Birmingham Women's and Children's NHS Foundation Trust

CCLG and Birmingham Women's and Children's Hospital Guideline on the Management of Chemotherapy Induced Nausea and Vomiting

(Applies to BCH site only)

Version:	2.1.1
Approved by:	Chemotherapy Working Group
Ratified by:	Drugs and Therapeutic Committee
Name of originator/author:	Eloise Neumann and Jason Patel
Name of responsible committee/individual:	Chemotherapy Working Group
Date issued:	24th July 2019
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Target audience:	Medical, nursing and pharmacy staff within the Haematology Oncology Specialty

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1. Introduction

This guideline has been developed in order to ensure that the prophylaxis and treatment of chemotherapy-induced nausea and vomiting is provided in a manner which aims to take account of the emetogenic stimulus provided by the chemotherapy and the known actions of the individual anti-emetic drugs.

2. Purpose

This guideline aims to provide a logically consistent framework within which prescribing will be done, and other support to the patient provided.

It also addresses the issue of costs. Expenditure on 5-HT_3 blockers such as ondansetron is still considerable and requires appropriate management.

3. Scope

3.1 Includes

All patients with a haematology/oncology diagnosis receiving chemotherapy.

3.2 Excludes

All patients without a haematology/oncology diagnosis and any patient NOT receiving chemotherapy.
These guidelines should be used with caution in patients undergoing allogenic stem cell transplant.

4. Duties

4.1 Duties within the Organisation

The lead officer for this document is identified on the title page.

4.2 Identification of Stakeholders

The following stakeholders have been identified within BCH: The Chemotherapy Working Group (CWG); the Cancer Locality Group; the Haematology Oncology Program meeting; nursing and support staff within the Haematology Oncology specialty.

Outside BCH: The Children's Cancer Expert Advisory Group to the West Midlands Cancer Alliance; West Midlands Cancer Alliance Chemotherapy Advisory Group.

5. Method for development

This guideline is derived from a national framework document for local implementation. It relies on the work undertaken by the Canadian-led POGO group who developed three clinical practice

guidelines for the prevention and management of chemotherapy-induced nausea and vomiting (CiNV) in children.

The POGO group convened an international guideline panel to create a clinical practice guideline based on accepted best-practice methods (similar to those used by NICE). The group undertook a series of focussed systematic reviews addressing management question in the prevention of CiNV, and the treatment of breakthrough, refractory and anticipatory CiNV. They then summarised this evidence and debated it, placing it in clinical context and developing recommendations. The guidelines were then subject to international stakeholder review before publication.

Now all phases of the management have been completed, the CCLG Supportive Care group has undertaken to summarise and contextualise in a UK framework to provide an up to date framework for local guidelines to be developed from. This involved the summarising of the guidelines, discussion of the recommendations made within a UK licencing context, and providing a quick-summary guide for use. Recommendations were then circulated via the CCLG Guideline Development Group panel and feedback incorporated.

The overall guideline has been updated by Eloise Neumann (ANP) and Jason Patel (Lead cancer pharmacist) to incorporate a prescribing flow diagram. Comments and suggestions were incorporated until a final version was agreed by the CWG and ratified by the Head of Chemotherapy (HoC) and Lead Cancer Clinician (LCC).

6. Content

Chemotherapy-induced nausea and vomiting (CINV) are said to be the most documented distressing side-effects of childhood cancer treatment, potentially influencing compliance with future treatments if not managed appropriately (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 co-ordinated by the vomiting centre situated in the medulla which receives input from the chemoreceptor trigger zone (CTZ) found in the area postrema and is outside of the blood-brain barrier. It 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 G.I input. CINV may result from chemo or CSF fluid 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.

The different stages of CINV are acute (0-24hrs after 1st dose); delayed (24hrs-5 days post chemo) 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 NK_1 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 guidelines, but not developed according to the recommendations of the NICE Guideline Methodology. An international collaboration, centred in the Canadian POGO group, 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.

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 the 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)
- Moderately emetogenic chemotherapy (MEC)
- Low emetogenicity chemotherapy
- 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, adapted to their own personal experience.

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

Prophylaxis: Highly emetogenic chemotherapy

For children and young people receiving highly emetogenic chemotherapy a combination of 5HT3 antagonist, dexamethasone and aprepitant should be prescribed unless there is a contraindication

Contraindications include

- Age < 6 months (aprepitant, refer to the drug section below)
- Contraindication to dexamethasone (e.g. steroids included in treatment protocol). Refer to the drug section, see below.
- Drug interaction with aprepitant. Refer to the drug section see below.

For children and young people receiving highly emetogenic chemotherapy with a contraindication to aprepitant a combination of 5HT3 antagonist and dexamethasone should be prescribed unless there is a contraindication

Contraindications include

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

For children and young people receiving highly emetogenic chemotherapy with a contraindication to aprepitant and dexamethasone receive a)Ondansetron or b) combination of 5HT3 antagonist (Ondansetron) and levomepromazine / metoclopramide (see table below)/or nabilone (in adolescents).

Prophylaxis: Moderately emetogenic chemotherapy

For children and young people receiving moderately emetogenic chemotherapy a combination of 5HT3 antagonist, dexamethasone should be prescribed unless there is a contraindication.

Contraindications include

- Contraindication to dexamethasone (e.g. steroids included in treatment protocol). See table below with dexamethasone.

For children and young people receiving moderately emetogenic chemotherapy with a contraindication to dexamethasone a combination of 5HT3 antagonist and aprepitant should be prescribed unless there is a contraindication.

Contraindications include

- Age < 6 months
- Drug interaction with aprepitant

For children and young people receiving moderately emetogenic chemotherapy with a contraindication to aprepitant and dexamethasone receive a) ondansetron or b) combination of 5HT3 antagonist and levomepromazine/ metoclopramide (see table below or nabilone).

Prophylaxis: Low emetogenic chemotherapy

For children and young people receiving moderately emetogenic chemotherapy, a 5HT3 antagonist should be prescribed.

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 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, addition of levomepromazine or metoclopramide (see table below) to the treatment should be considered

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, substitution ondansetron for a) granisetron in treatment should be considered./Granisetron patches can be used -refer to table.

- 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/ young people who continue to suffer refractory nausea &/or vomiting, addition of
  a) Levomepromazine infusion instead of IV or lorazepam or
  b) Acupressure should be considered.

Anticipatory nausea or vomiting

Anticipatory refers to significant nausea or vomiting prior to the delivery of chemotherapy. Research in this area is particularly weak. Lorazepam is used with good effect in centres. Refer to dosing info below. Some centres use ondansetron+/- levomepromazine up to 24hrs prior to chemotherapy.

For children and young people who develop anticipatory nausea &/or vomiting, psychological interventions such as hypnosis or systematic desensitization may be offered

For children and young people who develop anticipatory nausea &/or vomiting, low dose lorazepam 0.05-0.1 mg/kg may be prescribed the day before, and the first day of, chemotherapy

7. Education & Training

All staff prescribing anti-emetics for haematology / oncology patients will be expected to familiarize themselves and comply with these guidelines. Anti-emetic prescribing will be included in induction for new doctors and supplementary prescribers joining the specialty. Nursing staff will be educated on the pathophysiology of chemotherapy-induced nausea and vomiting and how to manage it.

8. References

Source Guidelines:

POGO Guidelines for the management of chemotherapy induced nausea and vomiting. http://www.pogo.ca/healthcare/practiceguidelines/

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), e1542–e1549.

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.

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.889-89.

Other References:

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

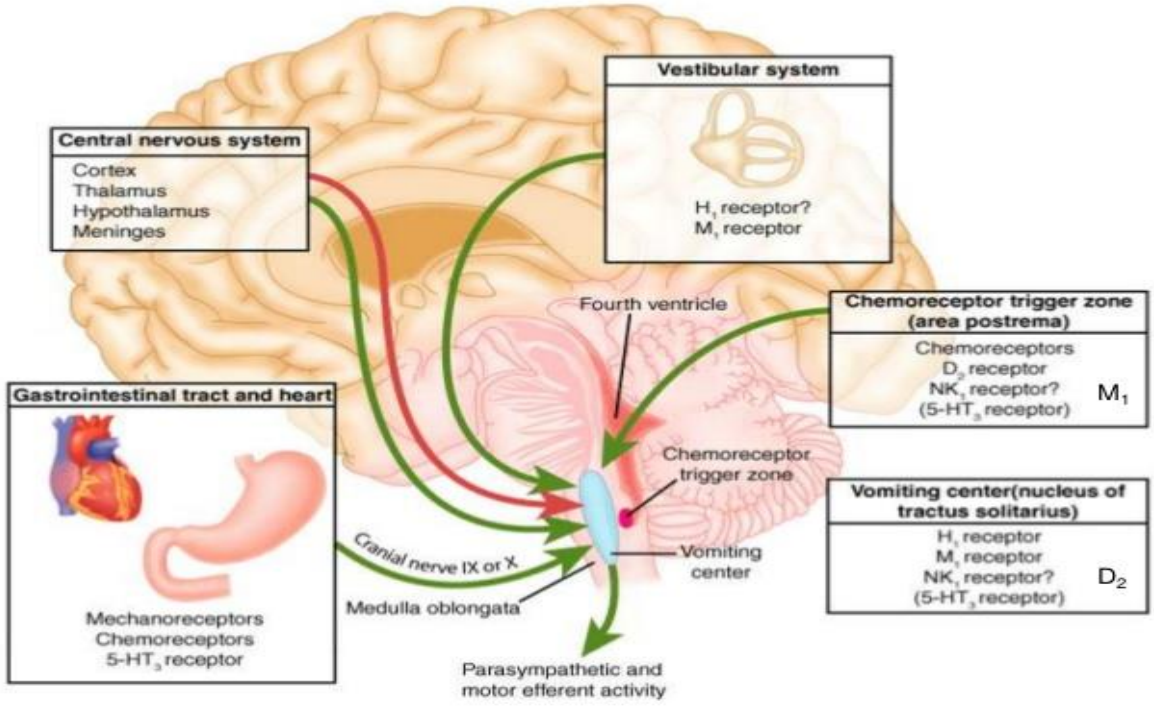
Krakauer, E., Zhu, A., Bounds, B., Sahani, D., McDonald, K. and Brachtel, E. (2005) Case 6-2005 — A 58-Year-Old Man with Esophageal Cancer and Nausea, Vomiting, and Intractable Hiccups. *New England Journal of Medicine,* 352, pp.817-825.

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., Kollar, D., Taylor, o., Bryant, r., Crockett, K., Gregurich and Hockenberrry, M. (2012) Nausea and Vomiting Perspectives among Children Receiving Moderate to Highly Emetogenic Chemotherapy Treatment. *Cancer Nursing*. 35(3), pp. 203-210.

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

APPENDIX 1: SITE OF ACTIONS OF ANTI-EMETICS



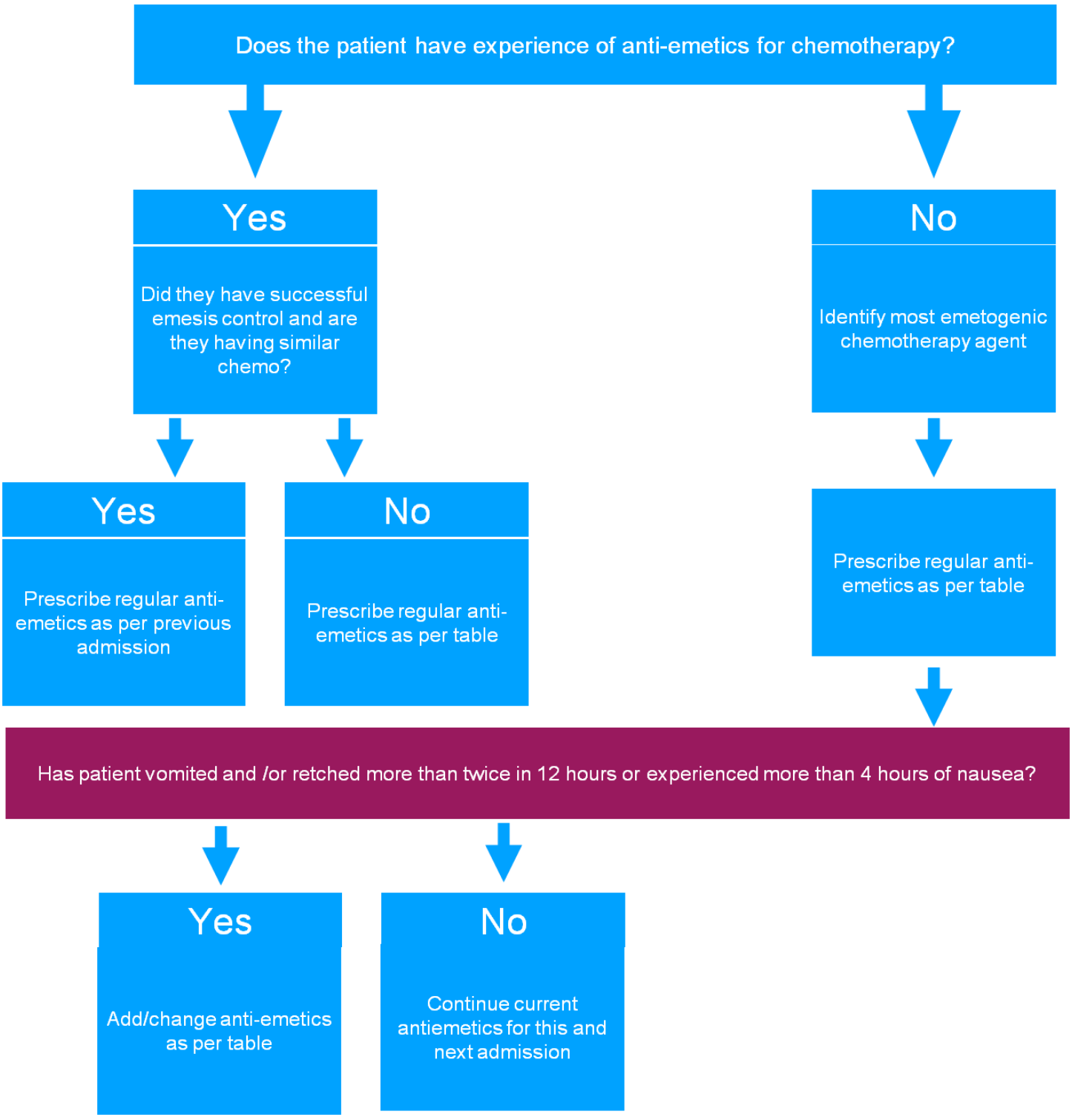
Krakauer et al. (2005). New England Journal of Medicine, 352, 817.

	Dopamine$_2$-receptor antagonist (D2)	Histamine$_1$-receptor antagonist (H1)	Acetylcholine receptor antagonist	5-hydroxytryptamine receptor$_3$-receptor antagonist	5-hydroxytryptamine receptor$_2$-receptor antagonist	5-hydroxytryptamine receptor$_4$-receptor agonist	NK1 inhibitor (NK1)
Dexamethasone				+++			
Aprepitant							+++
Cyclizine		++	++				
Hyoscine hydrobromide			+++				
Levomepromazine	++	+++	++		+++		
Metoclopramide	++			+		++	
Ondansetron				+++			

Avoid Cyclizine and Metoclopramide together – Metoclopramide is a prokinetic (stimulates the gut) while Cyclizine slows it down. Can be used together in palliative scenario.

Levomepromazine covers actions of Metoclopramide, Cyclizine and Hyoscine but has a greater number of side effects.

APPENDIX 2: OVERALL APPROACH FLOW-CHART



APPENDIX 3: EMETOGENICITY OF CHEMOTHERAPY NB BONE MARROW TRANSPLANT PATIENTS SEE SEPARATE LOCAL GUIDANCE

Very High emetogenic potential	High emetogenic potential
Cisplatin Cyclophosphamide > 2g/m^2 Ifosfamide Melphalan Thiotepa ***Combination chemotherapies:*** Cyclophosphamide + anthracycline Cyclophosphamide + etoposide Etoposide + Ifosfamide Doxorubicin + Ifosfamide Cytarabine 300 mg/m^2 + etoposide Doxorubicin + methotrexate 5g/m^2	Dactinomycin (actinomycin-D) Carboplatin Carmustine Cyclophosphamide 1g/m^2 - 2g/m^2 Cytarabine 3g/m^2/dose Dacarbazine Methotrexate ≥8 g/m^2

Moderate emetogenic potential		
Aldesleukin	Daunorubicin	Irinotecan
Arsenic trioxide	Daunorubicin liposomal	Lomustine
Azacitidine	Docetaxel	MTX
Cladribine	Doxorubicin	≥1g/m^2 to <12g/m^2
Clofarabine	Etoposide	Mitoxantrone
Cyclophosphamide	Idarubicin	Procarbazine
< 1g/m^2	Imatinib	Temozolomide
Cytarabine >200mg/m^2 to <3g/m^2	Inotuzumab	Treosulfan

Low emetogenic potential		
Alemtuzumab	CH14.18 Antibodies	Nelarabine
ATG	Cyclophosphamide <300 mg/m^2	Rituximab
Aspariginase	Cytarabine <200 mg/m^2	Tioguanine
Bevacizumab	Fludarabine**	Topotecan
Bleomycin	Gemcitabine	Vinblastine
Busulfan**	Gemtuzumab	Vincristine
Chlorambucil	Mercaptopurine	Vindesine
	Methotrexate < 1g/m^2	Vinorelbine

Anticipatory Nausea and Vomiting	
Anticipatory refers to significant nausea or vomiting prior to the delivery of chemotherapy.	**<u>Lorazepam PO:</u> Give one dose evening before and one dose 1 hr before starting chemotherapy**

APPENDIX 4: ANTI-EMETICS RECOMMENDED DOSAGES AND USAGE INSTRUCTIONS

Aprepitant

Drug class:

NK1 receptor antagonist

Formulations:

125mg, 80mg capsule, 125mg powder for oral suspension

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

Or use 3mg/kg on Day 1 and 2mg/kg on Days 2 & 3. Round to the nearest 5mg.

Weight	Day 1	Day 2	Day 3
<6kg	Not recommended for <6 months old		
6kg–7.9kg	25mg	15mg	15mg
8kg–9.9kg	30mg	20mg	20mg
10kg–11.9kg	35mg	25mg	25mg
12kg–14.9kg	45mg	30mg	30mg
15kg–19.9kg	60mg	40mg	40mg
20kg–24.9kg	75mg	50mg	50mg
25kg–29.9kg	90mg	60mg	60mg
30 kg and above	125mg	80mg	80mg

Diarrhoea, hiccups, headache, decreased appetite, cough, neutropenia (slightly prolonged compared to without aprepitant).

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. Not to be given with the following:

Etoposide, Ifosfamide, Imatinib, Irinotecan, vincristine, vinblastine, Vinorelbine, Phenytoin, carbamazepine, phenobarbitone, warfarin, BZD (lorazepam), clarithromycin and Rifampicin. Also do not give the above chemotherapy if aprepitant was given in the last two weeks.

Dose of dexamethasone must be halved.

<table>
<tr>
<td>Cyclizine

Drug class:

Antihistamine

Formulations:

50mg tablets, IV injection</td>
<td>IV/Oral:

<table>
<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>
</td>
<td>Drowsiness, Dry mouth

Blurred vision

Urinary retention

Restlessness

Insomnia, Tachycardia</td>
<td>Avoid using with Hyoscine and Levomepromazine

For the purpose of this guidelines use for emesis of raised intracranial pressure. Palliative care, irradiation sickness and opiate induced vomiting.

For continuous IV or SC infusion – dilute with Glucose 5%.</td>
</tr>
</table>

<table>
<tr>
<td>Dexamethasone

Drug class:

Corticosteroid

Formulations:

2mg tablets

0.5mg tablets

2mg/5mL liquid

IV injection</td>
<td>IV/Oral:

<u>Contra-indicated</u>: Brain tumour patients and those already on steroids - Consultant decision ONLY

<table>
<tr><th><u>Weight</u></th><th><u>Dose</u></th></tr>
<tr><td></=15kg</td><td>1mg</td></tr>
<tr><td>16-25kg</td><td>2mg</td></tr>
<tr><td>26-35kg</td><td>3mg</td></tr>
<tr><td>36-45kg</td><td>4mg</td></tr>
<tr><td>46-55kg</td><td>5mg</td></tr>
<tr><td>>55kg</td><td>6mg</td></tr>
</table>

Frequency can be BD or TDS.</td>
<td>Adrenal suppression

Gastric irritation

Osteoporosis

Weight gain, insomnia

Mood and behavioural problems</td>
<td>Give 1st dose with Ondansetron, before chemotherapy. For maximum of 5 days

IV Doses should be infused. Effective for delayed emesis

Dose of dexamethasone must be halved when used in combination with Aprepitant.

Contra-indicated: <u>Brain tumour patients and those already on steroids</u> (allogenic BMT, SCT, and AML&ALL) & those on mifamurtide. Caution in osteosarcoma patients (discuss with the consultant).</td>
</tr>
</table>

<table>
<tr>
<td>Granisetron patch 3.1mg/24 hours</td>
<td><u>12 years -18yrs</u>

Only available as 2nd line therapy and if no ondansetron is available. DISCUSS WITH PHARMACY.</td>
<td>Constipation, headache, rash.

Transient increase in liver enzymes.</td>
<td>Patch can be kept on for 7 days

Remove at least 24 hours after chemotherapy has been completed.

Not licenced 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.</td>
</tr>
<tr>
<td>Hyoscine Hydrobromide

Drug class:

Anticholinergic/

Antimuscarinic

Formulations:

Topical Patch 1mg/72 hrs</td>
<td>Topically:

Will take up to 6 hours to work

<table>
<tr><td>1 month – 2 years</td><td>1/4 of a patch every 72 hours</td></tr>
<tr><td>3 – 9 years</td><td>1/2 of a patch every 72 hours</td></tr>
<tr><td>10 years+</td><td>1 patch every 72 hours</td></tr>
</table>
</td>
<td>Drowsiness

Dry mouth

Dizziness

Blurred vision

Difficulty with micturition</td>
<td>Avoid using with Cyclizine, metoclopramide and Levomepromazine

For refractory emesis

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.</td>
</tr>
</table>

Levomepromazine

Drug class:

Phenothiazine

Formulations:

6mg tablet, 25mg Tablets

(tablets may be halved and dispersed)

IV Injection

Oral

1 month – 11 years	**0.05-0.2mg/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- 6.25 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 6mg tablet in 6mL of water and give proportion. **Doses greater than 3mg** – round to nearest 3mg or 12.5mg. Liquid can be manufactured in some centres.

Slow IV Infusion/bolus:

0.005mg/kg TWICE daily or daily

Continuous IV or SC Infusion:

1 month – 11 years	Maximum 25mg/24 hours continuous infusion 100-400microgram/kg in 24 hrs
12-17 years	**5mg to 25mg over 24 hours** increasing as necessary to a max of 25mg/24 hours

Somnolence

Asthenia

Dry mouth

Hypotension

Sedation

Site reaction

constipation

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

Avoid use in hepatic impairment.

Reduce dose in renal impairment.

Effective for delayed emesis.

Can be useful in vomiting due to raised intracranial pressure.

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

Lorazepam Drug class: *Benzodiazepine* Formulations: 1mg &2mg tablets (tablets may be halved), IV Injection	**Slow IV bolus/Oral:** **0.05-0.1mg/kg (max 4mg) every 8–12 hours** For anticipatory nausea and vomiting, give one dose evening before and one dose 1 hour before starting chemotherapy.	Drowsiness Amnesia Confusion and ataxia Pain with IV injection	

Metoclopramide

Drug class:

Dopamine antagonist

Formulations:

10mg Tablets

5mg/5mL liquid

10mg/2ml Injection

IV/Oral: Prevention of delayed chemotherapy-induced nausea and vomiting

0.2mg/kg THREE a day – OR dose banded as per below

Prescribe for as short a duration as possible and review regularly

Contraindicated in children <1 year.
Maximum 10mg per dose TDS.
See MHRA alert 2013.

Weight	Oral Dose	IV Dose
10–14.9kg	**1mg**	**1mg**
15–19.9kg	**2mg**	**2mg**
20–29.9kg	**2.5mg**	**2.5mg**
30–60kg	**5mg**	**5mg**
>60kg	**10mg**	**10mg**

Extrapyramidal effects

Hyperprolactinaemia

Drowsiness

Restlessness

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 cyclizine and hyoscine – will reduce prokinetic effects

Treat dystonic reactions with IV bolus of **PROCYCLIDINE:**

<2 yrs.	0.5-2mg as a single dose
2–10 yrs.	2-5mg as a single dose
>10 yrs.	5-10mg as a single dose

Usually effective in 5-10 min but may take up to 30min

Nabilone **<u>Preparations:</u>** Capsule 1mg	Oral >30kg 1mg three times a day	Dizziness, drowsiness, behavioural alterations, dry mouth, ataxia, and postural hypotension. Hallucination, 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.	A cannabinoid drug with central action. <u>Used</u> in adolescents when refractory to dexamethasone and ondansetron. It is used for acute, delayed and refractory emesis. Used for high & very high when 1st, 2nd & 3rd line failed for subsequent cycles. Start the night before, duration of chemo and until 48 hours after chemo. Do not use with levomepromazine and lorazepam.

Ondansetron

Drug class:

$5HT_3$ antagonist

Formulations:

4mg tablets

8mg tablets

4mg/8mg orodispersible film*

4mg/5mL liquid

IV 2mg/ml

Sublingual melts:4mg&8mg

IV/Oral:

5mg/m^2 TWO or THREE times a day (Max 8mg per dose) – dose banding can be used in as below

Weight	SA m^2	Oral Dose	IV Dose
4–4.9kg	**0.26–0.29**	**1mg**	**1.5mg**
5–6.9kg	**0.30–0.37**	**2mg**	**1.5mg**
7–8.9kg	**0.38–0.45**	**2mg**	**2mg**
9–11.9kg	**0.46–0.55**	**2mg**	**2.5mg**
12–16.9kg	**0.56–0.70**	**4mg**	**3mg**
17–23.9kg	**0.71–0.89**	**4mg**	**4mg**
24–29.9kg	**0.9–1.09**	**4mg**	**5mg**
30–38.9kg	**1.1– 1.2**	**6mg**	**6mg**
>39	**>1.2**	**8mg**	**8mg**

Constipation

Headache

Flushing

Occasional diarrhoea

*Use **Orodispersible film** if possible as it is cheaper than liquid ondansetron for patients with SA >0.56m^2 or wt. >12kg.

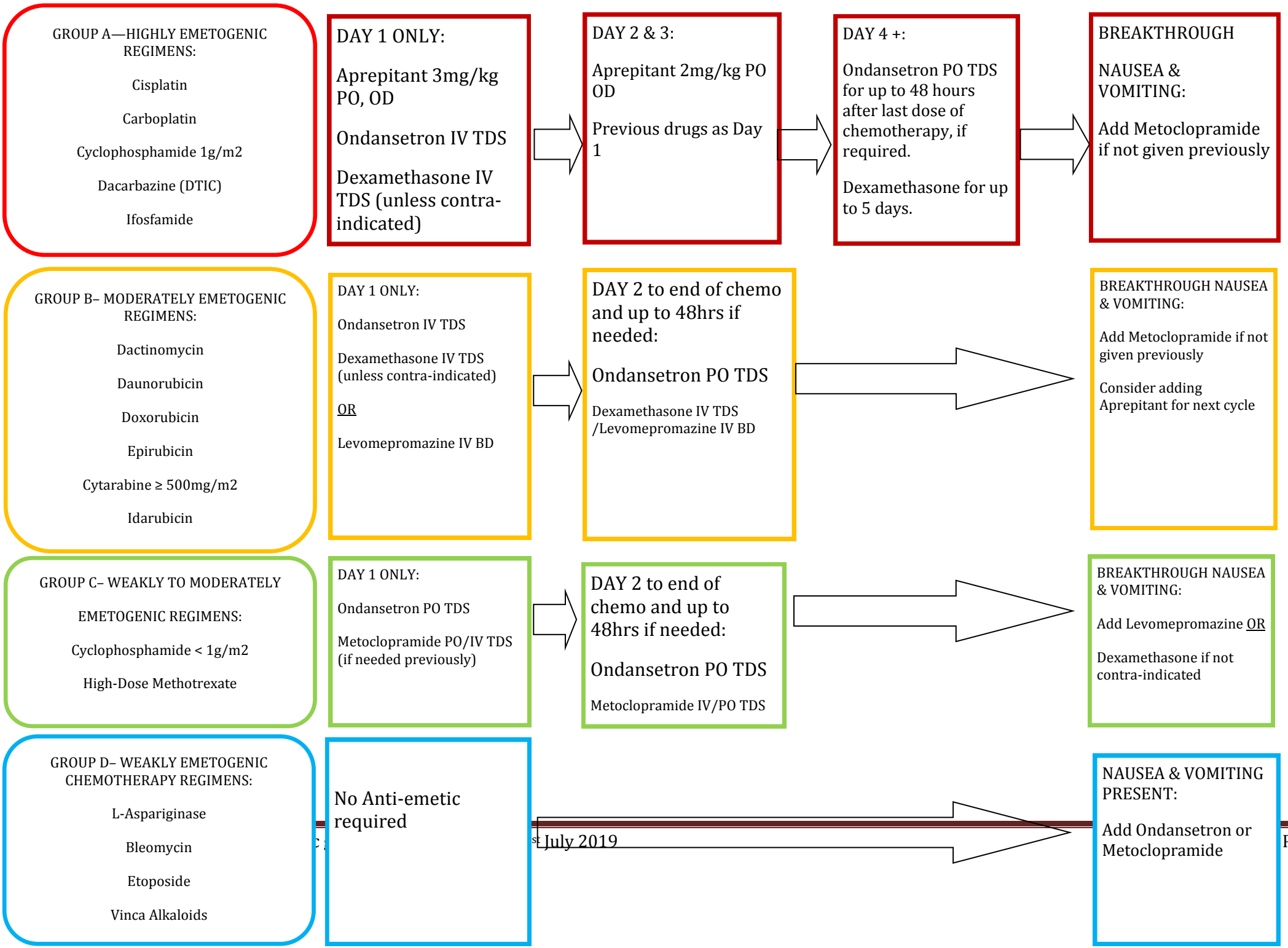
Each film is a 4mg dose and it cannot be halved.

Reduce dose in moderate or severe hepatic impairment

Do not use with drugs that prolong QT interval

Less effective for delayed emesis use metoclopramide

PALONOSETRON *$5HT_3$ antagonist* **Preparation:** **250 micrograms/5ml injection**	**<u>Dosing:</u>** **Please speak to Jason Patel, Siema Akram, Dr. Jenny Adamski, Eloise Neumann or Fran Thompson before prescribing this drug. It is for restricted use ONLY.** **Dosing is per the SPC.**	headache. dizziness jerky body movements abnormal heart rate coughing or shortness of breath	


GROUP A—HIGHLY EMETOGENIC REGIMENS:
Cisplatin
Carboplatin
Cyclophosphamide 1g/m2
Dacarbazine (DTIC)
Ifosfamide
DAY 1 ONLY:
Aprepitant 3mg/kg PO, OD
Ondansetron IV TDS
Dexamethasone IV TDS (unless contra-indicated)
DAY 2 & 3:
Aprepitant 2mg/kg PO OD
Previous drugs as Day 1
DAY 4 +:
Ondansetron PO TDS for up to 48 hours after last dose of chemotherapy, if required.
Dexamethasone for up to 5 days.
BREAKTHROUGH NAUSEA & VOMITING:
Add Metoclopramide if not given previously
GROUP B– MODERATELY EMETOGENIC REGIMENS:
Dactinomycin
Daunorubicin
Doxorubicin
Epirubicin
Cytarabine ≥ 500mg/m2
Idarubicin
DAY 1 ONLY:
Ondansetron IV TDS
Dexamethasone IV TDS (unless contra-indicated)
OR
Levomepromazine IV BD
DAY 2 to end of chemo and up to 48hrs if needed:
Ondansetron PO TDS
Dexamethasone IV TDS /Levomepromazine IV BD
BREAKTHROUGH NAUSEA & VOMITING:
Add Metoclopramide if not given previously
Consider adding Aprepitant for next cycle
GROUP C– WEAKLY TO MODERATELY EMETOGENIC REGIMENS:
Cyclophosphamide < 1g/m2
High-Dose Methotrexate
DAY 1 ONLY:
Ondansetron PO TDS
Metoclopramide PO/IV TDS (if needed previously)
DAY 2 to end of chemo and up to 48hrs if needed:
Ondansetron PO TDS
Metoclopramide IV/PO TDS
BREAKTHROUGH NAUSEA & VOMITING:
Add Levomepromazine OR
Dexamethasone if not contra-indicated
GROUP D– WEAKLY EMETOGENIC CHEMOTHERAPY REGIMENS:
L-Aspariginase
Bleomycin
Etoposide
Vinca Alkaloids
No Anti-emetic required
NAUSEA & VOMITING PRESENT:
Add Ondansetron or Metoclopramide