenous and consideration should be given to giving ondansetron/granisetrone/palonosetron with longer than standard intervals if the oral route is not possible.

B. Antiemetic management for subsequent cycles of chemotherapy and for patients who have been without treatment for an extended interval (for example a relapse patient)

Follow algorithms if previous cycle was optimally managed. If antiemetic therapy was not effective in spite of appropriate management based on the algorithms, antiemetic doses should be maximized, alternate antiemetics should also be considered or addition of a different class of antiemetic. This should be done in consultation with the pediatric hematology/oncology team.

2. Route of Administration for Antiemetic Agents

Whenever appropriate, antiemetics should be administered orally. If the oral route is not appropriate, antiemetic should be administered intravenously.

3. Duration of Antiemetic Administration

- Continue antiemetics “around the clock” not PRN for at least 24 hours after the end of chemotherapy.
- Dexamethasone if used should be discontinued 24 hours after the end of the chemotherapy.
- Antiemetics may need to be continued as needed (PRN).

4. Management of Antiemetic Failure

The following is a guide and management is not limited to these options.

A) Breakthrough nausea and vomiting treatment recommendations: (see Algorithm 1, Appendix 4)

Breakthrough CINV is defined as nausea and/or vomiting presumed to be attributable to antineoplastic chemotherapy and with no other pathological cause that occurs during the acute or delayed phase despite CINV prophylaxis as per these guidelines. Breakthrough nausea and vomiting occurs when the patient experiences 2 vomits or retches within a 24 hour period, or experiences greater than or equal to 3 hours of significant nausea per day, such that it affects the patient’s level of activity.

***Note:** The current recommendation is to prescribe dimenhydrinate.

1. For children receiving acute CINV prophylaxis recommended for minimally, low, or moderately emetogenic chemotherapy, clinicians should upgrade or escalate the acute CINV prophylaxis provided to that recommended for chemotherapy of the next higher level of emetogenic risk.
2. For children receiving acute CINV prophylaxis recommended for highly emetogenic chemotherapy, we suggest that olanzapine be added to CINV prophylaxis.
3. For children receiving acute CINV prophylaxis recommended for highly emetogenic chemotherapy and who cannot receive olanzapine (consult clinical pharmacist for drug interactions and contraindications), we suggest that one of the following antiemetic agents be added to CINV prophylaxis:
 - methotrimeprazine (also known as levomepromazine)
 - Scopolamine patch

Given the possibility of extrapyramidal reactions with olanzapine and methotrimeprazine, the risks and benefits of their use should be weighed carefully and co-administration of prophylaxis aimed at preventing extrapyramidal symptoms (EPS) should be considered. Patients and families should also be educated about the possible occurrence of EPS.

B) Refractory nausea and vomiting treatment recommendations: (see Algorithm 2, Appendix 5)

Refractory CINV is defined as nausea and/or vomiting presumed to be attributable to antineoplastic chemotherapy and with no other pathological cause which occurs during the acute or delayed phase despite appropriate CINV prophylaxis in patients who have experienced breakthrough CINV in a previous chemotherapy block. Refractory nausea and vomiting occurs when antiemetic regimens stop working. This may happen after a few cycles of chemotherapy.

1. For children receiving acute CINV prophylaxis recommended for minimally, low, or moderately emetogenic chemotherapy, clinicians should upgrade or escalate the acute CINV prophylaxis provided to that recommended for chemotherapy of the next higher level of emetogenic risk.
2. For children receiving acute CINV prophylaxis recommended for highly emetogenic chemotherapy, we suggest that the 5-HT₃ antagonist given for CINV prophylaxis be changed from ondansetron or granisetron to palonosetron. In jurisdictions where palonosetron is not available, we suggest that granisetron be substituted for ondansetron.
3. For children experiencing refractory CINV despite initiation of above recommendations and who have not previously received aprepitant because it is known or suspected to interact with the chemotherapeutic agent(s) being given, we suggest that the addition of aprepitant to acute CINV prophylaxis be considered.
4. For children experiencing refractory CINV despite initiation of the above recommendations, we suggest that one of the following interventions be added to the CINV prophylaxis provided:
 - interventions that were employed successfully for the treatment of breakthrough CINV in previous treatment blocks (olanzapine, methotrimeprazine, Scopolamine patch) **OR**
 - stimulation of Nei Gaun (P6) by means of acupressure or electro acupuncture (please consult pediatric oncologist to determine safety of acupuncture for the patient).

C) Delayed nausea and vomiting treatment recommendations: (See Algorithm 3, Appendix 6)

Delayed nausea and vomiting occurs after the first 24 hours after chemotherapy and usually within 7 days.

1. Add corticosteroids if not contraindicated
2. If corticosteroids alone fail add palonosetron with or without aprepitant
3. If corticosteroids are contraindicated give palonosetron with or without aprepitant

***Note:** Palonosetron is more effective in control of delayed nausea and vomiting than Ondansetron and granisetron as its half-life is 40 hours and 5HT₃ receptors blockage lasts for 5 days

D) Anticipatory nausea and vomiting treatment recommendations: (See Algorithm 4, Appendix 7)

Anticipatory nausea and vomiting occurs before the patient receives chemotherapy and is thought to be associated with previously poorly controlled nausea and vomiting. If patient is anxious prior to start of chemotherapy or experiences anxiety during chemotherapy add lorazepam and start the evening before the start of chemotherapy.

Other Considerations:

- A) A multidisciplinary approach to managing CINV will assist in providing appropriate supportive care and effective antiemetic regimens to the pediatric oncology patient.
- B) Poorly controlled CINV can result in dehydration, electrolyte imbalance, anorexia and, fatigue.
- C) Antiemetic therapies should be routinely administered during chemotherapy administration known to induce nausea and vomiting, not just PRN when patients develop symptoms of nausea.
- D) If a patient is being discharged with antiemetic medications, the patient and/or caregivers should be given instructions on management of antiemetic regimens at home, prior to discharge.

DEVELOPMENT AND REVIEW:

Prepared by: Tamara MacDonald PharmD

Expert Review: Dr. Jason Berman, Jennifer Bowdridge RN, Dr. Lynette Bowes, Dr. Bruce Crooks, Stephanie Eason RN, Dr. Conrad Fernandez, Dr. Lisa Goodyear, Dr. Ketan Kulkarni, Dr. Paul Moorehead, Deborah Parker RN, Dr. Vicky Price

Stakeholder Review: APPHON/ROHPPA Multidisciplinary Health Care Providers (For more information please contact APPHON/ROHPPA)

REFERENCES:

1. L. Lee Dupuis, M.Sc.Pharm., FCSHP, Anna Taddio, Ph.D., Elizabeth N. Kerr, Ph.D., Andrea Kelly, B.Sc.Pharm., and Linda MacKeigan, Ph.D. Development and Validation of the Pediatric Nausea Assessment Tool for Use in Children Receiving Antineoplastic Agents. *Pharmacotherapy*, 2006;26(9).
2. 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.
3. Dupuis LL, Boodhan S, Sung L, Holdsworth M, Robinson PD, Hain R, Portwine C, McCarthy P and Sung L. Guideline for classification of the acute emetogenic potential of antineoplastic medication in pediatric cancer patients. Pediatric Oncology Group of Ontario; Toronto. 2010.
4. Dupuis LL, Robinson PD, Boodhan S, Holdsworth M, Portwine C, Gibson P, Phillips R, Maan C, Stefin N and Sung L. Guideline for the Prevention and Treatment of Anticipatory Nausea and Vomiting due to Chemotherapy in Pediatric Cancer Patients. Pediatric Oncology Group of Ontario; Toronto. 2014.
5. Flank J, Robinson P, Holdsworth M, et al. Guideline for the Treatment of Breakthrough and the Prevention of Refractory Chemotherapy-Induced Nausea and Vomiting in Children With Cancer. *Pediatric Blood and Cancer*. 2016;63(7):1144-1151.
6. Patel P, Robinson PD, Thackary J et al. Guideline for the prevention of acute chemotherapy-induced nausea and vomiting in pediatric cancer patients: A focused update. *Pediatric Blood Cancer*. 2017 Oct; 64(10).
7. Flank J, Thackray J, Nielson D et al. Olanzapine for treatment and prevention of acute chemotherapy-induced vomiting in children: A retrospective, multi-center review. *Pediatric Blood and Cancer*. 2015 Mar;62(3):496-501

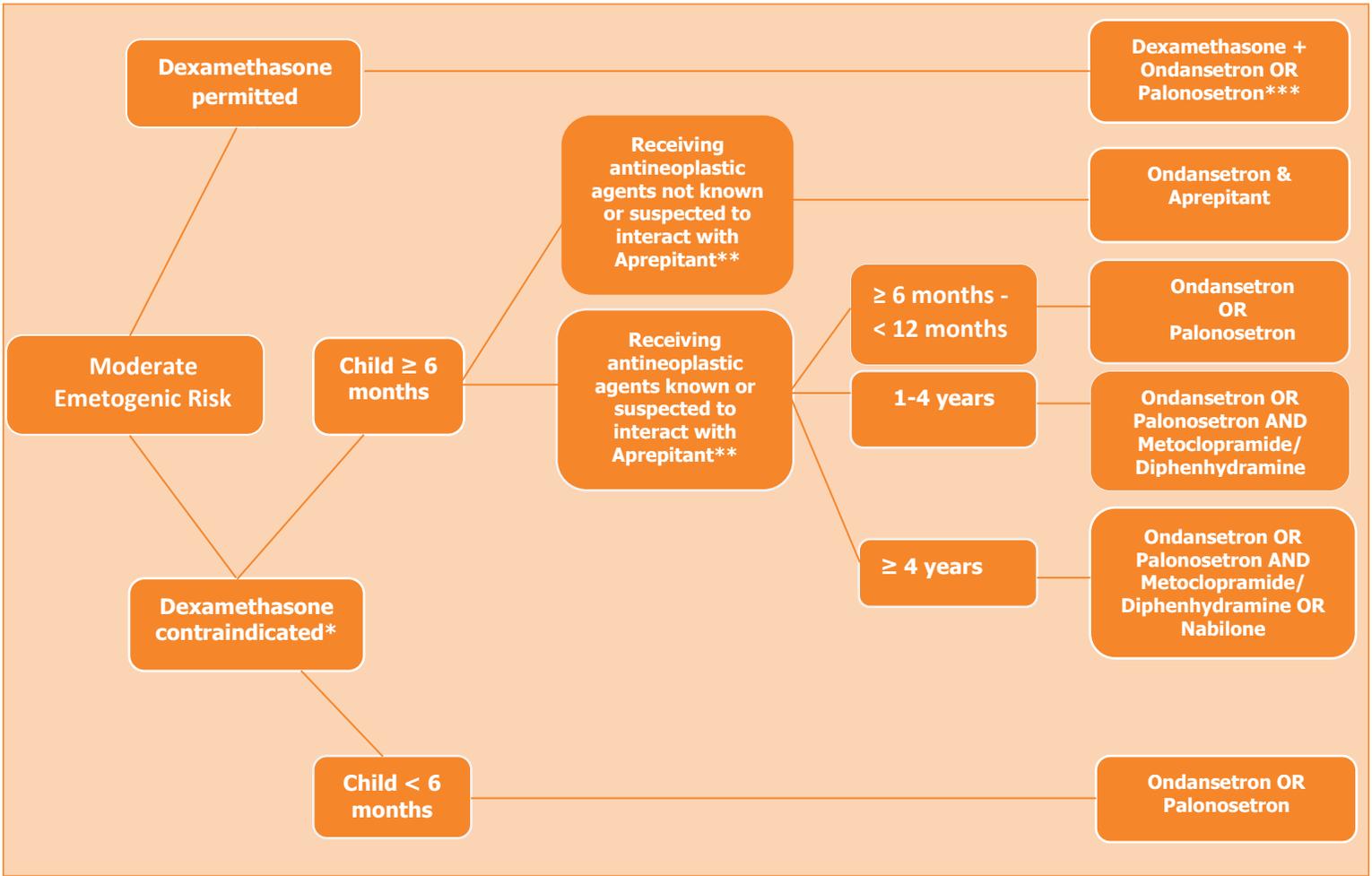
**APPENDIX 1: APPHON/ROHPPA Prevention of Acute CINV in Pediatric Cancer Patients
Minimal and Low Emetogenic Risk**

Minimal Emetogenic Risk		No Routine Prophylaxis	
Antineoplastic Agents with <u>MINIMAL</u> Emetic Risk <10% frequency of emesis in absence of prophylaxis			
Single agent antineoplastic therapy			
Alemtuzumab Alpha interferon Asparaginase (IM or IV) Bevacizumab Bleomycin Bortezomib Cladribine Dasatinib Decitabine Dexrazoxane	Erlotinib Fludarabine Gemtuzumab ozogamicin Hydroxyurea (oral) Lenalidomide Melphalan (oral low-dose) Mercaptopurine (oral) Methotrexate ≤50 mg/m ² Nelarabine	Rituximab Sorafenib Sunitinib Temsirolimus Thalidomide Thioguanine (oral) Trastuzumab Vinblastine Vincristine Vinorelbine	
For multiple agent and multi-day antineoplastic therapy – Please refer to recommendations in Low emetic risk table.			

Low Emetogenic Risk		Ondansetron	
----------------------------	--	--------------------	--

Antineoplastic Agents with <u>LOW</u> Emetic Risk 10% to <30% frequency of emesis in absence of prophylaxis		Antiemetic Dosage Recommendations for Children receiving <u>LOW</u> Emetic Risk Antineoplastic Therapy	
Single agent antineoplastic therapy		Drug	Dose
Cytarabine ≤200 mg/m ² Cytarabine (Intrathecal) Docetaxel Doxorubicin (liposomal) Etoposide Fludarabine (oral) 5-Fluorouracil Gemcitabine	Methotrexate >50 mg/m ² to <250 mg/m ² Methotrexate (intrathecal) Mitoxantrone Nilotinib Topotecan Vorinostat	Ondansetron	0.1 - 0.2 mg/kg/dose (max 8 mg/dose) IV/PO pre-therapy x 1 and up to TID prn OR 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
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.			

**APPENDIX 2: APPHON/ROHPPA - Prevention of Acute CINV in Pediatric Cancer Patients
Moderate Emetogenic Risk**



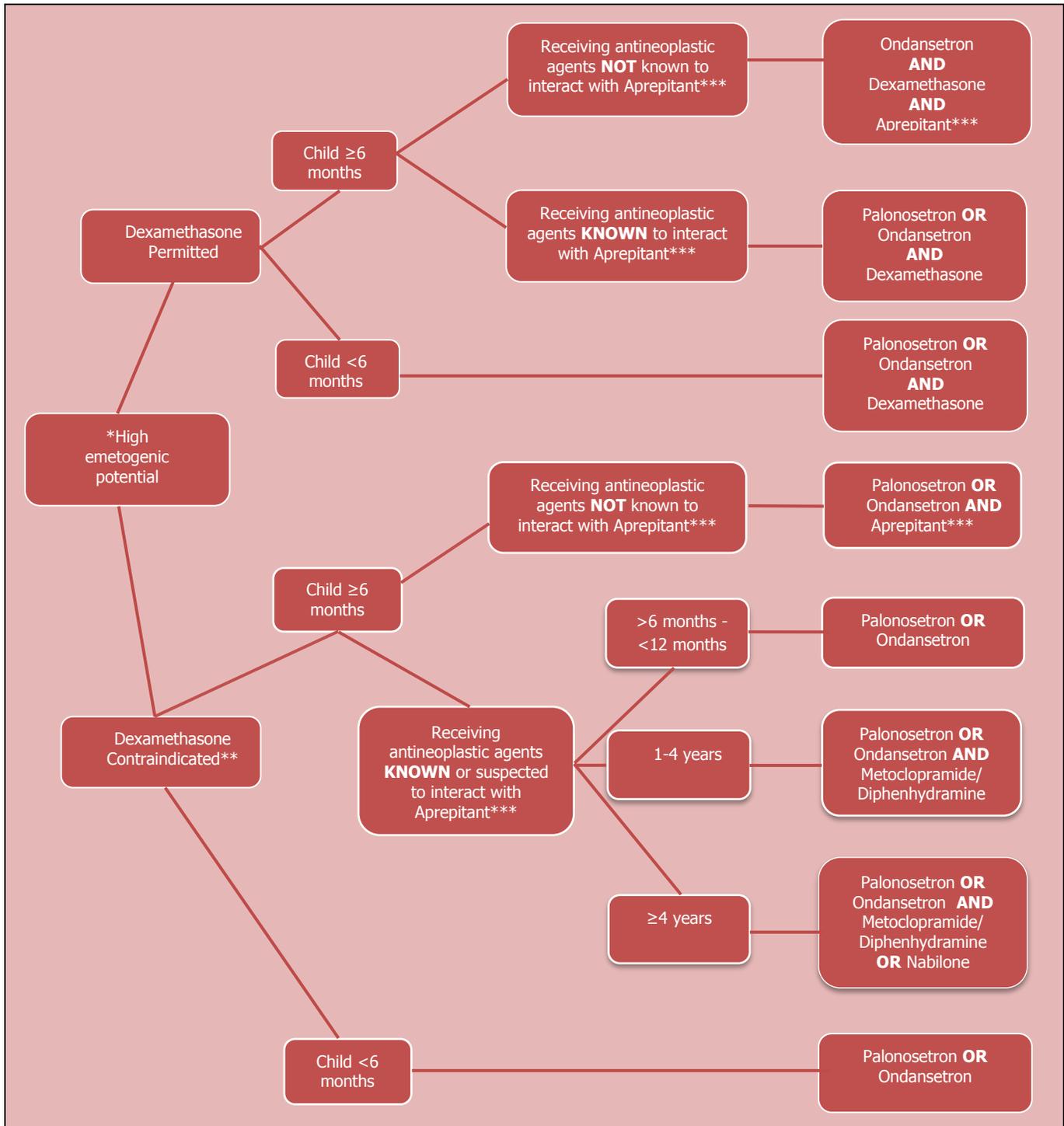
* The use of dexamethasone as an antiemetic is contraindicated in treatment of CNS tumours, AML and any study that prohibits their use as an antiemetic.

**When prescribing aprepitant always check for interactions with chemotherapy agents especially cyclophosphamide, ifosfamide and vincristine.

***If palonosetron not available consult pediatric clinical oncology pharmacist or pediatric oncologist.

Antineoplastic Agents with MODERATE Emetic Risk 30-90% frequency of emesis in absence of prophylaxis	Antiemetic Dosage Recommendations for Children receiving MODERATELY Emetogenic Antineoplastic Therapy	
<p align="center">Single agent antineoplastic therapy</p> <p>Adesleukin > 12 to 15 million units/m² Arsenic trioxide Azacitidine Bendamustine Carmustine ≤250 mg/m² Clofarabine Cyclophosphamide <1 g/m² Cyclophosphamide (oral) Cytarabine >200 mg to <3 g/m² Daunorubicin Doxorubicin Epirubicin Etoposide (oral) Idarubicin Ifosfamide Imatinib Irinotecan Lomustine Methotrexate ≥250 mg to <12 g/m² Oxaliplatin >75 mg/m² Temozolomide</p>	<p align="center">Drug</p> <p>Aprepitant</p> <p>Dexamethasone</p> <p>Metoclopramide</p> <p>Nabilone</p> <p>Ondansetron</p>	<p align="center">Dose</p> <p>Greater than or equal to 6 months: Day 1: 3 mg/kg (maximum 125 mg) PO x 1 Day 2 & 3: 2 mg/kg (maximum 80 mg) PO once daily</p> <p>≤0.6 m²: 2 mg/dose IV/PO q12 hr >0.6m²: 4 mg/dose IV/PO q12hr If given concurrently with aprepitant, reduce dexamethasone dose by half</p> <p>Age greater than 1 year 1 mg/kg/dose IV (max 40mg/dose) Give diphenhydramine 1 mg/kg/dose IV (max 50 mg/dose) concurrently.</p> <p>≥ 4 years <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</p> <p>Note: May need to titrate to effect.</p> <p>(0.1-0.2 mg/kg/dose; maximum 8 mg/dose) IV/PO pre-therapy x 1 and then q8h</p>
<p align="center">Multiple agent antineoplastic therapy</p>		
<p>With the <u>exceptions</u> listed under high emetic risk, emetogenicity is classified based on the most highly emetogenic agent.</p>		
<p align="center">Multi-day antineoplastic therapy</p>		
<p>Emetogenicity is classified based on the most highly emetogenic agent on each day of therapy.</p>	<p align="center">Palonosetron</p>	<p>1 month to less than 17 years: 0.02 mg/kg IV once (maximum: 1.5 mg/dose) pre-chemotherapy. May repeat once in 48 hours for multiday chemotherapy.</p> <p>Greater than or equal to 17 years: 0.25 mg/dose IV or 0.5 mg/dose PO once pre-chemotherapy. May repeat once in 48 hours for multiday chemotherapy</p>

**APPENDIX 3: APPHON/ROHPPA - Prevention of Acute CINV in Pediatric Cancer Patients
High Emetogenic Risk**



* For patients receiving cisplatin and anthracycline consider prescribing palonosetron in place of ondansetron as palonosetron is more effective in the management of delayed nausea and vomiting.

* For patients receiving cisplatin alone or with other agents please consult the pediatric oncologist or the clinical oncology pharmacists to determine appropriate use of palonosetron in these patients.

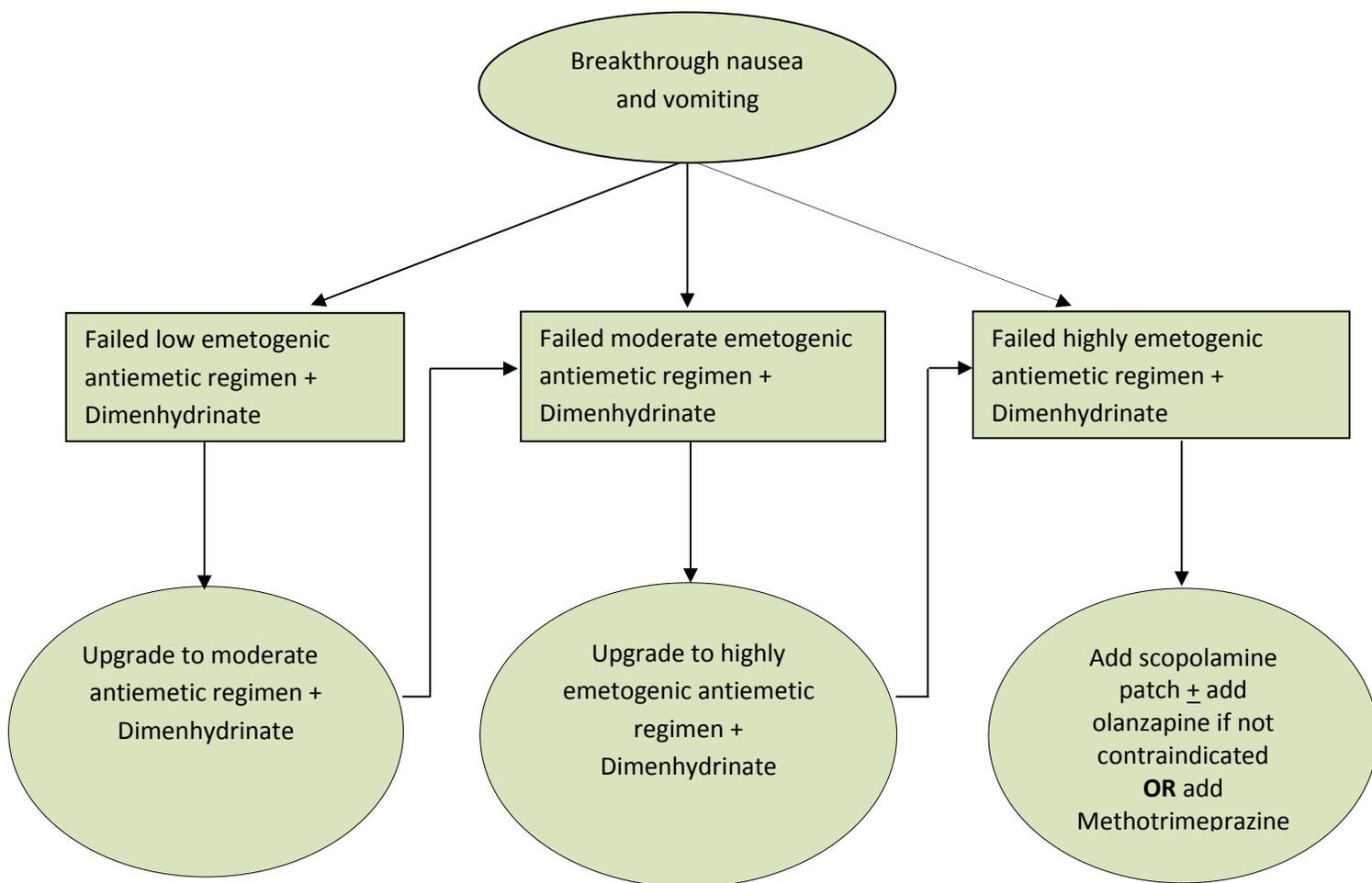
** Corticosteroid contraindicated in CNS tumours, AML and any study that prohibits their use as an antiemetic.

***When prescribing aprepitant always check for interactions with chemotherapy agents especially cyclophosphamide, ifosfamide and vincristine.

Antineoplastic Agents with HIGH Emetic Risk >90% frequency of emesis in absence of prophylaxis	
Single agent antineoplastic therapy	
Carboplatin Carmustine >250 mg/m ² Cisplatin Cyclophosphamide ≥1 g/m ² Cytarabine ≥3 g/m ² /dose Dacarbazine	Dactinomycin Methotrexate ≥12 g/m ² Procarbazine (oral)
Multiple agent antineoplastic therapy	
<p>With the <u>exceptions</u> listed below, emetogenicity is classified based on the most highly emetogenic agent.</p> <p>The following are <u>also</u> classified as high emetic risk: Cyclophosphamide + anthracycline Cyclophosphamide + etoposide Cytarabine 150-200 mg/m² + daunorubicin Cytarabine 300 mg/m² + etoposide Cytarabine 300 mg/m² + teniposide Doxorubicin + ifosfamide Doxorubicin + methotrexate 5 g/m² Etoposide + ifosfamide</p>	
Multi-day antineoplastic therapy	
Emetogenicity is classified based on the most highly emetogenic agent on each day of therapy.	

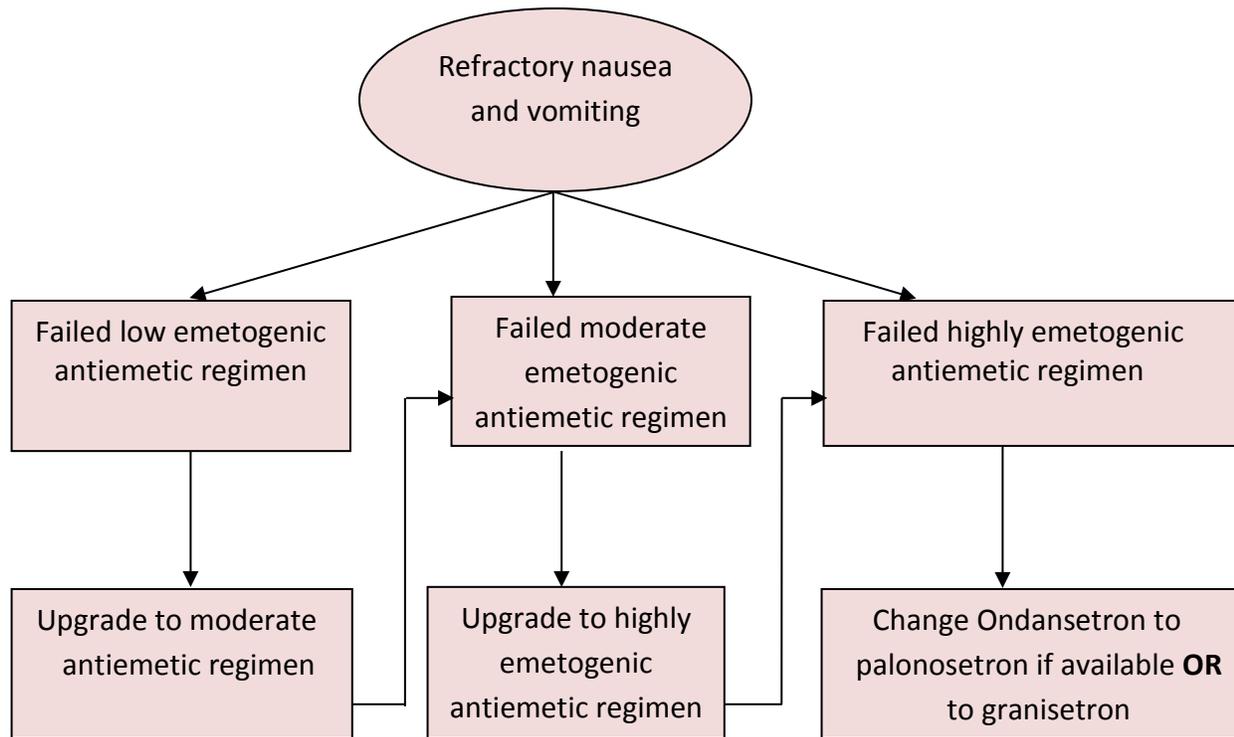
Antiemetic Dosage Recommendations for Children receiving HIGHLY Emetogenic Antineoplastic Therapy	
Drug	Dose
Aprepitant**	Greater than or equal to 6 months: Pre-Chemotherapy Day 1: 3 mg/kg (maximum 125 mg) PO x 1 Day 2 & 3: 2 mg/kg (maximum 80 mg) PO once daily
Dexamethasone	6 mg/m ² /dose IV/PO once daily pre-chemotherapy may increase to q 12 h (maximum 20 mg/day) If given concurrently with aprepitant, reduce dexamethasone dose by half
Metoclopramide	Age greater than 1 year 1 mg/kg/dose IV (max 40 mg/dose) Give diphenhydramine 1 mg/kg/dose IV (max 50 mg/dose) concurrently.
Nabilone	≥ 4 years <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 Note: May need to titrate to effect
Ondansetron	0.1-0.2 mg/kg/dose (maximum 8 mg/dose) IV/PO pre-therapy x 1 and then every 8 hours
Palonosetron	1 month to less than 17 years: 0.02 mg/kg IV once (maximum: 1.5 mg/dose) pre-chemotherapy. May repeat once in 48 hours for multiday chemotherapy. Greater than or equal to 17 years: 0.25 mg/dose IV or 0.5 mg/dose PO once pre- chemotherapy. May repeat once in 48 hours for multiday chemotherapy.

APPENDIX 4: Algorithm 1: Management of Breakthrough Nausea and Vomiting

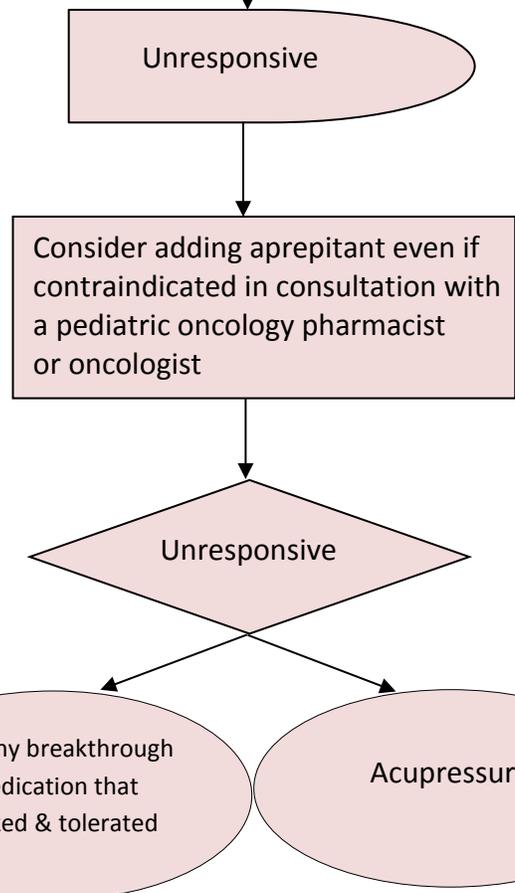


Dimenhydrinate	1 mg/kg (maximum 50 mg/dose) IV/PO q4h as needed for breakthrough nausea and vomiting upfront in all patients. Children less than 1 year should start with 0.5 mg/kg and titrate to effect to minimize paradoxical reactions
Methotrimeprazine	Infants, Children and Adolescents (oral dosing): 0.25 mg/kg/24hrs in 2 to 3 divided doses; may titrate to effect (maximum dose for children <12 years: 25 mg/day) Children and Adolescents (IV dosing): (IWK oncology/palliative care service recommendation): 0.0625 mg/kg/24hrs (maximum 2 mg/dose) IV over 30 minutes-1 hour if given through a central line q q8h-24hrs (monitor for hypotension)
Olanzapine	0.1 mg/kg/dose (maximum 10 mg/dose) once daily x 3 days Day 1-3 of chemotherapy and reassess Caution in children with psychiatric conditions Only available orally
Scopolamine patch	1 patch prior to chemotherapy for children greater than or equal to 18 kg and ½ patch for children less than 18 kg – tape half of the patch do not cut). Reapply a new patch every 72 hours.

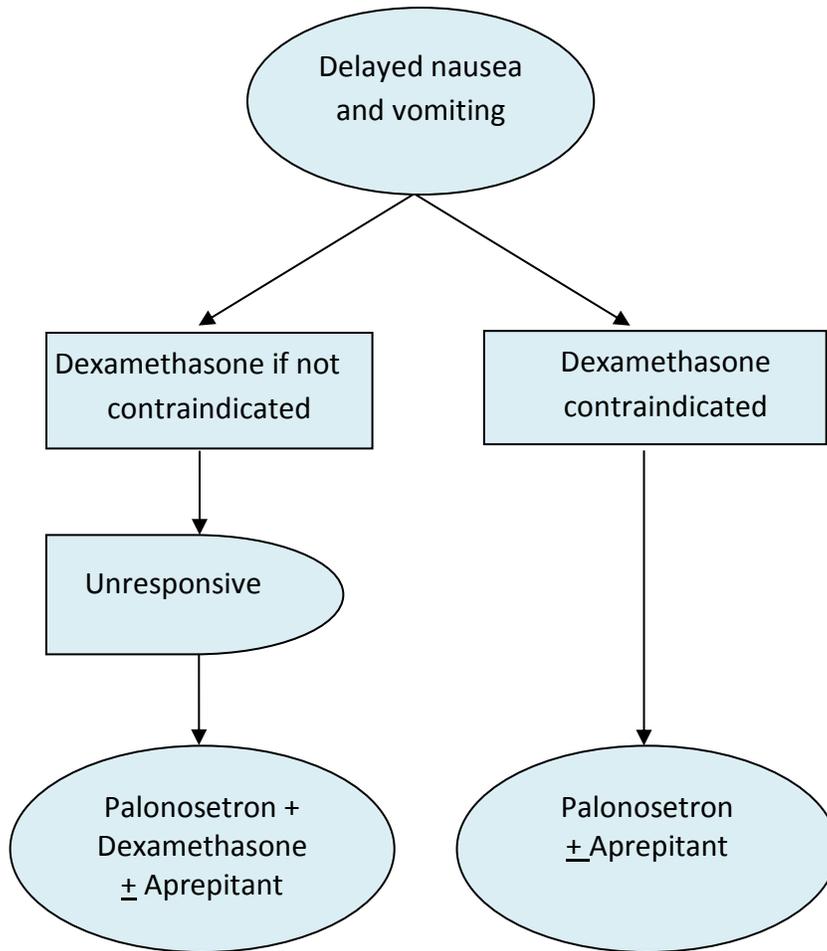
APPENDIX 5: Algorithm 2: Management of Refractory Nausea and Vomiting
 (follow these recommendations if patient fails breakthrough nausea and vomiting management)



Aprepitant	Greater than or equal to 6 months: Pre-chemotherapy Day 1: 3 mg/kg (maximum 125 mg) PO x 1 Day 2 & 3: 2 mg/kg (maximum 80 mg) PO once daily
Granisetron	40 micrograms/kg/dose PO q12hours (maximum 2 mg/dose)
Palonosetron	1 month to less than 17 years: 0.02 mg/kg IV once (maximum: 1.5 mg/dose) pre-chemotherapy. May repeat once in 48 hours for multiday chemotherapy. Greater than or equal to 17 years: 0.25 mg/dose IV or 0.5 mg/dose PO once pre- chemotherapy. May repeat once in 48 hours for multiday chemotherapy

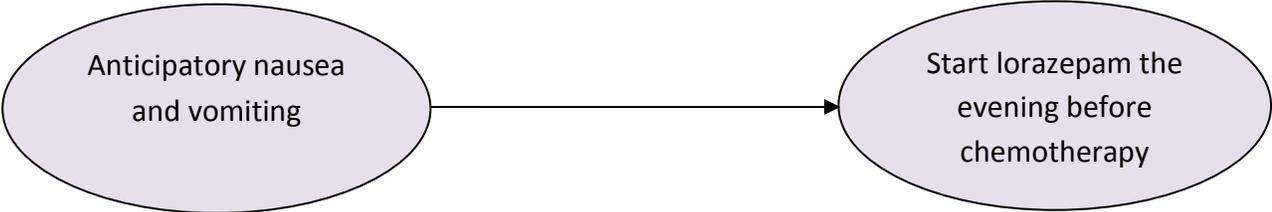


APPENDIX 6: Algorithm 3: Management of Delayed Nausea and Vomiting



Aprepitant	Greater than or equal to 6 months: Pre-chemotherapy Day 1: 3 mg/kg (maximum 125 mg) PO x 1 Day 2 & 3: 2 mg/kg (maximum 80 mg) PO once daily
Dexamethasone	Moderately emetogenic regimen : $\leq 0.6 \text{ m}^2$: 2 mg/dose IV/PO q12hr $> 0.6 \text{ m}^2$: 4 mg/dose IV/PO q12hr If given concurrently with aprepitant, reduce dexamethasone dose by half Highly emetogenic regimen: 6 mg/m ² /dose IV/PO once daily may increase to q 12 h (maximum 20 mg/day) If given concurrently with aprepitant, reduce dexamethasone dose by half
Palonosetron	1 month to less than 17 years: 0.02 mg/kg IV once (maximum: 1.5 mg/dose) pre-chemotherapy. May repeat once in 48 hours for multiday chemotherapy. Greater than or equal to 17 years: 0.25 mg/dose IV or 0.5 mg/dose PO once pre-chemotherapy. May repeat once in 48 hours for multiday chemotherapy

APPENDIX 7: Algorithm 4: Management of Anticipatory Nausea and Vomiting



Lorazepam	0.04-0.08 mg/kg/dose (maximum 2 mg/dose PO/SL/IV first dose night before chemotherapy and repeat a dose morning before chemotherapy and then q8h as needed)
------------------	---

APPENDIX 8: Table 1: Dosing of Antiemetics

	DOSING
Aprepitant	Greater than or equal to 6 months: Day 1: 3 mg/kg (maximum 125 mg) PO x 1 Day 2 & 3: 2 mg/kg (maximum 80 mg) PO once daily
Dexamethasone	Moderately emetogenic regimen : $\leq 0.6 \text{ m}^2$: 2 mg/dose IV/PO q12 hr >0.6m ² : 4 mg/dose IV/PO q12hr. If given concurrently with aprepitant, reduce dexamethasone dose by half Highly emetogenic regimen: 6 mg/m ² /dose IV/PO once daily may increase to q12 h (maximum 20 mg/day) If given concurrently with aprepitant, reduce dexamethasone dose by half
Dimenhydrinate	1 mg/kg (maximum 50 mg/dose) IV/PO q4h as needed for breakthrough nausea and vomiting upfront in all patients. Children less than 1 year should start with 0.5 mg/kg and titrate to effect to minimize paradoxical reactions
Granisetron	40 micrograms/kg/dose PO q12hours (maximum 2 mg/dose)
Lorazepam	0.04-0.08 mg/kg/dose (maximum 2 mg/dose) PO/SL/IV first dose night before chemotherapy and repeat a dose morning before chemotherapy and then q8h as needed
Methotrimeprazine	Infants, Children and Adolescents (oral dosing): 0.25 mg/kg/24hrs in 2 to 3 divided doses; may titrate to effect (maximum dose for children ≤ 12 years: 25 mg/day) Children and Adolescents (IV dosing): (IWK oncology/palliative care service recommendation): 0.0625 mg/kg/24hr (maximum 2 mg/dose) IV over 30 minutes-1 hour if given through a central line q8h –q24hr (monitor for hypotension)
Metoclopramide/Diphenhydramine	Age greater than 1 year: Metoclopramide 1 mg/kg/dose (max 40 mg/dose) Give diphenhydramine 1 mg/kg/dose (max 50 mg/dose) concurrently
Nabilone	≥ 4 years <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 Note: May need to titrate to effect
Olanzapine	0.1 mg/kg/dose (maximum 10 mg/dose) once daily x 3 days Day 1-3 of chemotherapy and reassess Caution in children with psychiatric conditions Only available orally. Round doses based on measurable portions of tablets. (Dosing evidence available in reference 7)
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 OR 0.1 - 0.2 mg/kg/dose (max 8 mg/dose) IV/PO pre-therapy x 1 and up to TID prn
Palonosetron	1 month to less than 17 years: 0.02 mg/kg IV once (maximum: 1.5 mg/dose) pre-chemotherapy. May repeat once in 48 hours for multiday chemotherapy. Greater than or equal to 17 years: 0.25 mg/dose IV or 0.5 mg/dose PO once pre- chemotherapy. May repeat once in 48 hours for multiday chemotherapy
Scopolamine patch	1 patch prior to chemotherapy for children greater than or equal to 18 kg and ½ patch for children less than 18 kg – tape half of the patch do not cut. Reapply a new patch every 72 hours.

APPENDIX 9:

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

	POGO	APPHON	COMMENTS
Dexamethasone	<p>Highly emetogenic regimen: 6 mg/m² /dose IV/PO q6h If given concurrently with aprepitant, reduce dexamethasone dose by half.</p> <p>Weak recommendation Low quality evidence</p>	<p>Highly emetogenic regimen: 6 mg/m²/dose IV/PO once daily may increase to q 12 h (maximum 20 mg/day) If given concurrently with aprepitant, reduce dexamethasone dose by half</p>	<p>Adult guidelines (NCCN, ASCO) recommend the use of dexamethasone as an antiemetic with a daily maximum of 20 mg. Usually given as a 12 mg in the morning and followed by 8mg in the evening for highly emetogenic chemotherapy regimens. Giving higher than adult recommended dose and possibly as high as 50 mg of dexamethasone per day was not felt to be best practice as dexamethasone has many adverse effects and anecdotally the 20 mg maximum has been sufficient with little evidence to suggest that higher doses provide better antiemetic control.</p>
Metoclopramide	<p>1 mg/kg/dose IV pre-therapy x 1 then 0.0375 mg/kg/dose PO q6h</p> <p>Strong recommendation Low quality evidence</p>	<p>Age greater than 1 year 1 mg/kg/dose (max 40 mg/dose) every 4-6 hours</p>	<p>The dose recommended after the pre-therapy dose is considered a low or motility dose and not in accordance with NCCN guidance document and as such not felt supported as best practice.</p>