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

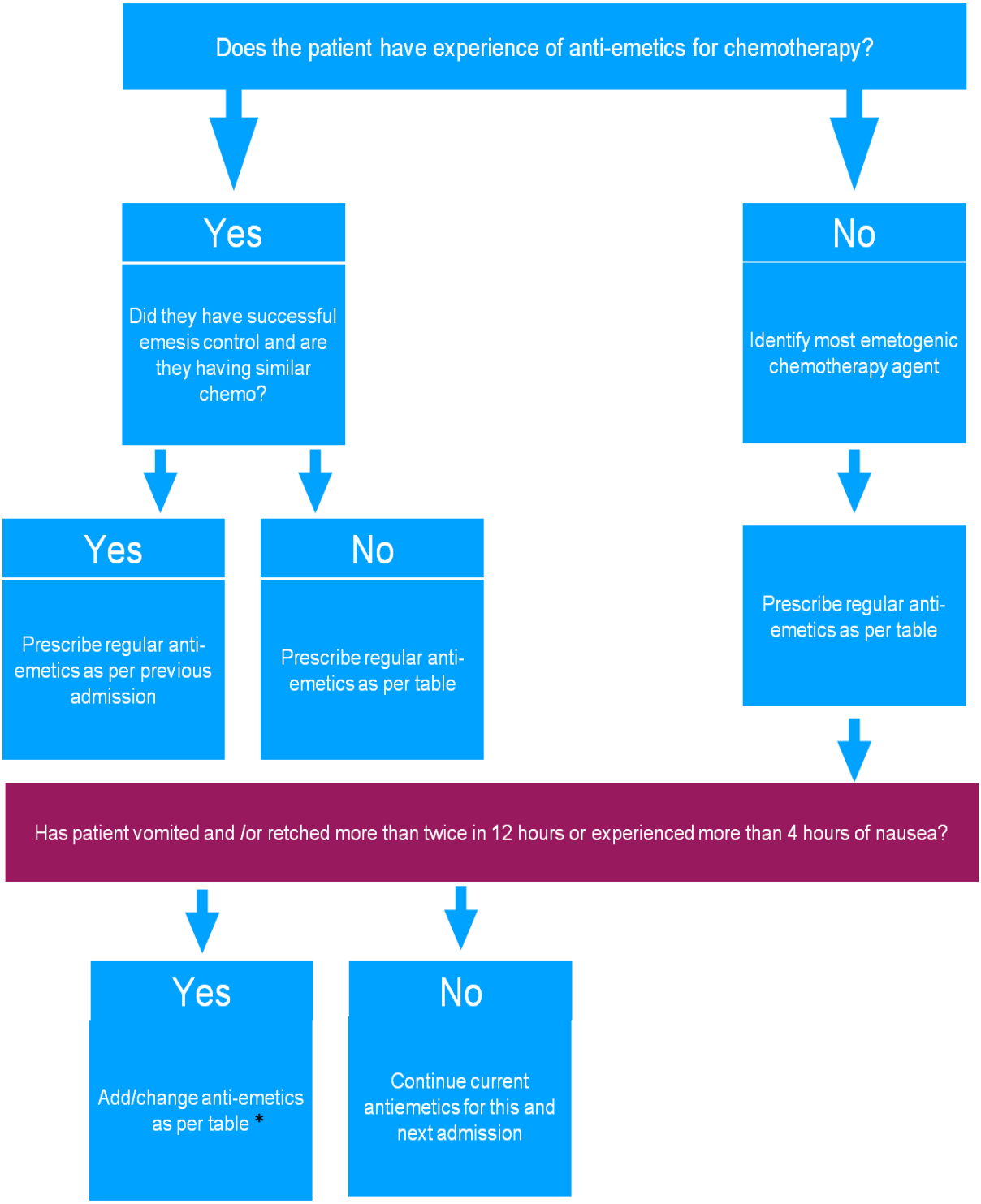

Table 1: MANAGEMENT OF CHEMOTHERAPY INDUCED NAUSEA AND VOMITING (CINV)

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 ≥ 3 concurrent days. Do not prescribe any other 5HT3 antagonist (e.g. ondansetron) within 5 days of receiving palonosetron.

Very Highly Emetogenic Chemotherapy (1)	
Cisplatin **Melphalan**	**Step 1:** Aprepitant + ondansetron/palonosetron** + dexamethasone* (50% dose) **Step 2:** Add regular levomepromazine If fails step 1: For subsequent cycles (if ≥ 6 months old) : Aprepitant + ondansetron/palonosetron** + dexamethasone* (50% dose) + levomepromazine For patients < 6 months old or <6kg do not give aprepitant: **Step 1:** Ondansetron + levomepromazine **Step 2:** Add regular dexamethasone* If fails step 1: For subsequent cycles (if <6 months old or <6kg): Ondansetron + levomepromazine + dexamethasone* **Delayed CINV** Oral aprepitant + dexamethasone* (50% dose) Consider addition of levomepromazine if not achieving satisfactory control
Very Highly Emetogenic Chemotherapy (2)	
Cyclophosphamide >2g/m² **Ifosfamide** **Cyclophosphamide + anthracycline** **Cyclophosphamide + etoposide** **Doxorubicin + Ifosfamide** **Cytarabine 300mg/m² + etoposide**	**Step 1:** Ondansetron/palonosetron** + levomepromazine + PRN dexamethasone* **Step 2:** Add regular dexamethasone* If fails step 2: For subsequent cycles escalate to treatments from the "very highly emetogenic chemotherapy regimens (1)" i.e. (if ≥ 6 months old and >6kg) aprepitant + ondansetron/palonosetron** + dexamethasone* (50% dose) **Delayed CINV** Oral levomepromazine

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

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

IV fosaprepitant must only be prescribed when the oral route of aprepitant is not possible. The decision to use must be made by the consultant only.

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
Aprepitant (oral) (NK1 receptor antagonist) **Preparations:** **Capsules:** 80mg, 125mg **125mg powder for oral suspension:** (to give 25mg/ml suspension)	**6 months to <12 years old and ≥6kg:** Day 1: 3mg/kg once daily (max. dose 125mg) Day 2 & 3: 2mg/kg once daily (max. dose 80mg) **≥12 years old:** Day 1: 125mg once daily Day 2 & 3: 80mg once daily **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.** **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.**	NB. Can increase ifosfamide mediated neurotoxicity and irinotecan toxicity – discuss with consultant before prescribing. Can increase exposure to vinca alkaloids. Can increase exposure to tyrosine kinase inhibitors. Monitor closely. Dose of dexamethasone must be reduced by 50% when given with aprepitant. Caution – check for drug interactions.
Cyclizine (Antihistamine) **Preparations:** **IV:** 50mg/mL **Tablets:** 50mg scored **Oral solution:** 5mg/5mL	**IV bolus/oral:** 1 month – 5 years: 0.5-1mg/kg (max 25mg) up to three times daily 6 – 11 years: 25mg up to three times daily 12 – 18 years: 50mg up to three times daily	Avoid using with levomepromazine or olanzapine.
Dexamethasone (Corticosteroid) **Preparations:** **IV:** 6.6mg/2ml **Oral Liquid:** 10mg/5mL **Tablets:** 500microgram, 2mg	**IV/oral:** SA ≤ 0.6m^2 : 2mg twice a day SA ≥ 0.6m^2 : 4mg twice a day **Use for maximum of 5 days.** Doses can be increased to 2.5-5mg/m^2 up to three times a day.	Dose of dexamethasone must be reduced by 50% when given with aprepitant. **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

Fosaprepitant (IV) (NK1 receptor antagonist) **Preparations:** **IV:** 150mg vial	**<u>For multi-day chemotherapy regimens:</u>** **>6kg and >6 months to <12 years old (IV infusion over 60 minutes):** Day 1: 3mg/kg once daily (max. dose 115mg) Day 2 & 3: 2mg/kg once daily (max. dose 80mg) **≥ 12 years old (IV infusion over 30 minutes):** Day 1: 115mg once daily Day 2 & 3: 80mg once daily **<u>For single day chemotherapy regimens:</u>** **> 6kg and > 6 months to < 2 years old (IV infusion over 60 minutes):** 5mg/kg as a single dose (max. dose 150mg) **>2 years to < 12 years old (IV infusion over 60 minutes):** 4mg/kg as a single dose (max. dose 150mg) **> 12 years old (IV infusion over 30 minutes):** 150mg as a single dose	NB: Can increase ifosfamide mediated neurotoxicity and irinotecan toxicity – discuss with consultant before prescribing. Can increase exposure to vinca alkaloids. Can increase exposure to tyrosine kinase inhibitors. Monitor closely. Dose of dexamethasone must be reduced by 50% when given with fosaprepitant. Caution – check for drug interactions.
Levomepromazine (Phenothiazine) **Preparations:** **IV:** 25mg/mL **Oral suspension:** 5 mg/mL **Tablets:** 25mg scored	**IV infusion (over 30 minutes):** 0.1mg/kg twice daily (max single dose 6.25mg) **IV continuous infusion:** 0.25-0.5mg/kg/24 hours (max dose 25mg/24 hours) **Oral:** 0.1 – 0.2 mg/kg twice daily (max single dose 12.5mg)	Monitor for drowsiness. Do not use with cyclizine, olanzapine or 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 as sedation may mask signs of encephalopathy.
Lorazepam (Benzodiazepine) **Preparations:**	**Oral:** 50 – 100 micrograms/kg (max 4mg) every 8-12 hours	Care in patients receiving ifosfamide since sedation may mask signs of encephalopathy

Tablets: 500 microgram, 1mg, **Oral Suspension:** 200 microgram/mL (note – this is an extemporaneous preparation made in pharmacy, so there may be a delay in obtaining this product)	**For anticipatory nausea and vomiting, give one dose the evening before and once dose 1 hour before starting chemotherapy.**	
Metoclopramide (dopamine antagonist) **Preparations:** **Tablets:** 10mg **Oral solution:** 5mg/5mL **IV:** 5mg/1mL injection	**>1 year:** 100-150 microgram/kg (max 10mg) every 8-12 hours **To be used for a maximum of 5 days – not for long term use.**	To be used on advice of consultant only. Do not use with levomepromazine or olanzapine. Treat dystonic reactions with procyclidine (dosing as per BNFc).
Nabilone (oral) (Cannabinoid) **Preparations:** **Capsules:** 0.25mg and 1mg	**>12 years and >30kg:** 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. **First dose should be taken the night before chemotherapy and the second dose 1-3 hours before the first dose of chemotherapy.** **Max 6mg per day, given in 3 divided doses.**	Note – Schedule 2 Controlled Drug Do not use with levomepromazine or lorazepam. To be used on advice of consultant only.
Olanzapine (Atypical Antipsychotic) **Preparations:** **Tablets:** 2.5mg, 5mg, 7.5mg, 10mg	**>1 year and >10kg:** 140 microgram/kg once daily. Increase as necessary to a max dose of 10mg per day in one or two divided doses Doses to be rounded to nearest 1.25mg.	Do not use with levomepromazine, metoclopramide and cyclizine. Note – very long half life with a long onset of action

Orodispersible tablets: 2.5mg, 5mg, 7.5mg, 10mg **Tablets can be halved or quartered. Tablets can be crushed and dispersed in water.**		To be used on advice of consultant only.
Ondansetron ($5HT_3$ antagonist) **Preparations:** **IV:** 8mg/4mL **Oral Liquid:** 4mg/5mL **Tablets:** 4mg, 8mg **Sublingual melts:** 4mg, 8mg **Orodispersible films:** 4mg, 8mg	**IV infusion (over 15 minutes):** 5mg/m² three times daily (max single dose 8mg) **Oral:** every 8 or 12 hours <0.3m² - 1mg 0.3-0.6m² 2mg 0.6-0.9m² 4mg 0.9-1.2m² 6mg >1.2m² 8mg (max single dose 8mg)	Reduce dose in moderate/severe hepatic impairment. Do not use with drugs that prolong QT interval. Dosing is for CINV only. Not recommended for delayed CINV
Palonosetron ($5HT_3$ antagonist) **Preparations:** **IV:** 250 microgram/5ml	**≥ 1 month old:** IV infusion (over 15 minutes): 20 micrograms/kg (max 1500 micrograms) beginning approximately 30 minutes before the start of chemotherapy	**Do not prescribe any other 5HT3 antagonist (e.g. ondansetron) within 5 days of receiving palonosetron.**

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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Version Control Table				
Version	Date	Author(s)	Status	Comment(s)
5	May 25	Colin Thorbinson Rachael Ruddin	Current	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,	Archived	

		Felicity Heard		
2	Aug 10	Lisa Howell, Felicity Heard	Archived	
1	Pre Sep 01	Pharmacy	Archived	

Review and Revision(s) Log *Record of revision(s) made to guidelines since Version 1*			
Section Number	Page Number	Revision(s) made	Reason for revision(s)
	2 & 3	Ondansetron IV 15 min infusion	SPC change
	2 & 3	Additional information on infusion times	For completeness
	3	Cyclizine added	In line with current usage
	3	Metoclopramide added	MHRA guidance
		Updated to reflect new national guidance on chemotherapy induced nausea and vomiting, produced by Children's Cancer and Leukaemia Group (CCLG)	CCLG guidance
		Updated to reflect new national guidance on chemotherapy induced nausea and vomiting, produced by Children's Cancer and Leukaemia Group (CCLG)	CCLG guidance