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DOCUMENT CONTROL PAGE

Title:	Chemotherapy induced nausea and vomiting (CINV) management guidelines (children's)
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Application:	Patients – Paediatric Haematology/Oncology patients receiving treatment with anticancer/chemotherapy agents All Staff

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Table of Contents

1 Introduction

Chemotherapy induced nausea and vomiting (CINV) is one of the most documented distressing side effects of childhood cancer and is a major limiting factor to compliance and effective treatment if not managed appropriately. Left untreated, it can lead to electrolyte imbalance, poor nutrition, dehydration, prolonged hospitalisation, and reduced quality of life.

Emesis is generated by the vomiting centre in the medulla, which receives input from the chemoreceptor trigger zone (CTZ) and can be activated by drugs (including chemotherapy), smells, sights or gastrointestinal input. Receptors that can be found in the CTZ include 5HT3, NK1 and dopamine, which form the basis for antiemetic therapy. Optimal management of CINV may require targeting the peripheral pathways with a 5HT3 receptor antagonist, and the central pathway with an NK1 receptor.

CINV can be acute (0-24hours after first chemotherapy dose), delayed (24 hours – 5 days post chemotherapy) and anticipatory (prior to the start of chemotherapy). Adequate control of CINV is crucial. Owing to the physiological differences between acute and delayed CINV, different therapeutic approaches may be required. Acute CINV is mediated by the neurotransmitter serotonin, whereas delayed CINV is mediated by substance P. Symptoms of nausea and vomiting may also arise as a result of other 'non-chemotherapy' related management of malignant disease (opioids, establishment of feeding regimes etc). It is important that treatment is directed towards the underlying cause in order to manage symptoms effectively.

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 guideline is for the management of CINV in paediatric haematology / oncology and haemopoietic stem cell transplant (HSCT) patients.

The guidance should be used in conjunction with the individual patient's anti-emetic history.

The scope of the guideline is to advise on the management of nausea and/or vomiting as a direct side effect of chemotherapy.

This guideline is for the management of patients in the acute setting and is not intended for use in palliative/end-of-life care.

3 Roles and Responsibilities

The Paediatric Medicines Management Group and the Chemotherapy Group will approve the content of the guideline

The Pharmacy Medicines Management Team will make available the 'Chemotherapy induced nausea and vomiting (CINV) management guidelines (Children's)' on the Trust intranet

The Chemotherapy Group will ensure the guideline is updated if legislation, recommendations, evidence or good practice change.

Departmental managers will disseminate procedural documents and facilitate any further training or discussion required.

All Trust staff: It is the personal responsibility of all staff to follow Trust procedural documents.

It will be the responsibility of the individual POSCUs to ensure that this guidance is ratified locally.

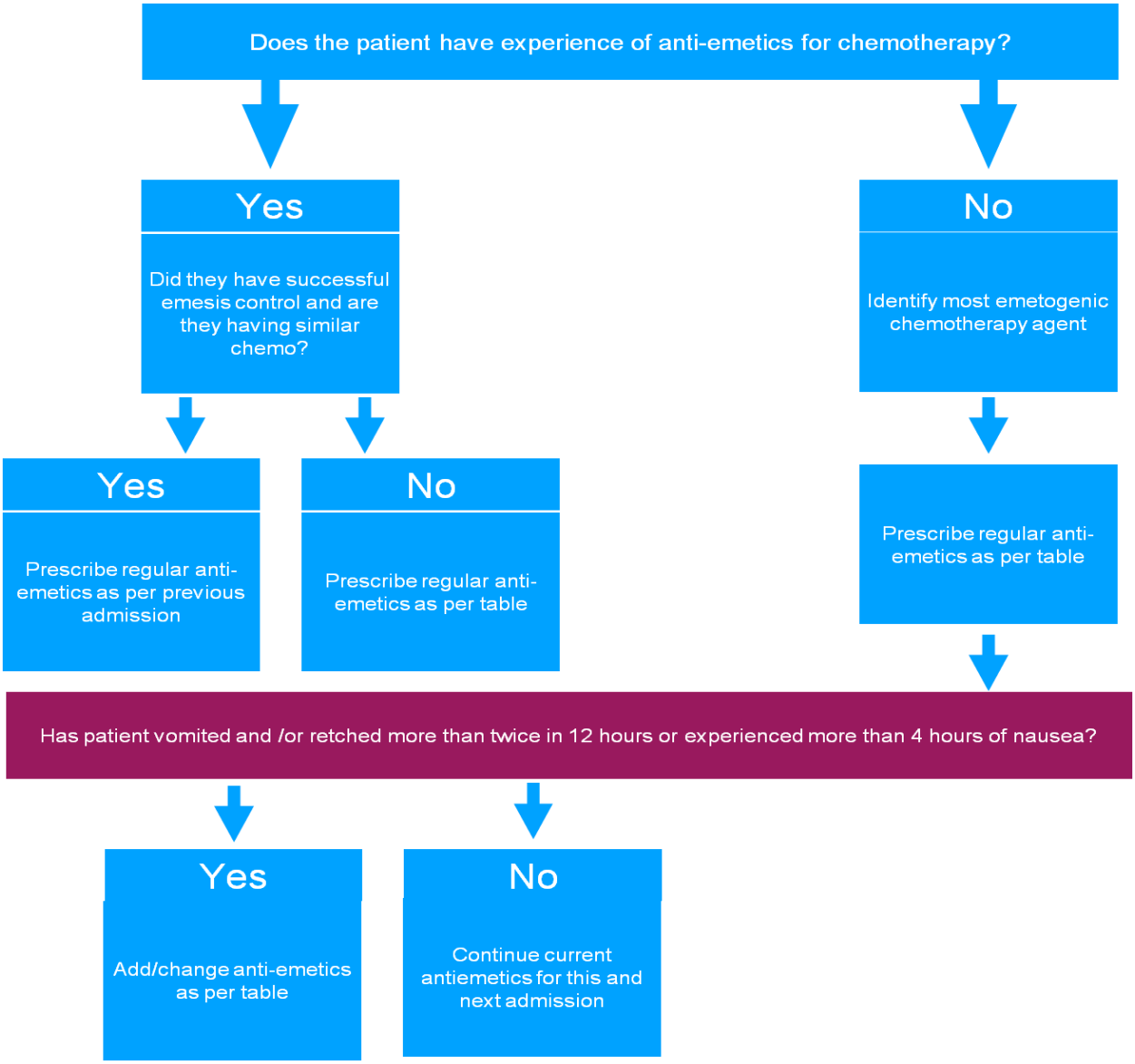
4 Recommendations: Over-riding principles

Patients being treated for malignant disease or undergoing HSCT can experience symptoms of nausea and vomiting for several different reasons including treatment with chemotherapy, establishing feeding and use of opioids. Symptoms can be distressing to both the patient and the family and can lead to refusal of further treatment if not managed effectively.

Children and young people about to undertake chemotherapy should have their chemotherapy assessed for emetogenicity. The CCLG have recommended chemotherapy be divided into four strata per the POGO-developed system:

- Highly emetogenic chemotherapy (HEC) including very highly emetogenic chemotherapy (vHEC)
- Moderately emetogenic chemotherapy (MEC)
- Low emetogenicity chemotherapy (LEC)
- Mininal emetogenicity

5 Flowchart: Overall step-wise approach to selecting anti-emetics



Prophylaxis: Very highly/highly emetogenic chemotherapy (>90%)	
Individual drugs: Asparaginase IV (erwina) (Erwinase) Busulfan IV/PO Carboplatin IV Cisplatin IV Cyclophosphamide IV ≥ 1200mg/m^2 Cytarabine IV ≥ 3g/m^2/day Dacarbazine IV Dactinomycin IV Doxorubicin IV ≥ 30mg/m^2/day Ifosfamide IV Melphalan IV Methotrexate IV ≥ 12g/m^2/day Thiotepa IV *Combination chemotherapies:* Cyclophosphamide IV + dactinomycin IV Cyclophosphamide IV + anthracycline IV Cyclophosphamide IV + etoposide IV Cytarabine IV + methotrexate IV Cytarabine IV + etoposide IV Dacarbazine IV + doxorubicin IV Dactinomycin IV + ifosfamide IV Doxorubicin IV + ifosfamide IV Etoposide IV + ifosfamide IV	<u>Step 1:</u> • Ondansetron + dexamethasone (50% dose) + aprepitant* (unless contraindicated, see drug monographs in section 10) • Levomepromazine + palonosetron** + dexamethasone where there is a contraindication to aprepitant. • Levomepromazine + palonosetron** + aprepitant* where there is a contraindication to dexamethasone • Levomepromazine + palonosetron** if there is a contraindication to dexamethasone and aprepitant <u>Step 2 (if inadequate control with step 1)</u> • Switch ondansetron to palonosetron** if not already using palonosetron • Add levomepromazine if not used in step 1. If used, switch levomepromazine to either metoclopramide or olanzapine • Consider changing to levomepromazine continuous IV infusion if persistent nausea/vomiting • Lorazepam may be added for refractory cases or where there is anticipatory nausea/vomiting • Add Nabilone PO short course for adolescents. Not to be used with levomepromazine and lorazepam * IV fosaprepitant may be used instead of PO aprepitant in patients unable to tolerate medication orally ** Palonosetron may be prescribed for patients receiving chemotherapy for ≥3 days and is the preferred 5HT3 antagonist for use in the acute phase for patients at high risk of CINV. Ensure no other 5HT3 antagonist (i.e. ondansetron) is used within 5 days of receiving palonosetron.

Prophylaxis: moderately emetogenic chemotherapy (30-90%)		
Arsenic trioxide IV Azacitidine SC Clofarabine IV Cyclophosphamide IV 500-1200mg/m^2 Cytarabine IV 200mg/m^2 to 3000mg/m^2 Daunorubicin IV Doxorubicin IV 10-30mg/m^2/dose Epirubicin IV Etoposide IV/PO Gemtuzumab IV Idarubicin IV Imatinib PO >260mg/m^2/day Inotuzumab IV Intrathecal chemotherapy	Irinotecan IV Lomustine PO Methotrexate IV ≥250mg/m^2 - <12g/m^2/dose Midostaurin PO Oxaliplatin IV >75mg/m^2 Topotecan IV/PO Trabectedin IV Venetoclax PO *Combination chemotherapies:* Cytarabine 60-90mg/m^2/dose + methotrexate 120mg/m^2/dose	<u>Step 1:</u> • Ondansetron + dexamethasone (unless contraindicated). • Ondansetron + aprepitant* where there is a contraindication to dexamethasone. • Ondansetron + levomepromazine (where there is a contraindication to aprepitant and dexamethasone) <u>Step 2:</u> • Add levomepromazine if not used in step 1. If used, switch levomepromazine to either metoclopramide or olanzapine • Change ondansetron to palonosetron** • Consider the addition of aprepitant in subsequent cycles, where CINV not controlled <u>Step 3:</u> • Consider levomepromazine continuous IV infusion for uncontrolled CINV • Add Nabilone PO short course for adolescents. Not to be used with levomepromazine and lorazepam. * IV fosaprepitant may be used instead of PO aprepitant in patients unable to tolerate medication orally ** Palonosetron may be prescribed for patients receiving chemotherapy for ≥3 days. Ensure no other 5HT3 antagonist (i.e. ondansetron) is used within 5 days of receiving palonosetron.

Prophylaxis: low emetogenic chemotherapy (10-30%)		
ATG Blinatunomab IV Bortezomib IV Cyclophosphamide IV <500 mg/m^2 Cyclophosphamide PO Cytarabine IV <200mg/m^2 Dinutuximab IV Docetaxel IV Everolimus PO 5-Fluorouracil IV Gemcitabine IV Kinase inihibitors PO (*dabrafenib, dasatinib, erlotinib, imatinib ≤ 260mg/m^2/day, nilotinib, polatinib, regorafenib, selumetinib, sorafenib, sunitinib, trametinib*)	Melphalan PO Mercaptopurine PO Methotrexate IV <250mg/m^2 Mitomycin IV Mitoxantrone IV Paclitaxel IV Procarbazine PO Temozolomide PO Thalidomide PO	<u>Step 1:</u> • Single agent ondansetron IV/PO is recommended for the acute phase (no routine prophylaxis normally required for the delayed phase). Note: occasionally patients on low emetogenic chemotherapy require the addition of a second agent. At RMCH, the agent of choice is levomepromazine or metoclopramide.

Prophylaxis: minimal emetogenic chemotherapy (<10%)		
Alemtuzumab Asparaginase IM (e.coli) (Oncaspar) ≤6000 units/m^2/dose Asparaginase IM (erwina) (Erwinase) ≤25,000 units/m^2/dose Bevacizumab Bleomycin Chlorambucil Cladribine Dexrazoxane Doxorubicin <10mg/m^2/dose Fludarabine	Hydroxycarbamide PO Methotrexate PO/SC Nelarabine Nivolumab Rituximab Thioguanine Vinblastine Vincristine Vindesine Vinorelbine	<u>Step 1:</u> • No routine prophylaxis is normally required • Single agent ondansetron IV/PO may be added per patient response

6 Breakthrough CINV

Breakthrough CINV refers to the reoccurrence of significant nausea and vomiting following a period of acceptable control. Where breakthrough CINV occurs, management should be escalated to the next intensity level outlined in the tables above.

minEC → LEC → MEC → HEC/vHEC

This should be clearly documented in the patient's notes and prophylaxis at the increased level should be considered for subsequent cycles of chemotherapy where the same drug/combinations or drug/combinations of similar emetogenic potential are given.

For patients with breakthrough nausea and vomiting on highly emetogenic chemotherapy regimens, consider:

- Switching ondansetron to palonosetron
- Addition of olanzapine or levomepromazine if not already tried
- Addition of aprepitant, dexamethasone or lorazepam (unless contraindicated)

7 Refractory nausea or vomiting

Refractory CINV refers to the continuation of significant nausea or vomiting without a period of acceptable control. This requires timely escalation of treatment to the next level up.

For patients with refractory nausea and vomiting on highly emetogenic chemotherapy regimens, consider:

- Switching ondansetron to palonosetron
- Review previous contraindication to aprepitant
- Addition of olanzapine, levomepromazine or metoclopramide
- Switching levomepromazine to continuous IV infusion rather than IV bolus
- Additional of lorazepam (PO or IV slow bolus)
- Addition of nabilone for adolescents (if antiemetics from at least 3 different groups already tried)
- Applying hyoscine patches for subsequent courses, applied the night before chemotherapy is due (at least 12 hours prior to chemotherapy)

Consider other possible causes for refractory nausea and vomiting that might not be directly related to chemotherapy.

8 Anticipatory nausea or vomiting

Anticipatory refers to significant nausea or vomiting prior to the delivery of chemotherapy. In severe cases, low-dose lorazepam may be prescribed the day before, and from the first day of chemotherapy.

9 Delayed nausea and vomiting

5HT3 antagonists are not recommended in the delayed phase and therefore should be stopped and not restarted. Alternative agents to consider for use include:

- Aprepitant/fosaprepitant
- Dexamethasone
- Olanzapine/levomepromazine

10 Discharge medication

'As needed' anti-emetics are not routinely recommended and 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 important. These should not routinely include ondansetron.

11 Drug dosing and recommendations for use: *(alphabetical)*

<table>
<tr><th>Drug name</th><th>Dosing and administration</th><th>Side effects</th><th>Additional information</th></tr>
<tr>
<td>

Aprepitant

Drug class:
NK1 receptor antagonist

Formulations:
- 125mg and 80mg capsules
- 125mg powder for oral suspension (reconstitutes to 25mg/mL)

Licensing:
- Capsules are licensed in ≥12 years (but safe to use in younger ages ≥10kg and ≥6 months)
- Oral suspension is licensed ≥6 months and <12 years (not for <6kg)

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Administered orally 1 hour prior to chemotherapy on days 1, 2 and 3. Consider extending for up to 48 hours post chemotherapy in previous refractory/delayed nausea cases.

First line: capsules. Dose banding for >10kg and <12 years:

Weight	Day 1	Day 2	Day 3
6kg–9.9kg	Use suspension		
10kg–11.9kg	30mg	20mg	20mg
12kg–14.9kg	40mg	25mg	25mg
15kg–18.9kg	50mg	35mg	35mg
19kg–25.9kg	60mg	40mg	40mg
26kg–29.9kg	80mg	55mg	55mg
30kg–33.9kg	100mg	60mg	60mg
34kg – 36.9kg	100mg	80mg	80mg
>37kg	125mg	80mg	80mg

Contents of capsules can be dispersed in a suitable volume of water prior to administration

Dose of capsules for ≥12 years:

Day 1	Day 2	Day 3
125mg	80mg	80mg

Dose using oral suspension (25mg/mL):

Day 1	Day 2	Day 3
3mg/kg (max dose 125mg)	2mg/kg (max dose 80mg)	2mg/kg (max dose 80mg)

</td>
<td>

Constipation

GI discomfort

Hiccups

Headache,

Decreased appetite

Cough

Neutropenia (slightly prolonged compared to without aprepitant).

</td>
<td>

Can increase ifosfamide mediated neurotoxicity and irinotecan toxicity. Monitor closely.

Can increase exposure to vinca alkaloids and tyrosine kinase inhibitors. Also cautioned with etoposide and irinotecan.

Not recommended if <6 months or <6kg

Not to be used in chemotherapy regimens that include steroids.

Moderate CYP3A4 inhibitor and mild CYP2C9 inducer. Caution when administered with concomitant substances metabolised primarily through CYP3A4 and with a narrow therapeutic range.

Avoid: *Phenytoin, carbamazepine, phenobarbitone, warfarin, benzodiazepines (lorazepam), clarithromycin and rifampicin.*

Reduce dose of **dexamethasone** by 50% if administering alongside aprepitant (see dexamethasone monograph)

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</tr>
</table>

<table>
<tr>
<td>Cyclizine

Drug class:
Antihistamine

Formulations:
• 50mg tablets
• IV injection</td>
<td>IV/Oral:
<table><tr><th>Age</th><th>IV/Oral Dose</th></tr><tr><td>1 month–5 yrs</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>
Tablets can be crushed and dispersed in a suitable volume of water.</td>
<td>Drowsiness
Dry mouth
Blurred vision
Urinary retention
Restlessness
Insomnia
Tachycardia
Headache
Dizziness</td>
<td>Avoid using with hyoscine, levomepromazine or olanzapine

Concomitant use with metoclopramide should be avoided where possible. Discuss with Pharmacy</td>
</tr>
<tr>
<td>Dexamethasone

Drug class:
Corticosteroid

Formulations:
• 2mg and 0.5mg tablets
• 2mg/5mL liquid
• IV injection 6.6mg/2mL</td>
<td>Give 1st dose 30-60 mins before chemotherapy.

IV/Oral: <u>with</u> aprepitant/fosaprepitant
<table><tr><th>BSA</th><th>IV/Oral Dose</th></tr><tr><td>≤ 0.6m²</td><td>1mg twice daily</td></tr><tr><td>> 0.6m2</td><td>2mg twice daily</td></tr></table>
Doses can be increased per the below table at least 24 hours after the last aprepitant/fosaprepitant dose

IV/Oral: <u>without</u> aprepitant/fosaprepitant
<table><tr><th>BSA</th><th>IV/Oral Dose</th></tr><tr><td>≤ 0.6m²</td><td>2mg twice daily</td></tr><tr><td>> 0.6m²</td><td>4mg twice daily</td></tr></table>
Use for a maximum of 5 days.

Doses can be increased to 2.5mg-5mg/m2 up to THREE times a day if needed.

Aim to space out doses to avoid night-time administration, to reduce the incidence of insomnia (doses do not need to be strictly 8 or 12 hours apart).</td>
<td>Adrenal suppression

Gastric irritation

Osteoporosis

Weight gain

Insomnia

Mood and behavioural problems</td>
<td>Dose of dexamethasone must be halved when used in combination with aprepitant or fosaprepitant

<u>Contra-indicated (as anti-emetic) for</u>:
Brain tumour patients
Patients already on steroids as part of their treatment (e.g. allogenic BMT, SCT, AML & ALL – discuss with consultant)
Patients on mifamurtide.

Caution in osteosarcoma patients (discuss with consultant)</td>
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</table>

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<tr>
<td>

Fosaprepitant

Drug class:
NK1 receptor antagonist

Formulations:
- 150mg powder for solution for infusion

</td>
<td>

IV infusion over 60 minutes for <12 years; administer over 30 minutes for ≥12 years

Dose for multi-day regimens:

Weight/Age	Day 1	Day 2	Day 3
<6kg	**Not recommended**		
>6kg and >6 months to <12 years	**3mg/kg IV (max 115mg)**	**2mg/kg IV (max 80mg)**	**2mg/kg IV (max 80mg)**
≥12 years	**115mg**	**80mg**	**80mg**

Alternative dosing for single day regimens:

BSA	IV/Oral Dose
>6 months and <2 years AND >6kg	**5mg/kg IV (max 150mg) as a single dose**
>2 years and <12 years	**4mg/kg IV (max 150mg) as a single dose**
≥12 years	**150mg as a single dose**

</td>
<td>

Constipation

Hiccups

Headache

Decreased appetite

Fatigue

GI discomfort

Raised ALT

</td>
<td>

Reserved for patients unable to take oral aprepitant

Can increase ifosfamide-mediated neurotoxicity and irinotecan toxicity. Monitor closely.

Not to be used with chemotherapy regimens that include steroids.

Known CYP3A4 inhibitor; caution in patients receiving concomitant medication metabolised primarily via CYP3A4.

Reduce dose of dexamethasone by 50% if administering alongside fosaprepitant (see dexamethasone monograph)

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<tr>
<td>

Hyoscine hydrobromide

Drug class:
Antimuscarinic

Formulations:
- Topical patch 1mg/72h

</td>
<td>

Topically:

Age	Dose
1 month – 2 years	**¼ patch every 72 hours**
3 – 9 years	**½ patch every 72 hours**
10 years +	**1 patch every 72 hours**

Useful for refractory nausea and vomiting

Will take up to 6 hours to work.

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<td>

Confusion
Constipation
Drowsiness
Dry Mouth
Dizziness
Blurred vision
Difficulty with micturition

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<td>

Avoid using with cyclizine and levomepromazine

Apply to a clean, dry and hairless area of skin behind the ear, avoiding any cuts or irritation.

Wash hands after applying and the skin area after removal.

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</table>

Levomepromazine

Drug class:
Phenothiazine

Formulations:
- 6.25mg and 25mg tablets
- 5mg/mL liquid
- IV injection

Tablets may be crushed and dispersed in water prior to administration

Age	IV/Oral Dose
1 month – 11 years	**IV 0.05mg/kg twice a day** (max 12.5mg/dose) **PO tablet 0.1mg/kg** (max 3.125mg) twice a day **PO liquid 0.1mg/kg** (max 3mg) twice a day
12-17 years	**IV 0.05mg/kg twice a day** (maximum 25mg/dose) **PO tablet 3.125- 6.25 mg twice a day.** (maximum 25 mg twice a day) **PO liquid 3-6mg twice a day** (maximum 25mg twice a day)

Note: Doses may be increased as tolerated if ineffective. If emetogenicity not controlled with BD dosing, consider increasing to TDS. Max dose 1mg/kg (max 25mg) twice daily

IV – administer as slow IV infusion over 30 minutes.

For oral 5mg/mL solution, consult with pharmacy if doses beyond 0.5mg/kg are required due to pegylated glycol content of liquid.

Age	Continuous IV infusion
1month – 11 years	**100-400 micrograms/kg over 24 hours (max 25mg/24 hours)**
12–17years	**5mg/24 hours (increased as necessary up to max 25mg/24 hours)**

Somnolence

Asthenia

Dry mouth

Hypotension

Sedation

Site reaction

Constipation

QT prolongation

Monitor for drowsiness.

Avoid using with cyclizine and hyoscine.
Use with caution with metoclopramide

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

Can be useful in vomiting due to raised intracranial pressure.

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

<table>
<tr>
<td>Lorazepam

Drug class:
Benzodiazepine

Formulations:
• 1mg & 2.5mg tablets (tablets may be halved)
• 4mg/mL IV Injection</td>
<td>IV/Oral:

<table><tr><th>Recommended dose</th></tr><tr><td>50 – 100 micrograms/kg (max 4mg) every 8 – 12 hours</td></tr></table>
IV administration: give as a slow bolus

For anticipatory nausea and vomiting, give one dose on the evening before and one dose 1 hour before starting chemotherapy.</td>
<td>Drowsiness

Amnesia

Confusion

Ataxia

Pain with IV injection</td>
<td>Useful for anticipatory, breakthrough and refractory CINV.

Care in patients receiving ifosfamide as sedation may mask signs of encephalopathy.</td>
</tr>
<tr>
<td>Metoclopramide

Drug class:
Dopamine antagonist

Formulations:
• 10mg tablets
• 5mg/5mL liquid
• 10mg/2ml injection</td>
<td>IV/Oral: See MHRA alert 2013

<table><tr><th>Age</th><th>Recommendation</th></tr><tr><td>< 1 year</td><td>Not recommended</td></tr><tr><td>1–18 years</td><td>0.15mg/kg every 8 – 12 hours (max 10mg per dose TDS)</td></tr></table>
OR
<table><tr><th>Weight</th><th>Oral/IV Dose</th></tr><tr><td>10–14.9kg</td><td>1mg three times a day</td></tr><tr><td>15–19.9kg</td><td>2mg three times a day</td></tr><tr><td>20–29.9kg</td><td>2.5mg three times a day</td></tr><tr><td>30–59.9kg</td><td>5mg three times a day</td></tr><tr><td>≥ 60kg</td><td>10mg three times a day</td></tr></table></td>
<td>Extrapyramidal effects

Hyper-prolactinaemia

Drowsiness

Restlessness</td>
<td>Review with consultant before using. Duration should not exceed 5 days.

Useful for delayed CINV and severe intractable vomiting due to radiotherapy.

Use after levomepromazine failed. Do not use with levomepromazine.

Reduce dose in renal and hepatic impairment

Use with caution with cyclizine and hyoscine – will reduce prokinetic effects

Treat dystonic reactions with IV bolus of PROCYCLIDINE:
<table><tr><td><2 yrs.</td><td>0.5-2mg as a single dose</td></tr><tr><td>2–9 yrs.</td><td>2-5mg as a single dose</td></tr><tr><td>≥ 10 yrs.</td><td>5-10mg as a single dose</td></tr></table></td>
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<table>
<tr>
<td>Nabilone

Drug class:
Cannabinoids

Note: CD Schedule 2

Formulations:
• 250 micrograms capsules
• 1mg capsules</td>
<td>Oral:

<table><tr><th>Age</th><th>Recommendation</th></tr><tr><td>≥ 12 years and ≥ 30kg</td><td>Initial dose 1mg twice daily

Can increase to 2mg twice daily

Maximum daily dose is 6mg per day in 3 divided doses</td></tr></table>
Administer the first dose the night before chemotherapy is due.

Second dose to be administered 1-3 hours before chemotherapy and can be continued for 24-48 hours post last chemotherapy dose.</td>
<td>Drowsiness

Abdominal pain

Hallucination
Vertigo/visual impairment

Euphoria

Gastro-intestinal side effects (e.g., abdominal pain, reduced appetite)

Mood and behavioural changes (may persist 48-72 hours after stopping)</td>
<td>To be started on consultant advice only in adolescents with delayed or refractory CINV, particularly refractory to dexamethasone and ondansetron.

Only prescribed with vHEC where at least 3 anti-emetics from different classes have been used with no benefit.

Not to be used with levomepromazine and lorazepam.

Avoid in severe hepatic impairment.

Cautions: heart disease, psychiatric disorders, hypertension.

Caution with other CNS depressant drugs due to synergistic effects.</td>
</tr>
<tr>
<td>Olanzapine

Drug class:
Atypical antipsychotic

Formulations:
• 2.5mg, 5mg, 10mg, 15mg, 20mg tablets
• 5mg, 10mg and 20mg orodispersible tablets</td>
<td>Oral:

<table><tr><th>Age</th><th>Dose</th></tr><tr><td>>1 year and >10kg</td><td>140micrograms/kg ONCE a day (max per dose 10mg)</td></tr></table>
Round doses to the nearest 1.25mg
Observe slow dose titration to minimise sedation.

Tablets can be halved, quartered, or crushed and dispersed in water to give a proportion.

Orodispersible tablets may be halved and quartered.

NB: use of olanzapine for CINV is an unlicensed indication</td>
<td>Somnolence
Weight gain / increased appetite
Elevated triglycerides
Sedation
Dry mouth
Constipation
Urinary retention
Drowsiness
QTc interval prolongation
Agitation
UV light sensitivity
Bone marrow suppression</td>
<td>Consultant decision to commence after MDT discussion.

Useful for breakthrough and refractory CINV

Only prescribed with vHEC where at least 3 anti-emetics from different classes have been used with no benefit.

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

Do not use with levomepromazine, metoclopramide, cyclizine or hyoscine. Significant risk of increased side effects.</td>
</tr>
</table>

<table>
<tr>
<td>Ondansetron

Drug class:
5HT₃ antagonist

Formulations:
• 4mg and 8mg tablets
• 4mg and 8mg orodispersible tablets
• 4mg/5mL liquid
• 2mg/ml IV injection</td>
<td>IV/Oral:

<table><tr><th>Age</th><th>Dose</th></tr><tr><td>All ages</td><td>5mg/m^2 three times a day (max 8mg/dose)</td></tr></table>
IV: administer as an infusion over 15 minutes

OR for oral dosing (outpatient/discharge)
<table><tr><th>Surface Area m^2</th><th>Oral Dose</th></tr><tr><td><0.3</td><td>1mg three times a day</td></tr><tr><td>0.3 – 0.6</td><td>2mg three times a day</td></tr><tr><td>0.6 – 0.9</td><td>4mg three times a day</td></tr><tr><td>0.9 – 1.2</td><td>6mg three times a day</td></tr><tr><td>≥1.2</td><td>8mg three times a day</td></tr></table></td>
<td>Constipation

Headache

Flushing

Occasional diarrhoea

QT prolongation</td>
<td>Reduce dose in moderate or severe hepatic impairment

Caution with drugs that prolong QT interval (however safe to use with olanzapine)

Dosing for CINV only.

Not recommended for delayed CINV.

Unlicensed for CINV in <6 months. Consider palonsetron as a licensed alternative in this age group.</td>
</tr>
<tr>
<td>Palonosetron

Drug class:
5HT₃ antagonist

Formulations:
• 250 micrograms solution for injection</td>
<td>IV infusion over 15 minutes

<table><tr><th>Age</th><th>Dose</th></tr><tr><td>≥1 month</td><td>20 micrograms/kg (max dose 1500 micrograms) administered as a single 15 minute IV infusion beginning approximately 30 minutes before the start of chemotherapy</td></tr></table>
Avoid the use of 5HT3 antagonists for 5 days after a single dose is given.

Repeat dosing: there is limited evidence on repeat dosing of palonsetron. Based on a mean half-life of 40 hours, where repeat dosing or an alternative 5HT3 antagonist is required, an interval of 5 days in between doses is recommended.</td>
<td>Constipation

Headache

Diarrhoea

Dizziness

Electrolyte imbalance

QTc prolongation</td>
<td>Avoid the use of 5HT3 antagonists for 5 days after a single dose is given.

Ensure this is communicated to POSCUs where shared cared centres are involved.</td>
</tr>
</table>

12 Equality Impact Assessment.

An Equality Impact Assessment (EqIA) has been completed for this document.

This provides assurance that this Trust approved procedural document does not discriminate on the grounds of:

- Religion or belief
- Disability
- Sex or gender
- Human Rights
- Age
- Race or ethnicity
- Sexual orientation
- Socio economic
- Marriage or Civil Partnership
- Pregnancy and Maternity
- Gender re-assignment

The EqIA Reference Number can be found on the document control page.

13 Consultation, Approval and Ratification Process

Consultation Process, Consultation and Communication with Stakeholders

Paediatric Haematology/Oncology Team

Policy Approval Process

Paediatric Chemotherapy Group

Ratification Process

Medicines Management Group – Paediatrics

14 Dissemination and Implementation

14.1 Dissemination

The document will be circulated to the Consultants, Lead Nurse for Haematology / Oncology (Children's Division) and Pharmacy via the Chemotherapy Group.

This guideline will be available on the Trust intranet site

Dissemination to the POSCU centres will be through the MacMillan Team and the Paediatric Cancer Administration and Quality Manager

14.2 Monitoring Compliance of Procedural Documents

Process for Monitoring Compliance.

Compliance with the guideline will be monitored during daily clinical ward visits. No formal audit of compliance is required.

15 References and Bibliograph

1. Paediatric Formulary Committee. BNF for children [online] Available from www.medicinescomplete.com [accessed: 22/06/18].
2. Children's Cancer and Leukaemia Group (CCLG), "Guideline on the management of chemotherapy induced nausea and vomiting" CCLG Supportive Care Group, Version 3, 2025
3. Tomlin S., 2018. Guy's and St Thomas' Paediatric Formulary [online] Available from http://cms.ubqo.com/public/d2595446-ce3c-47ff-9dcc-63167d9f4b80 [accessed 22/06/18].
4. Dupuis LL, Nathan PC. Options for the prevention and management of acute chemotherapy-induced nausea and vomiting in children. Paediatr Drugs. 2003;5(9):597-613. doi: 10.2165/00148581-200305090-00003 [Accessed 12/05/23]
5. Simonian JS, Varanasi S, Richards GJ, Nguyen AV, Diaz-Fong JP, Le J. A critical narrative review of medical cannabis in pediatrics beyond epilepsy, part III: chemotherapy-induced nausea and vomiting and inflammatory bowel disease. Pediatr Med 2020;3:12. doi: 10.21037/pm-20-70 [Accessed 12/05/23]