

## MANAGEMENT OF CHEMOTHERAPY INDUCED NAUSEA AND VOMITING

### 1. **INTRODUCTION**

Chemotherapy induced nausea and vomiting (CINV) is said to be one of the most distressing side effects of childhood cancer treatment, and if not managed appropriately can affect compliance with future treatment. If not controlled, CINV can also lead to complications such as malnutrition, dehydration, electrolyte imbalances, prolonged hospitalisation and psychological issues including anticipatory nausea and vomiting.

CINV can be:

- acute (0–24 hours after dose),
- delayed (24 hours–5 days post last dose of chemotherapy)
- anticipatory (prior to the start of chemotherapy)

Physiological differences exist between the acute and delayed CINV, therefore optimal management may require different therapeutic approaches to gain adequate control.

The Children's Cancer and Leukaemia Group (CCLG) have produced a national framework document to guide local implementation, which has been used to guide the content of this Trust guideline.

### 2. **PURPOSE/SCOPE**

The following guidelines are for the management of CINV in paediatric oncology/haematology patients. The guideline should be used in conjunction with the patient's individual anti-emetic history.

### 3. **RECOMMENDATIONS**

Children and young people about to receive chemotherapy should have their chemotherapy assessed for emetogenicity. The CCLG have recommended chemotherapy be divided into five strata:

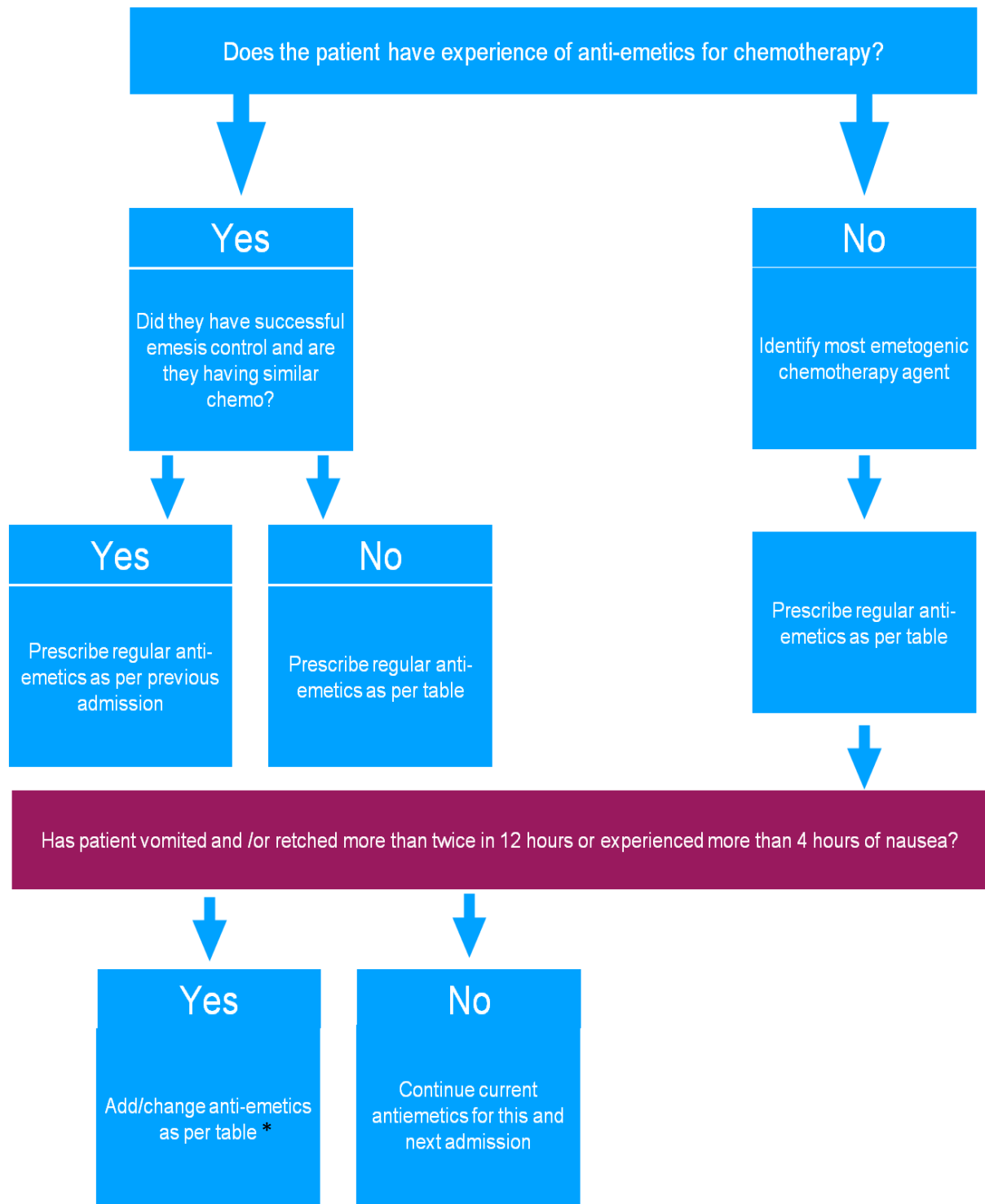
- Very highly emetogenic chemotherapy
- Highly emetogenic chemotherapy
- Moderately emetogenic chemotherapy
- Low emetogenic chemotherapy
- Minimal emetogenic chemotherapy

Children and young people should have their symptoms of nausea and vomiting assessed.

Children and young people about to undertake chemotherapy should have antiemetics prescribed prior to chemotherapy, adapted to their own personal experience.

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

**4. FLOWCHART – OVERALL APPROACH TO SELECTING ANTI-EMETICS**



**Table 1: MANAGEMENT OF CHEMOTHERAPY INDUCED NAUSEA AND VOMITING (CINV)**

**Using table 1:** move to the next step within the antiemetic intensity level. For subsequent cycles where the same drug/drug combinations or drug-combinations of similar emetogenic potential are given consider starting prophylaxis at the increased intensity level.

**\*Avoid dexamethasone in the following groups:**

1. Brain tumour patients
2. Any treatment cycles which include steroids as anti-cancer therapy e.g. ALL
3. Caution with immunotherapy, refer to guidance for individual drugs (e.g. mifamurtide)
4. Reduce dexamethasone dose to 50% when given with aprepitant.

**\*\*Palonosetron:**

Palonosetron can be considered for patients receiving chemotherapy for  $\geq 3$  concurrent days. Do not prescribe any other 5HT3 antagonist (e.g. ondansetron) within 5 days of receiving palonosetron.

**Very Highly Emetogenic Chemotherapy (1)**

<b>Cisplatin</b> <b>Melphalan</b>	<p><b>Step 1:</b> Aprepitant/fosaprepitant + ondansetron/palonosetron** + dexamethasone* (50% dose)</p> <p><b>Step 2:</b> Add regular levomepromazine</p> <p>If fails step 1: For subsequent cycles (if <math>\geq 6</math> months old) :          Aprepitant/fosaprepitant + ondansetron/palonosetron** + dexamethasone* (50% dose) + levomepromazine</p> <p><u>For patients &lt; 6 months old or &lt;6kg do not give aprepitant/fosaprepitant:</u></p> <p><b>Step 1:</b> Ondansetron + levomepromazine</p> <p><b>Step 2:</b> Add regular dexamethasone*</p> <p>If fails step 1: For subsequent cycles (if &lt;6 months old or &lt;6kg):          Ondansetron + levomepromazine + dexamethasone*</p> <p><b>Delayed CINV</b>          Oral aprepitant + dexamethasone* (50% dose)          Consider addition of levomepromazine if not achieving satisfactory control</p>
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**Very Highly Emetogenic Chemotherapy (2)**

<b>Cyclophosphamide</b> <b>&gt;2g/m<sup>2</sup></b> <b>Ifosfamide</b>  <b>Cyclophosphamide +</b> <b>anthracycline</b> <b>Cyclophosphamide +</b> <b>etoposide</b> <b>Doxorubicin +</b> <b>Ifosfamide</b> <b>Cytarabine 300mg/m<sup>2</sup></b> <b>+ etoposide</b>	<p><b>Step 1:</b> Ondansetron/palonosetron** + levomepromazine + PRN dexamethasone*</p> <p><b>Step 2:</b> Add regular dexamethasone*</p> <p>If fails step 2: For subsequent cycles escalate to treatments from the “very highly emetogenic chemotherapy regimens (1)” i.e. (if <math>\geq 6</math> months old and &gt;6kg) aprepitant/fosaprepitant + ondansetron/palonosetron** + dexamethasone* (50% dose)</p> <p><b>Delayed CINV</b>          Oral levomepromazine</p>
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<b>Doxorubicin + methotrexate 5g/m<sup>2</sup></b> <b>Etoposide + ifosfamide</b>	Consider addition of regular dexamethasone* if received regularly during admission or not achieving control on levomepromazine monotherapy
<b>Highly Emetogenic Chemotherapy</b>	
<b>Carboplatin</b> <b>Carmustine</b> <b>Cyclophosphamide &gt;1g/m<sup>2</sup></b> <b>Cytarabine &gt;1g/m<sup>2</sup></b> <b>Dacarbazine</b> <b>Methotrexate &gt;3g/m<sup>2</sup></b> <b>Thiotepa</b>	<p><b>Step 1:</b> Ondansetron/palonosetron** +/- levomepromazine</p> <p><b>Step 2:</b> Add regular levomepromazine if not given at step 1</p> <p><b>Step 3:</b> Add regular dexamethasone* for breakthrough</p> <p>If fails step 3: For subsequent cycles escalate to Very Highly Emetogenic Chemotherapy (1) (if ≥ 6 months old) i.e. aprepitant/fosaprepitant + ondansetron/palonosetron** +/- dexamethasone* (50% dose)</p> <p><b>Delayed CINV</b>          Oral levomepromazine          Consider addition of regular dexamethasone* if received regularly during admission or not achieving control on levomepromazine monotherapy</p>
<b>Moderately Emetogenic Chemotherapy</b>	
<b>Actinomycin D</b> <b>Amsacrine</b> <b>Azacitidine</b> <b>Busulfan IV</b> <b>Clofarabine</b> <b>Cyclophosphamide 300mg/m<sup>2</sup>- 1g/m<sup>2</sup></b> <b>Cytarabine 500mg- 1g/m<sup>2</sup></b> <b>Daunorubicin</b> <b>Doxorubicin</b> <b>Docetaxel</b> <b>Epirubicin</b> <b>Idarubicin</b> <b>Imatinib</b> <b>Inotuzumab</b> <b>Irinotecan</b> <b>Lomustine</b> <b>Midostaurin</b> <b>Mitoxantrone</b> <b>Oxaliplatin</b> <b>Procarbazine</b> <b>Temozolomide</b> <b>Treosulfan</b>	<p><b>Step 1:</b> Ondansetron/palonosetron** + PRN levomepromazine</p> <p><b>Step 2:</b> Add regular levomepromazine</p> <p><b>Step 3:</b> Add regular dexamethasone*</p> <p>If fails step 3: For subsequent cycles escalate to Very Highly Emetogenic Chemotherapy (1) (if ≥ 6months old) : aprepitant/fosaprepitant + ondansetron/palonosetron** +/- dexamethasone* (50% dose)</p> <p><b>Delayed CINV</b>          Oral levomepromazine          Consider addition of regular dexamethasone* if received regularly during admission or not achieving control on levomepromazine monotherapy</p>
<b>Arsenic trioxide</b>	For arsenic give PRN Cyclizine ONLY (Arsenic prolongs QT interval).

<b>Low Emetogenic Chemotherapy</b>	
<p>ATG Bortezomib Bleomycin Brentuximab Oral busulphan Capecitabine Cladribine Cyclophosphamide &lt;300mg/m<sup>2</sup> Cytarabine &lt;500mg/m<sup>2</sup> Chlorambucil Dasatinib Dinutuximab Etoposide 5-Fluorouracil Fludarabine Gemcitabine Gemtuzumab Hydroxyurea Mercaptopurine Methotrexate &lt;3g/m<sup>2</sup> Methotrexate oral Mitomycin Nilotinib Nelarabine Paclitaxel Ponatinib Regorafenib Ruxolitinib Sorafenib Sunitinib Thalidomide Thioguanine Topotecan Venetoclax Vinca Alkaloids</p>	<p><b>Step 1:</b> Ondansetron PRN</p> <p><b>Step 2:</b> Regular ondansetron</p> <p>If fails step 2: For subsequent cycles escalate to Step 2 of Moderately Emetogenic Chemotherapy i.e. regular ondansetron and levomepromazine</p>
<b>Minimally Emetogenic Chemotherapy</b>	
<p>Alemtuzumab Asparaginase Blinatumomab Bevacizumab Dabrafenib Lenolidomide Nivolumab Rituximab</p>	<p><b>Step 1:</b> No routine prophylaxis should be prescribed</p> <p>If fails step 1: For subsequent cycles escalate to Step 1 of Low Emetogenic Chemotherapy i.e. ondansetron PRN</p>

## 5. **REFRACTORY CINV**

Refractory CINV refers to the continuation of significant nausea or vomiting without a period of acceptable control. For those who continue to suffer with refractory CINV despite escalation through the intensity levels as detailed in table 1, consider alternate approaches e.g. olanzapine, switching levomepromazine from an IV intermittent infusion to IV continuous infusion or adding lorazepam. Management of refractory CINV must be discussed with a consultant and pharmacy.

Nabilone can be considered on consultant discretion only.

## 6. **ANTICIPATORY CINV**

Anticipatory CINV refers to significant nausea or vomiting prior to the delivery of chemotherapy. Consider home administration of ondansetron +/- levomepromazine up to 24 hours prior to administration of chemotherapy. Low dose lorazepam may be prescribed (must be discussed with a consultant). Offer psychological interventions.

## 7. **DELAYED CINV**

Delayed CINV refers to nausea or vomiting that occurs 24 hours – 5 days post the last dose of chemotherapy. 5HT3 antagonists are not recommended in delayed CINV and should never be given within 5 days of receiving palonosetron.

Recommendations for delayed CINV are included within the emetogenic risk stratifications.

Olanzapine or metoclopramide can be considered on consultant discretion only.

## 8. **PREFERRED ROUTE OF ADMINISTRATION**

Oral administration is preferred wherever possible. Dual IV and oral routes can be prescribed for ondansetron, dexamethasone and levomepromazine ONLY.

For duplicate route prescribing the prescriber must add a free text note in the 'Dose Instruction' field indicating there is a duplicate route 'see IV/ Oral also'.

The nurse should choose the route at the point of administration and for the route not given: select 'not given' and add free text – 'duplicate route'. If the patient is an outlier on a ward other than 3B, only one route of prescribing is allowable.

## 9. **DISCHARGE MEDICATION**

Ensure patients are discharged home with a supply of antiemetics to continue for up to 5 days post chemotherapy. This should not routinely include ondansetron.

## 10. **ACUTE LYMPHOBLASTIC LEUKAMIA (ALL) PATIENTS IN MAINTENANCE**

Routine use of antiemetics is unlikely to be required for ALL patients in maintenance. Use of antiemetics should regularly be reviewed.

## 11. ANTIEMETIC DRUG INFORMATION

Drug	Dose	Additional information
<p><b>Aprepitant (oral) (NK1 receptor antagonist)</b></p> <p><b>Preparations:</b> <b>Capsules:</b> 80mg, 125mg</p> <p>Note for patients who are unable to swallow capsules: capsules can be opened, and contents of the FULL capsule dispersed in water. A proportion of the capsule contents cannot be taken to give lower doses.</p>	<p><b>≥12 years old, or &lt;12 years old AND ≥40kg:</b> Day 1: 125mg once daily Day 2 &amp; 3: 80mg once daily</p> <p><b>For patients 6 months to &lt;12 years old AND ≥6kg to &lt;40kg – see fosaprepitant below.</b></p> <p><b>To be administered 1 hour prior to chemotherapy on Days 1, 2 and 3. If no chemotherapy is given on Day 2 and 3 then administer in the morning.</b></p> <p><b>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.</b></p>	<p>NB. Can increase ifosfamide mediated neurotoxicity and irinotecan toxicity – discuss with consultant before prescribing.</p> <p>Can increase exposure to vinca alkaloids. Can increase exposure to tyrosine kinase inhibitors. Monitor closely.</p> <p><b>Dose of dexamethasone must be reduced by 50% when given with aprepitant.</b></p> <p>Caution – check for drug interactions.</p>
<p><b>Cyclizine (Antihistamine)</b></p> <p><b>Preparations:</b> <b>IV:</b> 50mg/mL <b>Tablets:</b> 50mg scored <b>Oral solution:</b> 5mg/5mL</p>	<p><b>IV bolus/oral:</b> 1 month – 5 years: 0.5-1mg/kg (max 25mg) up to three times daily</p> <p>6 – 11 years: 25mg up to three times daily</p> <p>12 – 18 years: 50mg up to three times daily</p>	<p>Avoid using with levomepromazine or olanzapine.</p>
<p><b>Dexamethasone (Corticosteroid)</b></p> <p><b>Preparations:</b> <b>IV:</b> 6.6mg/2ml <b>Oral Liquid:</b> 10mg/5mL <b>Tablets:</b> 500microgram, 2mg</p>	<p><b>IV/oral:</b> SA ≤ 0.6m<sup>2</sup> : 2mg twice a day SA ≥ 0.6m<sup>2</sup> : 4mg twice a day</p> <p><b>Use for maximum of 5 days.</b></p> <p>Doses can be increased to 2.5-5mg/m<sup>2</sup> up to three times a day.</p>	<p>Dose of dexamethasone must be reduced by 50% when given with aprepitant.</p> <p><b>Avoid dexamethasone in the following groups:</b></p> <ol style="list-style-type: none"> <li>Brain tumour patients</li> <li>Any treatment cycles which include steroids as anti-cancer therapy e.g. ALL</li> <li>Caution with immunotherapy, refer to guidance for individual drugs e.g. mifamurtide</li> </ol>

<p><b>Fosaprepitant (IV)</b> <b>(NK1 receptor antagonist)</b></p> <p><b>Preparations:</b> <b>IV:</b> 150mg vial</p>	<p><b>For multi-day chemotherapy regimens:</b>  <b>&gt;6kg and &gt;6 months to &lt;12 years old (IV infusion over 60 minutes):</b>          Day 1: 3mg/kg once daily (max. dose 115mg)          Day 2 &amp; 3: 2mg/kg once daily (max. dose 80mg)</p> <p><b>≥ 12 years old (IV infusion over 30 minutes):</b>          Day 1: 115mg once daily          Day 2 &amp; 3: 80mg once daily</p> <p><b>For single day chemotherapy regimens:</b>  <b>&gt; 6kg and &gt; 6 months to &lt; 2 years old (IV infusion over 60 minutes):</b>          5mg/kg as a single dose (max. dose 150mg)</p> <p><b>&gt;2 years to &lt; 12 years old (IV infusion over 60 minutes):</b>          4mg/kg as a single dose (max. dose 150mg)</p> <p><b>&gt; 12 years old (IV infusion over 30 minutes):</b>          150mg as a single dose</p> <p><b>Fosaprepitant infusion should be completed 30 minutes before starting chemotherapy.</b></p>	<p>NB: Can increase ifosfamide mediated neurotoxicity and irinotecan toxicity – discuss with consultant before prescribing.</p> <p>Can increase exposure to vinca alkaloids. Can increase exposure to tyrosine kinase inhibitors. Monitor closely.</p> <p>Dose of dexamethasone must be reduced by 50% when given with fosaprepitant.</p> <p>Caution – check for drug interactions.</p>
<p><b>Levomepromazine (Phenothiazine)</b></p> <p><b>Preparations:</b>  <b>IV:</b> 25mg/mL  <b>Oral suspension:</b> 5 mg/mL  <b>Tablets:</b> 25mg scored</p>	<p><b>IV infusion (over 30 minutes):</b>          0.1mg/kg twice daily (max single dose 6.25mg)</p> <p><b>IV continuous infusion:</b> 0.25-0.5mg/kg/24 hours (max dose 25mg/24 hours)</p> <p><b>Oral:</b> 0.1 – 0.2 mg/kg twice daily (max single dose 12.5mg)</p>	<p>Monitor for drowsiness.</p> <p>Do not use with cyclizine, olanzapine or metoclopramide.</p> <p>Avoid use in hepatic impairment.          Reduce dose in renal impairment.</p> <p>Can be useful in vomiting due to raised intracranial pressure.</p> <p>Care in patients receiving ifosfamide as sedation may mask signs of encephalopathy.</p>

<p><b>Lorazepam (Benzodiazepine)</b></p> <p><b>Preparations:</b>  <b>Tablets:</b> 500 microgram, 1mg,</p> <p><b>Oral Suspension:</b>          200 microgram/mL (note – this is an extemporaneous preparation made in pharmacy, so there may be a delay in obtaining this product)</p>	<p><b>Oral:</b>          50 – 100 micrograms/kg (max 4mg) every 8-12 hours</p> <p><b>For anticipatory nausea and vomiting, give one dose the evening before and once dose 1 hour before starting chemotherapy.</b></p>	<p>Care in patients receiving ifosfamide since sedation may mask signs of encephalopathy</p>
<p><b>Metoclopramide (dopamine antagonist)</b></p> <p><b>Preparations:</b>  <b>Tablets:</b> 10mg</p> <p><b>Oral solution:</b>          5mg/5mL</p> <p><b>IV:</b> 5mg/1mL injection</p>	<p><b>&gt;1 year:</b>          100-150 microgram/kg (max 10mg) every 8-12 hours</p> <p><b>To be used for a maximum of 5 days – not for long term use.</b></p>	<p>To be used on advice of consultant only.</p> <p>Do not use with levomepromazine or olanzapine.</p> <p>Treat dystonic reactions with procyclidine (dosing as per BNFc).</p>
<p><b>Nabilone (oral) (Cannabinoid)</b></p> <p><b>Preparations:</b>  <b>Capsules:</b> 0.25mg and 1mg</p>	<p><b>&gt;12 years and &gt;30kg:</b>          Initially 1mg twice daily, increased if necessary to 2mg twice daily throughout each cycle of chemotherapy and, if necessary, for 48 hours after the last dose of each cycle.</p> <p><b>First dose should be taken the night before chemotherapy and the second dose 1-3 hours before the first dose of chemotherapy.</b></p> <p><b>Max 6mg per day, given in 3 divided doses.</b></p>	<p>Note – Schedule 2 Controlled Drug</p> <p>Do not use with levomepromazine or lorazepam.</p> <p>To be used on advice of consultant only.</p>
<p><b>Olanzapine (Atypical Antipsychotic)</b></p>	<p><b>&gt;1 year and &gt;10kg:</b>          140 microgram/kg once daily.</p>	<p>Do not use with levomepromazine, metoclopramide and cyclizine.</p>

<p><b>Preparations:</b>  <b>Tablets:</b> 2.5mg, 5mg, 7.5mg, 10mg</p> <p><b>Orodispersible tablets:</b> 2.5mg, 5mg, 7.5mg, 10mg</p> <p><b>Tablets can be halved or quartered. Tablets can be crushed and dispersed in water.</b></p>	<p>Increase as necessary to a max dose of 10mg per day in one or two divided doses</p> <p>Doses to be rounded to nearest 1.25mg.</p>	<p>Note – very long half life with a long onset of action</p> <p>To be used on advice of consultant only.</p>
<p><b>Ondansetron</b>        (5HT<sub>3</sub> antagonist)</p> <p><b>Preparations:</b>  <b>IV:</b> 8mg/4mL  <b>Oral Liquid:</b> 4mg/5mL  <b>Tablets:</b> 4mg, 8mg  <b>Sublingual melts:</b> 4mg, 8mg  <b>Orodispersible films:</b> 4mg, 8mg</p>	<p><b>IV infusion (over 15 minutes):</b> 5mg/m<sup>2</sup> three times daily (max single dose 8mg)</p> <p><b>Oral:</b> every 8 or 12 hours        &lt;0.3m<sup>2</sup> - 1mg        0.3-0.6m<sup>2</sup> 2mg        0.6-0.9m<sup>2</sup> 4mg        0.9-1.2m<sup>2</sup> 6mg        &gt;1.2m<sup>2</sup> 8mg        (max single dose 8mg)</p>	<p>Reduce dose in moderate/severe hepatic impairment.</p> <p>Do not use with drugs that prolong QT interval.</p> <p>Dosing is for CINV only.</p> <p>Not recommended for delayed CINV</p>
<p><b>Palonosetron</b>        (5HT<sub>3</sub> antagonist)</p> <p><b>Preparations:</b>  <b>IV:</b> 250 microgram/5ml</p>	<p><b>≥ 1 month old:</b>        IV infusion (over 15 minutes): 20 micrograms/kg (max 1500 micrograms) beginning approximately 30 minutes before the start of chemotherapy</p> <p><b>&gt;18 years old:</b> IV bolus: 250 microgram as a single dose, 30 minutes before the start of chemotherapy</p>	<p><b>Do not prescribe any other 5HT<sub>3</sub> antagonist (e.g. ondansetron) within 5 days of receiving palonosetron.</b></p>

## References

1. Children’s Cancer and Leukaemia Group (CCLG), “Guideline for the Management of Chemotherapy-Induced Nausea and Vomiting”. CCLG Supportive Care Group, Version 3, March 2025.
2. Children’s Cancer and Leukaemia Group (CCLG), “Guideline for the Management of Chemotherapy-Induced Nausea and Vomiting”. CCLG Supportive Care Group, Version 2.1, Nov 2023.
3. Children’s Cancer and Leukaemia Group (CCLG), “Guideline on the management of chemotherapy induced nausea and vomiting”. CCLG Supportive Care Group, Version 1, 2018.
4. Alder Hey Children’s NHS Foundation Trust. Management of Chemotherapy Induced Nausea and Vomiting. May 2020
5. British National Formulary for Children 2024 – 2025
6. Metoclopramide: risk of neurological adverse effects. Medicines and Healthcare products Regulatory Agency. December 2014

MANAGEMENT OF CHEMOTHERAPY INDUCED NAUSEA AND VOMITING	
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Name of originator/author:	<p><b>Review March 2025 undertaken by:</b> Colin Thorbinson (Consultant Paediatric Oncologist) Rachael Ruddin (Paediatric Oncology/Haematology Pharmacist)</p> <p><b>Review December 2019 undertaken by:</b> Barry Pizer (Consultant Paediatric Oncologist) Rachael Ruddin (Paediatric Oncology/Haematology Pharmacist) Caroline Osborne (Principal Pharmacist Oncology Team Manager)</p> <p><b>Original authors:</b> Lisa Howell (Consultant Paediatric Oncologist) Felicity Heard (Oncology Pharmacist)</p>
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Version Control Table				
Version	Date	Author(s)	Status	Comment(s)
6	April 26	Rachael Ruddin	Current	Fosaprepitant added in place of aprepitant sachets which have been discontinued. Palonsetron doses for >18 years added

5	May 25	Colin Thorbinson Rachael Ruddin	Archived	Updated to reflect new national guidance on chemotherapy induced nausea and vomiting, produced by Children's Cancer and Leukaemia Group (CCLG) Addition of following drugs: Palonosetron, Olanzapine, Nabilone
4.2	Apr 24	Rachael Ruddin	Archived	3-month extension to allow review and approval via MMOC.
4.1	November 2023	Barry Pizer, Rachael Ruddin, Caroline Osborne	Archived	Extended pending publication of national guidance
4	May 20	Barry Pizer, Rachael Ruddin, Caroline Osborne	Archived	4.5.23 - Author: Colin Thorbinson Expiry extended to 11.23
3	Jan 16	Lisa Howell, Felicity Heard	Archived	
2	Aug 10	Lisa Howell, Felicity Heard	Archived	
1	Pre Sep 01	Pharmacy	Archived	

Review and Revision(s) Log			
<i>Record of revision(s) made to guidelines since Version 1</i>			
Section Number	Page Number	Revision(s) made	Reason for revision(s)
	Various	Fosaprepitant added in place of aprepitant sachets	Aprepitant sachets discontinued
		Palonosetron doses for >18 years added	Clarification of dosing for older patients