CCLG Guideline for the Management of Chemotherapy-Induced Nausea and Vomiting (CINV)

November 2023

Adapted and approved for use at Birmingham Children's Hospital, June 2024.

Contents

Executive summary

The CCLG Supportive Care Group have compiled this national framework document based on excellent international guidelines with the aim of providing a comprehensive overview which may be taken to standardise therapy across CCLG Centres for the management of chemotherapy induced nausea and vomiting.

Introduction

Chemotherapy-induced nausea and vomiting (CINV) are said to be the most documented distressing side- effects of childhood cancer treatment, potentially influencing adherence with future treatments if not managed appropriately (Priya et al. 2022; Wood et al. 2015). Managed incorrectly, they can lead to physical problems such as anorexia, malnutrition and dehydration, plus psychological complications that in turn may lead to anticipatory nausea and vomiting (Rodgers et al. 2012; Dewan, Singhal and Harit, 2010).

Nausea and vomiting are reflexes initiated by the body to expel toxic substances from the stomach and intestine (Navari, 2013). Emesis is coordinated by the vomiting centre situated in the medulla which receives input from the chemoreceptor trigger zone (CTZ), found in the area postrema. It is outside of the blood-brain barrier and is simulated by circulating toxins or drugs such as chemotherapy. The CTZ possesses many $5HT_3$ receptors, NK1 receptors and Dopamine receptors (D2). The vomiting centre is stimulated by drugs, smells, sights, emotions etc. as well as Gastrointestinal (G.I) input. CINV may result from chemotherapy or Cerebrospinal Fluid (CSF) acting directly on the CTZ, in the vomiting centre, but chemotherapy may also induce the release of serotonin and substance P from cells within the gastric mucosa.

There are different stages of CINV described: acute (0-24hrs after 1st dose); delayed (24hrs-5 days post last dose of chemotherapy) and anticipatory (prior to the start of chemotherapy). Physiological differences exist in acute and delayed CINV. Acute is mediated by the neurotransmitter serotonin, whereas delayed is mediated by substance P. Therefore, optimal management of CINV may require targeting the peripheral pathways with a $5HT_3$ receptor antagonist and the central pathway with an NK1 receptor.

The provision of adequate preventative and responsive anti-nausea and vomiting therapies is key in all centres where children and treated with chemotherapy. The different centres have traditionally used their own ‘in-house’ guidelines, rarely developed according to the recommendations of the NICE Guideline Methodology (https://www.nice.org.uk/process/pmg20/chapter/introduction). An international collaboration, centred in the Canadian Pediatric Oncology Group of Ontario (POGO), developed a series of detailed evidence-based guidelines for the management of different phases of treatment-related nausea and vomiting. This document details the recommendations and explanatory notes where necessary, to explain different decisions from the Canadian-led panel. The research and main linking explanations are found in the accompanying guideline documents.

Methods

This guideline is a national framework document for local implementation. It relies on the work undertaken by the Canadian-led POGO group who developed clinical practice guidelines for the prevention and management of chemotherapy-induced nausea and vomiting (CINV) in children, as well as breakthrough and refractory.

The POGO group convened an international guideline panel to create a clinical practice guideline (CPG) based on accepted best-practice methods (similar to those used by NICE). The group undertook a series of focused systematic reviews addressing management questions in the prevention of CINV, and the treatment of breakthrough, refractory and anticipatory CINV. This evidence was summarised and debated, placing it in clinical context and resulted in a series of

recommendations. These guidelines were subject to international stakeholder review before publication and have been updated since first publication.

All phases of the management have now been completed and the CCLG Supportive Care Group has undertaken to summarise and contextualise in a UK framework, to provide an up-to-date resource to inform CCLG centre guidelines. This involved the summarising of the guidelines, discussion of the recommendations made within a UK licensing context and providing a summary guide as an example for use. Recommendations have been circulated via the CCLG Guideline Development Group panel and feedback incorporated.

The CCLG Supportive Care Group noted that each centre may have subtle variations on their interpretation of the evidence, some driven by local commissioning or drug procurement processes, which make cost-effectiveness decisions different and the local guideline marginally different. The CCLG Supportive Care Group were also vey mindful of the necessarily poor quality of evidence that underlies the banding of drugs into emetogenic potential. Such data in children are drawn from small studies, often confounded by expectation and prophylactic antiemetics. As such, CCLG centre variations may occur. Centres with experience and disagreement with a classification system (such as the POGO system) are encouraged to publish their experience to support the advancement of the knowledgebase and increase the potential for nationally agreed guidance.

Please note that where palonosetron, olanzapine or fosaprepitant are recommended, these drugs may need individual Trust Drugs and Therapeutic Committee (DTC) and funding stream approval. Alternative agents that have already been approved, can be used.

CCLG group

The adaptation group consisted of: Mrs. Eloise Neumann, Mr. Pritesh Patel, Mrs. Ghazala Javid, Professor Faith Gibson, Dr Jessica Bate, Dr Geoff Shenton, Dr Hugh Bishop and Dr Bob Phillips.

Recommendations: Over-riding principles

Children and Young People about to undertake chemotherapy should have their chemotherapy assessed for emetogenicity

Balancing the use of antiemetic against the chance of chemotherapy causing problems is a key principle. A number of systems have been proposed; for this guideline, the POGO-developed system will be used. It divides chemotherapy into four strata:

- Highly emetogenic chemotherapy (HEC) **including** very highly emetogenic chemotherapy (VHEC)
- Moderately emetogenic chemotherapy (MEC)
- Low emetogenicity chemotherapy (LEC)
- Minimal emetogenicity

Children and Young People should have their symptoms of nausea and vomiting assessed.

There are a range of assessment tools for nausea and vomiting (see 'References'). These guidelines strongly advise using them within practice in order to improve patient care. No clear data supports the use of any one system over another, and with varied age ranges, two scales may be preferred.

Children and Young People about to undertake chemotherapy, should have their emetogenicity-assessed treatment prescribed prior to chemotherapy, and adapted to their own personal experience.

While the evidence underpinning 'personalisation' of therapy is weak, it is common practice to use higher-level antiemetic's when a child or young person has experienced problems with nausea and/or vomiting previously. Good control is felt to reduce the chances of anticipatory, and breakthrough/refractory, nausea and vomiting in subsequent courses of chemotherapy.

Prophylaxis: Very highly <u>AND</u> highly emetogenic chemotherapy

A combination of ondansetron, dexamethasone and aprepitant should be prescribed, unless there is a contraindication.

Contraindications include:

- Age < 6 months or less than 6kg (aprepitant, see Table 4)
- Contraindication to dexamethasone (e.g. steroids included in treatment protocol). Refer to Table 4.
- Drug interaction with aprepitant. Refer to Table 4.

Where aprepitant is contraindicated, use:

- **5HT3 antagonist (preferentially palonosetron) and dexamethasone unless there is a contraindication.**

Contraindications include:

- Contraindication to dexamethasone (e.g. steroids included in treatment protocol or brain tumour diagnosis)

Where aprepitant and dexamethasone are contraindicated, use:
- **Palonosetron (Or ondansetron if palonosetron not available)**
- **Olanzapine or levomepromazine**
- **Consider adding nabilone in for adolescents**

Prophylaxis: Moderately emetogenic chemotherapy

A combination of ondansetron (or other 5HT3RA) and dexamethasone should be prescribed unless there is a contraindication.

Contraindications include:

- Contraindication to dexamethasone (e.g. steroids included in treatment protocol). See Table 4.

Where there is a contraindication to dexamethasone, use:
- **Palonosetron if available, or ondansetron**
- **Aprepitant (unless there is a contraindication)**

Contraindications include:

- Age < 6 months
- Drug interaction with aprepitant, see Table 4.

Where aprepitant and dexamethasone are contraindicated, use:
- **Palonosetron if available, or ondansetron**
- **Olanzapine or levomepromazine**
- **Consider adding nabilone in for adolescents**

Prophylaxis: Low emetogenic chemotherapy

For Children and Young People receiving low emetogenic chemotherapy, use ondansetron or another 5HT3 antagonist.

Prophylaxis: Minimally emetogenic chemotherapy

For Children and Young People receiving minimally emetogenic chemotherapy, no routine prophylaxis should be prescribed.

Breakthrough nausea or vomiting

Breakthrough refers to the reoccurrence of significant nausea or vomiting after a period of acceptable control. Should a child or young person experience this, a ‘next level up’ approach to prophylaxis should be strongly considered on subsequent cycles.

For Children and Young People receiving highly or very highly emetogenic chemotherapy, switching ondansetron to palonosetron (if not already prescribed), should be considered.

Addition of any of the below options should also be considered:

- **Olanzapine or levomepromazine, or**
- **Aprepitant, or**
- **Dexamethasone, or**
- **Lorazepam (See Table 3 below)**

Refractory nausea or vomiting

Refractory refers to the continuation of significant nausea or vomiting without a period of acceptable control. Should a child or young person experience this, a 'next level up' approach to prophylaxis should be strongly considered on subsequent cycles.

For Children and Young People receiving moderate, low or minimal emetogenic chemotherapy, escalation of treatment to the next highest level of intensity should be undertaken.

For Children and Young People receiving highly emetogenic chemotherapy, switch ondansetron to palonosetron, if not already prescribed, or consider granisetron.

For Children and Young People receiving highly emetogenic chemotherapy, who have previously been considered to have a contraindication to aprepitant, re-visiting that decision is strongly recommended.

For Children and Young People who continue to suffer refractory nausea and/or vomiting, addition of

- **Olanzapine, levomepromazine or metoclopramide, or**
- **Levomepromazine infusion instead of bolus injection, or**
- **Lorazepam, or**
- **Acupressure should be considered.**

Other alternative agents and approaches have been used. For example, hyoscine patches can be used for subsequent courses for refractory emesis failing to respond to other rescue therapy, applied the night before chemotherapy is due (at least 12 hours prior to chemotherapy). Hypnotherapy and distraction techniques are frequently employed. Others may use nabilone for refractory CINV for adolescents. Please note that data surrounding these interventions is sparse.

It is worth noting that refractory nausea and vomiting may not always be directly related to CINV so please consider other causes or alternative reasons at this point. A focus on non-pharmacological interventions may be useful. The evidence surrounding anti-emetics for breakthrough CINV is poor and further research is recommended.

Anticipatory nausea or vomiting

Anticipatory refers to significant nausea or vomiting prior to the delivery of chemotherapy. Research in this area is particularly weak.

For Children and Young People who develop anticipatory nausea and/or vomiting, psychological interventions such as hypnosis or systematic desensitization may be offered.

For Children and Young People who develop anticipatory nausea and/or vomiting, low dose lorazepam (Table 4), may be prescribed the day before, and from the first day of chemotherapy.

Delayed nausea & vomiting

The above regimens are intended to prevent both acute and delayed nausea and vomiting. 5HT3 antagonists are **not** recommended in the delayed phase and therefore should be stopped and not re-started. Agents to consider using include:

- Aprepitant (or Fosaprepitant)
- Dexamethasone
- Olanzapine/levomepromazine

Discharge medication:

Please note that the current CPG's from POGO do not routinely recommend 'as needed' anti-emetics therefore careful education and consideration should be given before discharging patients home with anti-emetics. However, ensuring patients are discharged home with a supply of anti-emetics to continue up to, but not beyond, the end of the delayed phase of CINV, is worth considering. **These should not routinely include ondansetron.**

Source guidelines

POGO Guidelines for the management of chemotherapy induced nausea and vomiting.
Chemotherapy-Induced Nausea and Vomiting - POGO

References to tools:

Baxter, A., Watcha, M., Baxter, W., Leong, T. and Wyatt, M. (2011) Development and Validation of a Pictorial Nausea Rating Scale for Children. Pediatrics, 127(6), pp.1542–1549.
Dupuis, L.L., Taddio, A., Kerr, E., Kelly, A. and MacKeigan, L. (2006) Development and Validation of the Pediatric Nausea Assessment Tool for Use in Children Receiving Antineoplastic Agents. Pharmacotherapy, 26(9), pp.1221-1231.

Patel, P., Robinson, P., Wahib, N., Cheung, T., Cabral, S., Parker, A.,Cohen, M., Devine, K., Gibson, P., Holdsworth, M.T., Neumann, E., Orsey, A., Phillips, R., Spinelli, D., Thackray; J., van de Wetering, M., Woods, D., Sung, L. and Dupuis, L.L (2022) Interventions for the prevention of acute phase chemotherapy-induced nausea and vomiting in pediatric patients: a systematic review and meta-analysis. Supportive Care in Cancer, 30, pp. 8855–8869.

Patel, P., Robinson, P., Cohen, M., Devine, K., Gibson, P., Holdsworth, M.T., Neumann, E., Orsey, A., Phillips, R., Spinelli, D., Thackray, J., van de Wetering, M., Woods, D., Cabral, S., Sung, L. and Dupuis, L.L. (2022) Prevention of acute and delayed chemotherapy-induced nausea and vomiting in pediatric cancer patients: A clinical practice guideline. Pediatric Blood and Cancer, 69(12).

Patel, P., Robinson, P., Phillips, R., Baggott, C., Devine, K., Gibson, P., Guilcher, G., Holdsworth, M.T., Neumann, E., Orsey, A., Spinelli, D., Thackray, J., van de Wetering, M., Cabral, S., Sung, L. and Dupuis, L.L. Treatment of breakthrough and prevention of refractory chemotherapy-induced

nausea and vomiting in pediatric cancer patients: Clinical practice guideline update. Pediatric Blood and Cancer, 70(8).

Rhodes, V. and McDaniel, R. (1999) The Index of Nausea, Vomiting, and Retching: A New Format of the Index of Nausea and Vomiting. Oncology Nursing Forum, 26(5), pp.889-894.

Wood, J.M., Chapman, K. and Eilers, J.(2011) Tools for Assessing Nausea, Vomiting, and Retching. Cancer Nursing, 34(1), E14-E24.

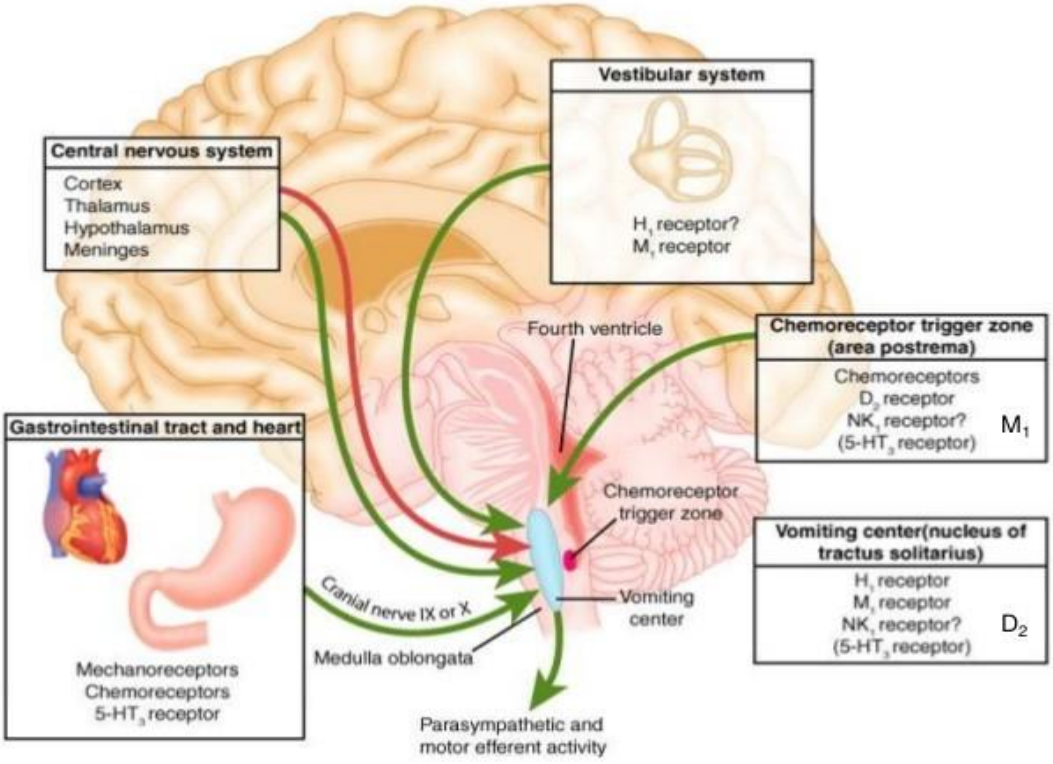
Other references:

Dewan, P., Singhal, S. and Harit, D. (2010) Management of Chemotherapy-Induced Nausea and Vomiting. Indian Pediatrics, 47, pp. 149-155.

Kraukauer , E.L., Zhu, A.X., Bounds, B.C., Sahani, D., McDonald, K.R., and Brachfel, E. (2005) Case 6-2005: A 58- Year Old Man with Esophageal Cancer and Nausea and Vomiting and Intractable Hiccups. New England Journal of Medicine, 352(8), pp.817-825.
Navari, R. (2013) Management of Chemotherapy-Induced Nausea and Vomiting: Focus on Newer Agents and New Uses for Older Agents. Drugs, 73, pp.249-262.

Rodgers, C., Norville, R., Taylor, O., Poon, C., Hesselgrave, J., Gregurich, M. and Hockenberry, M. (2012) Children's Coping Strategies for Chemotherapy-Induced Nausea and Vomiting. Oncology Nursing Forum, 39(2), pp.202-209.
Wood, M., Hall, L., Hockenberry, M. and Borinstein, S. (2015) Improving Adherence to Evidence-Based Guidelines for Chemotherapy-Induced Nausea and Vomiting. Journal of Pediatric Oncology Nursing, 32(4), pp.195 –20.

Figure 1. Site of actions of anti-emetics



Krakauer et al. (2005). New England Journal of Medicine, 352, 817.

Table 1. Site of actions of anti-emetics

	Dopamine2-receptor antagonist (D2)	Histamine1-receptor antagonist (H1)	Acetylcholine receptor antagonist	5-hydroxytryptamine receptor3-receptor antagonist	5-hydroxytryptamine receptor2-receptor antagonist	5-hydroxytryptamine receptor4-receptor agonist	NK1 inhibitor (NK1)
Aprepitant/ Fosaprepitant							+++
Cyclizine		++	++				
Hyoscine hydrobromide			+++				
Levomepromazine	++	+++	++		+++		
Metoclopramide	++			+		++	
Ondansetron/ Palonosetron				+++			
Olanzapine	++ (Also, D1 & D4)	+++	+++	+	+++		

Table 2. Overall approach flow-chart

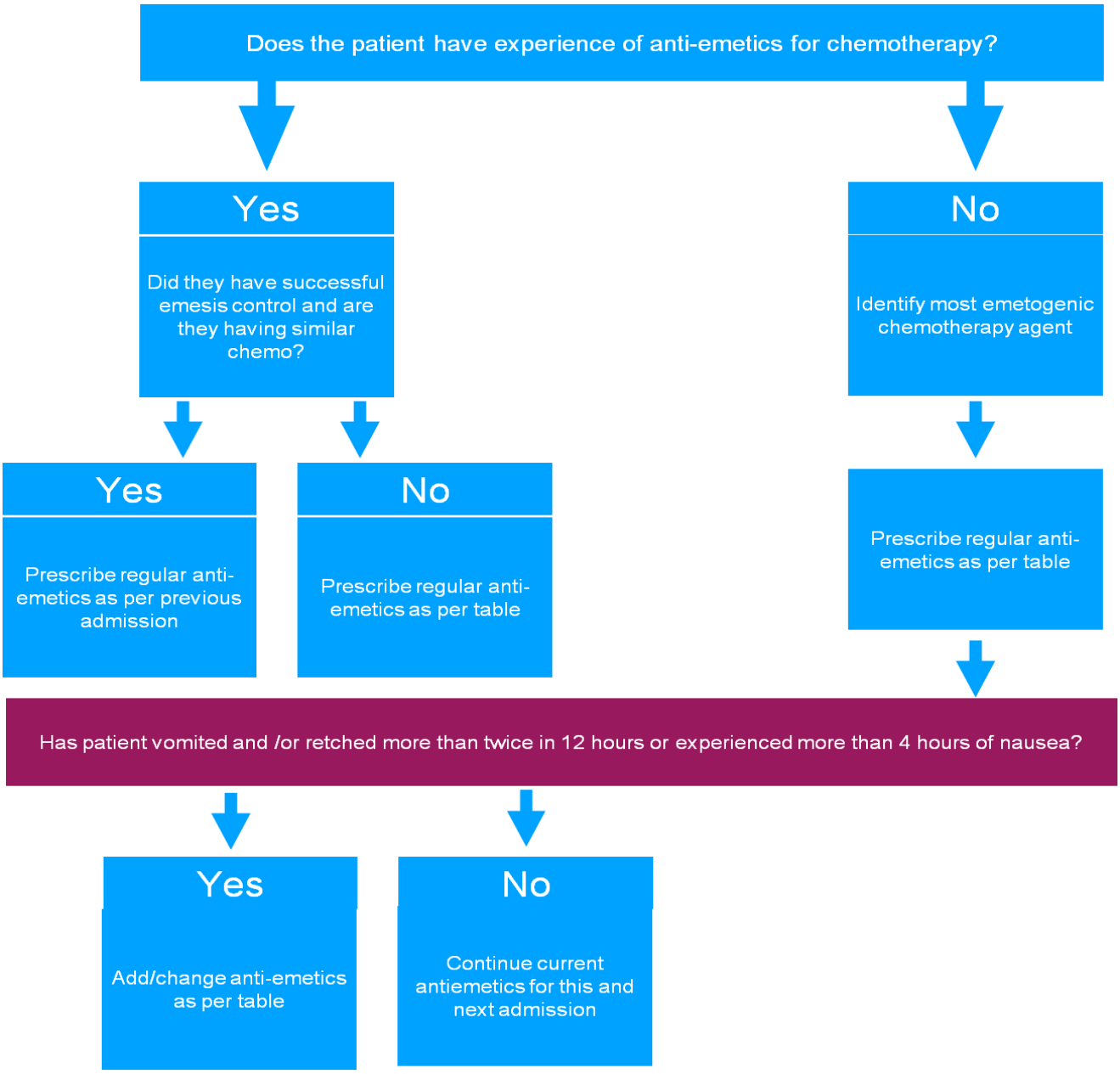
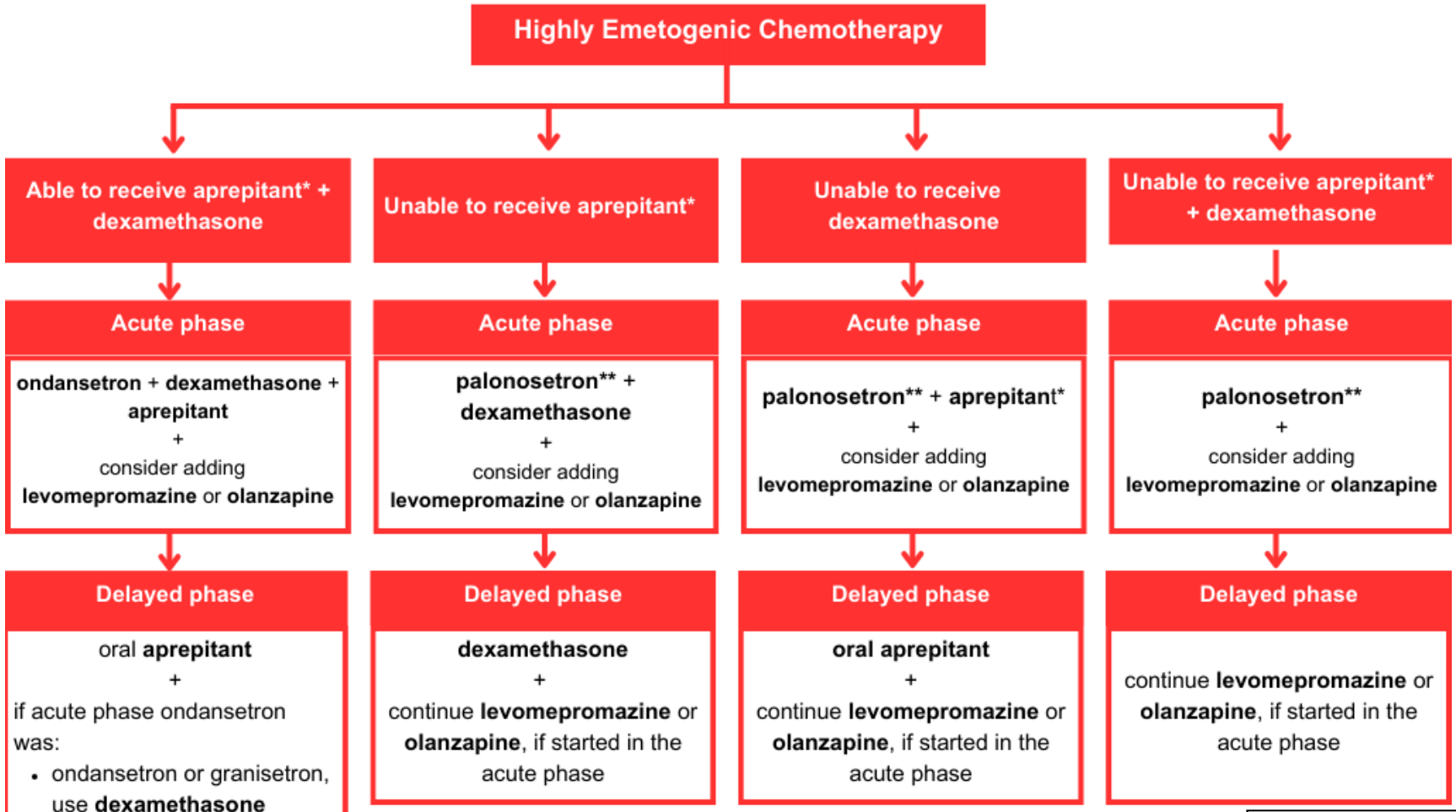


Table 3. Emetogenicity of chemotherapy (examples)

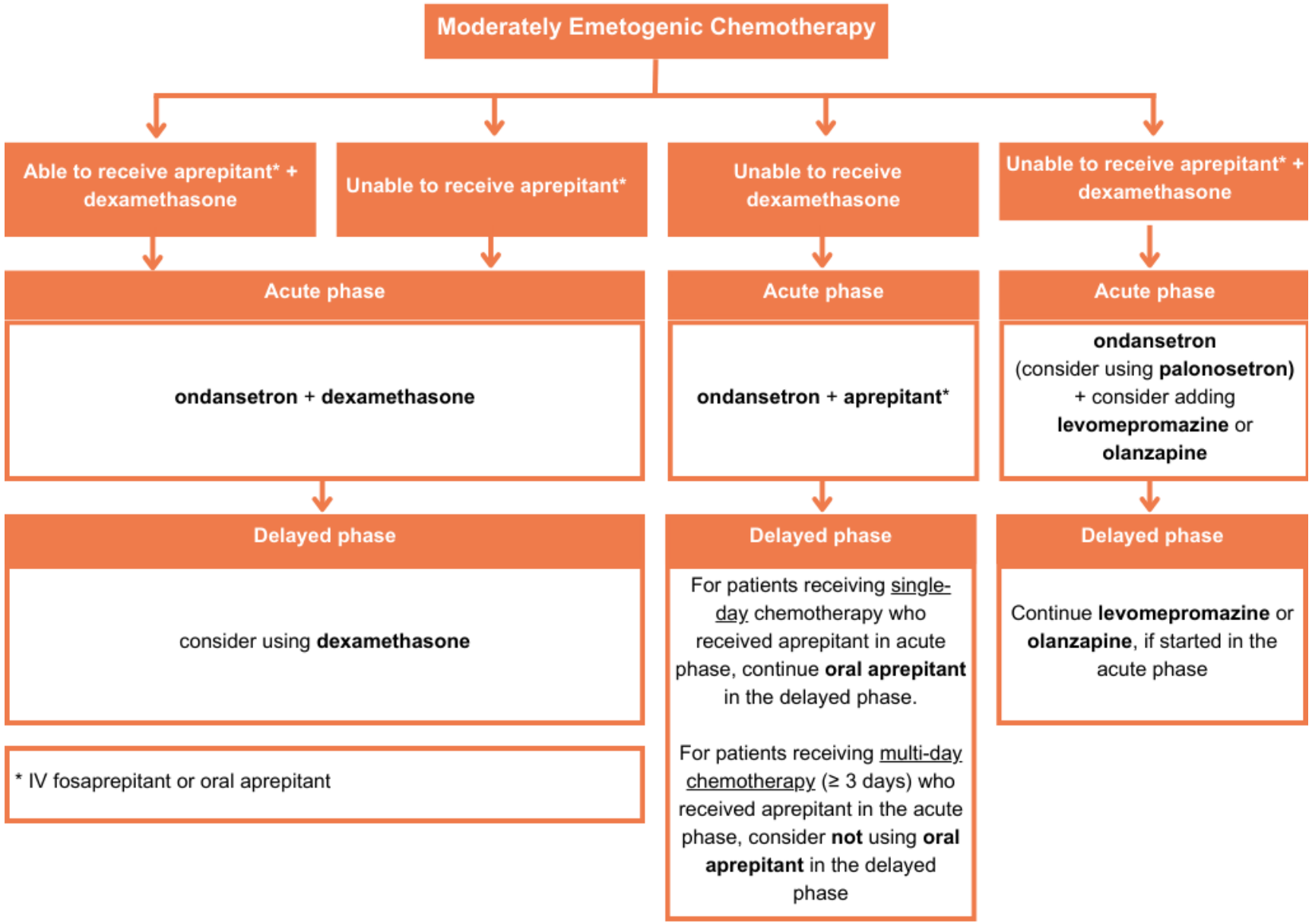
Very High emetogenic potential (>90%)	
• Cisplatin • Cyclophosphamide > 2g/m2 • Ifosfamide • Melphalan (IV) Combination chemotherapies: • Cyclophosphamide + anthracycline • Cyclophosphamide + etoposide • Etoposide + Ifosfamide • Doxorubicin + Ifosfamide • Cytarabine 300 mg/m2 + etoposide • Doxorubicin + methotrexate 5g/m2	
High emetogenic potential (>90%)	
• Dactinomycin • Carboplatin • Carmustine >250mg/m2 • Cyclophosphamide 1.5g/m2 - 2g/m2 • Cytarabine > 3g/m2/dose • Dacarbazine • Methotrexate ≥12 g/m2	
Moderate emetogenic potential (30%-90%)	
• Arsenic trioxide • Azacitidine • Clofarabine • Cyclophosphamide > 1500mg/m2 • Cytarabine 1g/m2 -3g/m2 • Daunorubicin • Doxorubicin • Epirubicin • Idarubicin 75mg/m2 • Imatinib	• Inotuzumab • Irinotecan • Lomustine • Methotrexate > 5g/m2 to <12g/m2 • Midostaurin (PO) • Oxaliplatin< 1g/m2 • Procarbazine • Temozolomide • Thiotepa • Trabectedin • Treosulfan
Low emetogenic potential (<30%)	
• Amsacrine • ATG • Bortezomib • Blinatumomab • Brentuximab • Capecitabine • Chlorambucil • CH14.18 Antibodies • Cyclophosphamide <300 mg/m2 • Cytarabine <1g/m2	• Methotrexate >1g/m2 to <5g/m2 • Methotrexate oral • Melphalan (oral) • Mitoxantrone• • Mitomycin • Nilotinib • Nelarabine • Paclitaxel • Ponatinib • Regorafenib

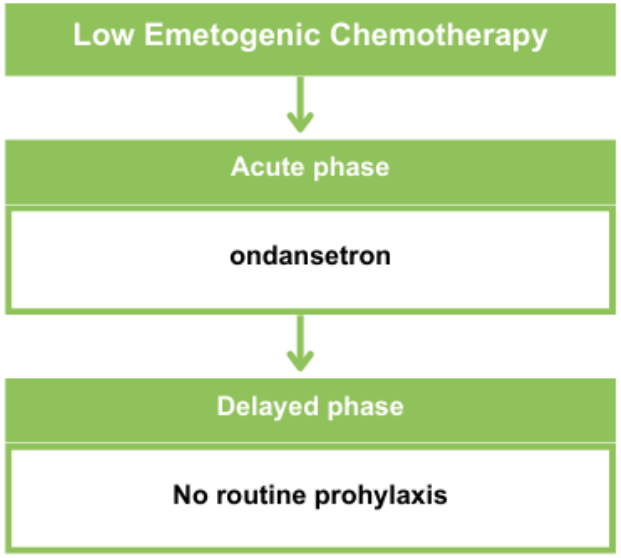
• Dasatinib • Dinutuximab • Docetaxel • Etoposide (IV and PO) • Everolimus • 5-fluorouracil • Gemcitabine • Gemtuzumab • Hydroxyurea • Intrathecals	• Ruxolitinib • Sorafenib • Sunitinib • Temsirolimus • Thalidomide • Topotecan • Venetoclax • Vinblastine • Vindesine • Vinorelbine
Minimal emetogenic potential (min) <10%	
• Alemtuzumab • Asparginase • Bevacizumab • Bleomycin • Busulfan • Cladribine • Dabrafenib • Fludarabine • Lenalidomide • Methotrexate < 1g/m2 • Mercaptopurine • Nivolumab • Rituximab • Thalidomide • Thioguanine • Vincristine	
Anticipatory nausea and vomiting	
Anticipatory refers to significant nausea or vomiting prior to the delivery of chemotherapy	**Lorazepam oral:** Give one dose evening before and one dose 1 hour before starting chemotherapy



* fosaprepitant may be used if oral aprepitant cannot be tolerated
** palonosetron is the preferred 5HT3RA for use in the acute phase for patients at high risk of delayed CINV, but ondansetron can be used if palonosetron is not available in your Trust.

NB: Patients < or = 16kg should all receive Palonosetron as their 5HT3 antagonist. Please round doses down to 1 vial of 250 micrograms. Patients unable to receive Dex/Aprep should receive Palonosetron regardless of weight.


Moderately Emetogenic Chemotherapy
Able to receive aprepitant* + dexamethasone
Unable to receive aprepitant*
Unable to receive dexamethasone
Unable to receive aprepitant* + dexamethasone
Acute phase
ondansetron + dexamethasone
Acute phase
ondansetron + aprepitant*
Acute phase
ondansetron (consider using palonosetron) + consider adding levomepromazine or olanzapine
Delayed phase
consider using dexamethasone
Delayed phase
For patients receiving single-day chemotherapy who received aprepitant in acute phase, continue oral aprepitant in the delayed phase.
For patients receiving multi-day chemotherapy (≥ 3 days) who received aprepitant in the acute phase, consider not using oral aprepitant in the delayed phase
Delayed phase
Continue levomepromazine or olanzapine, if started in the acute phase
* IV fosaprepitant or oral aprepitant


Low Emetogenic Chemotherapy
Acute phase
ondansetron
Delayed phase
No routine prohylaxis

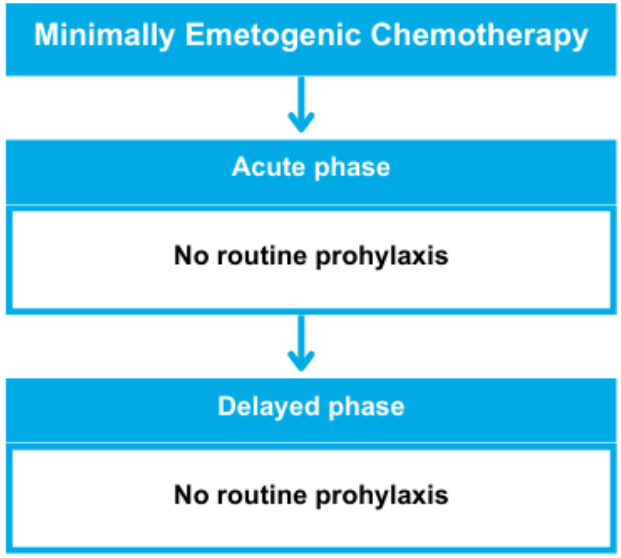

Minimally Emetogenic Chemotherapy
Acute phase
No routine prohylaxis
Delayed phase
No routine prohylaxis

Table 4. Anti-emetics recommended dosages and usage instructions (alphabetical)

<table>
<tr><th>Drug</th><th>Dose</th><th>Side Effects</th><th>Comments</th></tr>
<tr>
<td>Aprepitant
Drug class:
NK1 receptor antagonist

Formulations:
125mg, 80mg capsule
Contents of capsules can be dispersed in water. Recommended volume: For doses <80mg: Dissolve each capsule in 3.2mL of water.

125mg powder for oral suspension (to give a 25mg/ml suspension)
After reconstitution: The oral suspension can be kept at room temperature (not above 30°C) for up to 3 hours. It can also be stored refrigerated (between 2°C and 8°C) for up to 72 hours.

Indication:
Treat and prevent acute and delayed CINV</td>
<td>Administered orally 1 hour prior to chemotherapy on Days 1, 2 and 3. If no chemotherapy is given on Days 2 and 3, administer in the morning

<table>
<tr><th>Day 1</th><th>Day 2</th><th>Day 3</th></tr>
<tr><td>3 mg/kg orally
Maximum dose 125 mg</td><td>2 mg/kg orally
Maximum dose 80mg</td><td>2 mg/kg orally
Maximum dose 80mg</td></tr>
</table>
Continue beyond day 3 for longer courses of chemotherapy.

Suggested dose bands for ease of administration
<table>
<tr><th>Weight</th><th>Day 1</th><th>Day 2</th><th>Day 3</th></tr>
<tr><td><6kg</td><td colspan="3">Not recommended</td></tr>
<tr><td>6kg–7.9kg</td><td>20mg</td><td>10mg</td><td>10mg</td></tr>
<tr><td>8kg–11.9kg</td><td>30mg</td><td>20mg</td><td>20mg</td></tr>
<tr><td>12kg–14.9kg</td><td>40mg</td><td>25mg</td><td>25mg</td></tr>
<tr><td>15kg–17.9kg</td><td>50mg</td><td>35mg</td><td>35mg</td></tr>
<tr><td>18kg–22.9kg</td><td>60mg</td><td>45mg</td><td>45mg</td></tr>
<tr><td>23kg–29.9kg</td><td>80mg</td><td>55mg</td><td>55mg</td></tr>
<tr><td>30kg–36.9kg</td><td>100mg</td><td>70mg</td><td>70mg</td></tr>
<tr><td>37 kg and above</td><td>125mg</td><td>80mg</td><td>80mg</td></tr>
</table>
Consider extending duration of therapy, for up to 48 hours post chemotherapy in the event of refractory or delayed nausea and vomiting in previous cycle.</td>
<td>Diarrhoea, hiccups, headache, decreased appetite, cough, neutropenia (slightly prolonged compared to without aprepitant).</td>
<td>NB: Can increase Ifosfamide mediated neurotoxicity and Irinotecan toxicity. Monitor closely.
Caution in patients receiving concomitant substances that are metabolised primarily through CYP3A4 and with a narrow therapeutic range. Also, p450 2c9 inducer.

Always check for drug interactions – of note azole antifungals and immunosuppressants

Dose of dexamethasone must be halved.</td>
</tr>
<tr>
<td>Cyclizine
Drug class:
Antihistamine

Formulations:
IV injection
50mg tablets
Tablets can be crushed and dispersed in a small amount of water and a proportion given.

Indication:
For the purpose of this guideline, used for emesis of raised intracranial pressure,</td>
<td>IV/Oral:
<table>
<tr><th>Age</th><th>Oral/IV</th></tr>
<tr><td>1 month–5 years</td><td>0.5-1mg/kg up to 3 times daily (Max 25mg/dose)
Prescribe to the nearest 5mg.</td></tr>
<tr><td>6–11 years</td><td>25mg up to 3 times daily</td></tr>
<tr><td>12 years+</td><td>50 mg up to 3 times daily</td></tr>
</table>
Continuous IV or SC Infusion:
<table>
<tr><th>Age</th><th>IV continuous infusion</th></tr>
<tr><td>1–23 months</td><td>3mg/kg over 24 hours</td></tr>
<tr><td>2–5 years</td><td>50mg over 24 hours</td></tr>
<tr><td>6–11 years</td><td>75mg over 24 hours</td></tr>
<tr><td>12–17 years</td><td>150mg over 24 hours</td></tr>
</table></td>
<td>Drowsiness, Dry mouth
Blurred vision
Urinary retention
Restlessness
Insomnia,
Tachycardia</td>
<td>Avoid using with Hyoscine and Levomepromazine

For continuous IV or SC infusion – dilute with Glucose 5% or water for injection. Precipitation may occur if sodium chloride 0.9% is used.</td>
</tr>
</table>

<table>
<tr>
<td>palliative care, irradiation sickness and opiate induced vomiting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexamethasone
Drug class:
Corticosteroid

Formulations:
2mg tablets
0.5mg tablets
2mg/5mL liquid
IV injection

Indication:
Treat and prevent acute and delayed CINV</td>
<td>IV/Oral:
<table><tr><th>SA m²</th><th>IV/Oral Dose</th></tr><tr><td>≤ 0.6m²</td><td>2mg TWICE a day</td></tr><tr><td>> 0.6m²</td><td>4mg TWICE a day</td></tr></table>
Prescribe <u>TWICE</u> daily doses early morning and afternoon to reduce insomnia (e.g. 5am and 4pm) for maximum of 5 days. Give orally where possible.

Doses can be increased to 2.5mg-5mg/m2 up to THREE times a day</td>
<td>Adrenal suppression
Gastric irritation
Osteoporosis
Weight gain, insomnia</td>
<td>Dose of dexamethasone must be halved when used in combination with Aprepitant.

Contra-indicated:
Brain tumour patients and those already on & those on mifamurtide. Caution in osteosarcoma patients (discuss with the consultant).</td>
</tr>
<tr>
<td>Fosaprepitant
Drug class:
NK1 receptor antagonist

Formulations:
150mg powder for solution for infusion

Indication:
Treat and prevent acute and delayed CINV</td>
<td>Intravenous infusion:
<table><tr><th>Weight</th><th>Day 1</th><th>Day 2</th><th>Day 3</th></tr><tr><td><6kg</td><td colspan="3">Not recommended</td></tr><tr><td>>6kg and >6 months to <12 years</td><td>3mg/kg once a day (max. 115mg)</td><td colspan="2">2mg/kg once a day (max. 80mg)</td></tr><tr><td>=>12 years</td><td>115mg</td><td colspan="2">80mg</td></tr></table>
Not currently available at BCH.</td>
<td>Diarrhoea, hiccups, headache, decreased appetite, fatigue, raised ALT</td>
<td>NB: Can increase Ifosfamide mediated neurotoxicity and Irinotecan toxicity. Monitor closely.

Caution in patients receiving concomitant medication metabolised primarily via CYP3A4. Fosaprepitant is a known inhibitor of CYP3A4.

Dose of dexamethasone must be halved</td>
</tr>
</table>

Granisetron

Drug class:
5HT$_3$ antagonist

Formulations:
3.1mg/24 hours transdermal patch
1mg/ml injection
1mg tablet

Indication:
Treat and prevent acute and delayed CINV

Transdermal Patch:

Age	Dose
>=12 years	**Apply 3.1 mg/24 hours, apply patch to clean, dry, non-irritated, non-hairy skin on upper arm (or abdomen if upper arm cannot be used) 24–48 hours before treatment, patch may be worn for up to 7 days**

Oral:

Age	Dose
>=12 years	**1–2 mg, to be taken within 1 hour before start of treatment, then 2 mg daily in 1–2 divided doses for up to 1 week following chemotherapy**

IV:

Age	Dose
2–17 years	**10–40 micrograms/kg (max. per dose 3 mg), repeated if necessary, to be given before start of chemotherapy, for treatment, dose may be repeated within 24 hours if necessary, not less than 10 minutes after initial dose; maximum 2 doses per day.**

Side effects:
Constipation, headache, rash.

Transient increase in liver enzymes.

Not licensed in children. Only consider for nausea and vomiting induced by cytotoxic chemotherapy for planned duration of 3–5 days where oral antiemetics cannot be used.

Not currently available at BCH.

Hyoscine Hydrobromide

Drug class:
Anticholinergic/ Antimuscarinic

Formulations:
Topical Patch 1mg/72 hrs

Indication:
refractory CINV

Topically:
Will take up to 6 hours to work

Age	Dose
1 month – 2 years	**1/4 of a patch every 72 hours**
3 – 9 years	**1/2 of a patch every 72 hours**
10 years+	**1 patch every 72 hours**

Drowsiness
Dry mouth
Dizziness
Blurred vision
Difficulty with micturition

Avoid using with Cyclizine and Levomepromazine

Apply to a clean, dry, hairless area of skin behind the ear, avoiding any cuts or irritation. Wash hands after applying and the skin area after removal.
Scopaderm® patches can be cut

Levomepromazine

Drug class:
Phenothiazine

Formulations:
3mg tablet,
(tablets may be halved and dispersed)
IV Injection

Indication:
Delayed emesis, refractory and breakthrough CINV

Oral

Age	Dose
1 month – 11 years	**50-100 micrograms/kg once or twice a day.** Dose may be increased as necessary and as tolerated. Max 1mg/kg/dose once or twice a day (max 25mg/dose)
12-17 years	**3-6 mg once or twice a day.** Dose may be increased as necessary and as tolerated. Max 25 mg twice daily.
Dose rounding Important as no liquid formulation available	**Dose doses less than 3mg** – Prescribe to the nearest 0.5mg. Disperse one 3mg tablet in 5mL of water and give proportion. **Doses greater than 3mg** – round to nearest 3mg

Slow IV Infusion:

Somnolence
Asthenia
Dry mouth
Hypotension

Avoid using with Cyclizine and Hyoscine, Use with caution with metoclopramide

Avoid use in hepatic impairment.
Reduce dose in renal impairment.

Care in patients receiving ifosfamide since sedation may mask signs of encephalopathy.

<table>
<tr>
<td>Useful in vomiting due to raised intracranial pressure</td>
<td>
<table>
<tr><th>Dose</th></tr>
<tr><td>50-100 micrograms/kg TWICE daily</td></tr>
</table>
Continuous IV or SC Infusion:
<table>
<tr><th>Age</th><th>Dose</th></tr>
<tr><td>1 month – 11 years</td><td>100micrograms/kg/24 hours increasing as necessary to
a max of 0.4mg/kg/24 hours. Maximum 25mg/24 hours</td></tr>
<tr><td>12-17 years</td><td>5mg/24 hours increasing as necessary to
a max of 25mg/24 hours</td></tr>
</table>
</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorazepam
Drug class:
Benzodiazepine

Formulations:
1mg, 2mg tablets (tablets may be halved and dispersed), IV Injection

Indication:
Anticipatory nausea and vomiting. Breakthrough and refractory CINV.</td>
<td>Slow IV bolus/Oral:
<table>
<tr><th>Dose</th></tr>
<tr><td>50-100 micrograms/kg (max 4mg) every 8–12 hours</td></tr>
</table>
For anticipatory nausea and vomiting, give one dose evening before and one dose 1 hour before starting chemotherapy.</td>
<td>Drowsiness
Amnesia
Confusion and ataxia
Pain with IV injection</td>
<td>Care in patients receiving ifosfamide since sedation may mask signs of encephalopathy</td>
</tr>
</table>

<table>
<tr>
<td>Metoclopramide
Drug class:
Dopamine antagonist

Formulations:
10mg Tablets
5mg/5mL liquid
IV Injection

Indication:
Prevent delayed nausea and vomiting. Effective for severe intractable vomiting due to radiotherapy.</td>
<td>IV/Oral (from 1 month):
<table>
<tr><th>Age</th><th>Dose</th></tr>
<tr><td>> 1 year</td><td>100-150 micrograms/kg every 8-12 hours (Max 10mg/dose)</td></tr>
</table>
To use for a maximum of 5 days. Discuss with pharmacy if required for prolonged courses

Suggested doses:
<table>
<tr><th>Weight</th><th>Oral/IV Dose</th></tr>
<tr><td><10kg</td><td>100micrograms/kg</td></tr>
<tr><td>10–14.9kg</td><td>1mg</td></tr>
<tr><td>15–19.9kg</td><td>2mg</td></tr>
<tr><td>20–29.9kg</td><td>2.5mg</td></tr>
<tr><td>30–60kg</td><td>5mg</td></tr>
<tr><td>>60kg</td><td>10mg</td></tr>
</table>
</td>
<td>Extrapyramidal effects
Hyperprolactinaemia
Drowsiness
Restlessness</td>
<td>Should be used after levomepromazine failed for maximum 5-days. Review with consultant before using.

Reduce dose in renal and hepatic impairment
Use with caution with levomepromazine, cyclizine and hyoscine – will reduce prokinetic effects

Treat dystonic reactions with PROCYCLIDINE</td>
</tr>
<tr>
<td>Nabilone
Drug class:
A cannabinoid drug with central action.
Note: CD Schedule 2

Formulations:
Capsule 1mg

Indication: For delayed and refractory CINV in adolescents – particularly when refractory to dexamethasone and ondansetron and where failed all other lines of antiemetic treatment</td>
<td>Oral
<table>
<tr><th>Age</th><th>Dose</th></tr>
<tr><td>>12 years and >30kg</td><td>Initially 1 mg twice daily, increased if necessary to 2 mg twice daily throughout each cycle of chemotherapy and, if necessary, for 48 hours after the last dose of each cycle

First dose should be taken the night before chemotherapy and the second dose 1–3 hours before the first dose of chemotherapy, daily dose maximum should be given in 3 divided doses; maximum 6 mg per day.</td></tr>
</table>
</td>
<td>Side effects:
dizziness, drowsiness, behavioural alterations, dry mouth, ataxia, postural hypotension. Hallucinations, euphoria and other psychotic reactions in some patients. Patients and carers should be made aware of possible changes in mood and other adverse behavioural effects.</td>
<td>Do not use with levomepromazine and lorazepam.</td>
</tr>
</table>

<table>
<tr>
<td>Olanzapine
Drug class:
Atypical Antipsychotic

Formulations:
2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg tablets
2.5mg 5mg, 7.5mg, 10mg, 15mg, 20mg orodispersible / lyophilisate tablets

Indication:
Prevent and treat acute and delayed CINV</td>
<td>Oral
<table><tr><th>Age</th><th>Dose</th></tr><tr><td>>1 year and 10kg</td><td>140 micrograms/kg ONCE a day increasing as necessary to a max. of 10mg per day in one or two divided doses</td></tr></table>
Doses should be rounded to nearest 1.25mg Observe slow dose titration to minimise sedation. Tablets maybe halved or quartered. Tablets maybe crush and dispersed in water and a proportion given. Oro-dispersible tablets and oral lyophilisate tablets may be halved or quartered or dispersed in water and a proportion given.</td>
<td>Weight gain / Increase appetite
Elevated triglycerides
Sedation
Dry mouth
Constipation, urinary retention, dizziness, drowsiness , agitation
QT interval prolongation</td>
<td>Should be consider for those patients with significant refractory nausea and vomiting only.

Extremely long half life with long onset of action (measured in days rather than hours)

<u>DO NOT USE</u> IN COMBINATION WITH LEVOMEPROMAZINE, METOCLOPRAMIDE, CYCLIZINE OR HYOSCINE. Significant risk of increased side effects</td>
</tr>
<tr>
<td>Ondansetron
Drug class:
5HT₃ antagonist

Formulations:
4mg, 8mg tablets
4mg/8mg orodispersible film
4mg/5mL liquid
2mg/ml IV Injection
Sublingual melts 4mg/8mg

Indication:
Prevent acute and delayed CINV</td>
<td>IV/Oral:5mg/m² (Max 8mg per dose) loading dose followed by regular dose TWICE a day <u>until 2-3 days post chemo</u> (increased to THREE times a day if required)

Loading dose
<table><tr><th>Age/Surface Area</th><th>Dose</th></tr><tr><td>All ages</td><td>5mg/m²</td></tr></table>
Regular dose
<table><tr><th>Age/Surface Area</th><th>Dose</th></tr><tr><td><6months</td><td>150 micrograms/kg</td></tr><tr><td><0.6m2 and >=6months</td><td>2mg</td></tr><tr><td>0.6-<1.3m2</td><td>4mg</td></tr><tr><td>>=1.3m2</td><td>8mg</td></tr></table></td>
<td>Constipation
Headache
Flushing</td>
<td>Orodispersible film cannot be cut

Reduce dose in moderate or severe hepatic impairment

Do not use with drugs that prolong QT interval (however safe to use with olanzapine)

Less effective for delayed emesis.</td>
</tr>
<tr>
<td>Palonosetron
Drug class:
5HT₃ antagonist

Formulations:
250 micrograms solution for injection

Indication:
Prevent acute and delayed CINV</td>
<td>IV Infusion

<table><tr><th>Age</th><th>Dose</th></tr><tr><td>Age >=1 month</td><td>20 micrograms/kg (max 1500 micrograms) administered as a single 15 minute intravenous infusion beginning approximately 30 minutes before the start of chemotherapy.</td></tr></table>
Repeat dosing: There is limited evidence or research on repeat dosing of palonosetron. Based on a mean half-life of 40 hours, where repeat dosing or using an alternative 5HT3 antagonist is required, an interval of 5 days in between doses is recommended. Further research into this is required.</td>
<td>Constipation; headache, diarrhoea; dizziness; electrolyte imbalance</td>
<td>Where palonosetron is used, centres should ensure systems are in place to ensure patients do not have 5HT3 antagonist prescribed for them after receiving palonosetron with particular consideration for POSCUs.</td>
</tr>
</table>

<table>
<tr>
<td>Procyclidine
Drug class:
Anticholinergic

Formulations:
5mg/ml injection
5mg/5ml liquid SF, 2.5mg/5ml
5mg tablet</td>
<td>Intramuscular injection, or by intravenous injection:
Acute dystonia doses: single doses
dose usually effective in 5–10 minutes but may need 30 minutes for relief

<table>
<tr><th>Age</th><th>Dose</th></tr>
<tr><td>1 month- 1 year</td><td>0.5-2mg for 1 dose</td></tr>
<tr><td>2-9 years</td><td>2-5 mg for 1 dose</td></tr>
<tr><td>>10 years</td><td>5-10 mg</td></tr>
</table>
</td>
<td>Anti-cholinergic: Constipation; dry mouth; urinary retention; vision blurred</td>
<td>Contraindicated in Gastro-intestinal obstruction</td>
</tr>
</table>