Pan-Birmingham NHS
Cancer Network

Coversheet for Network Site Specific Group Agreed Documentation

This sheet is to accompany all documentation agreed by Pan Birmingham Cancer Network Site Specific Groups. This will assist the Network Governance Committee to endorse the documentation and request implementation.

Document Title	Anti Emetic Guidelines for Adults receiving Chemotherapy
Document Date	January 2009
Document Purpose	This Guideline has been produced to support the following: • The management of all patients likely to experience nausea and vomiting due to anti cancer treatment • The management of patients who experience anti cancer treatment related nausea and vomiting
Authors	Frances Shaw Principal Pharmacist Cancer Services (Heart of England NHS Foundation Trust)
References	See document
Consultation Process	Consultation was via the author, Chemotherapy Network Site Specific Group, Haematology Network Site Specific Group, Oncologists and the Network Drug and Therapeutics Committee via Andrew Stanley.
Review Date (must be within three years)	January 2012
Approval Signatures: Network Site Specific Group Clinical Chair	
Date Approved by Network Governance Committee	21 January 2009

ENDORSED BY THE GOVERNANCE COMMITTEE

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Anti Emetic Guidelines for Adults Receiving Chemotherapy

Version History

Version	Date	Comments
0.1	29.04.08	Guideline introduced into system and placed in Network format.
0.1	29.07.08	Circulated to Chemotherapy NSSG, Haematology NSSG, Network Pharmacist and Oncologists for consultation
0.2	29.07.08	With comments from Alison Rowe
0.3	17.10.08	Tables formatted following discussion at Chemotherapy NSSG
0.4	22.12.08	Document scope and background provided by author. NSSG approved
1	21.01.09	Endorsed by the Guidelines Review Sub Group once minor format changes are made

1. Scope of the Guideline

This Guideline has been produced to support the following:

- The management of all patients likely to experience nausea and vomiting due to anti cancer treatment
- The management of patients who experience anti cancer treatment related nausea and vomiting

1.1 This guideline is intended for nurses, pharmacists and doctors who are treating oncology and haematology patients with chemotherapy. It may also be used by GPs and other doctors within the Trust who would be looking for breakthrough treatment for patients who came to see them or who were admitted with nausea and vomiting when already taking prophylactic anti emetics.

2. Guideline Background

2.1 In 2006 the American Society for Clinical Oncology published its anti emetic guidelines. These guidelines have been used throughout the United Kingdom to optimise prophylactic use of anti emetics.

2.2 This guideline aims to combine up to date research, current thinking and local expert opinion to produce Network Guidelines for the management of nausea and vomiting that results from treatment with anti cancer agents. This guideline is intended to aid the Trusts in the Pan Birmingham Cancer Network area to rationalise anti emetic treatment.

3. Introduction

3.1 Nausea and vomiting are known side effects of many of the chemotherapy agents. The risk and severity of symptoms largely depends upon the dose and combination of cytotoxic agents used. However, patients who receIVe the same chemotherapy may experience different levels of nausea and vomiting. Prophylaxis and treatment guidelines need to take this issue into account.

Prophylaxis of nausea and vomiting from the first course of treatment is essential as uncontrolled symptoms can contribute to anorexia, fluid, electrolyte imbalance, and anticipatory nausea and vomiting.

3.2 There are three types of nausea and vomiting associated with chemotherapy:
ACUTE – usually within several hours of chemotherapy administration
DELAYED – can be delayed for several days after the treatment
ANTICIPATORY – If nausea and vomiting is not controlled with chemotherapy then the patient may experience a conditioned response of nausea and vomiting before treatment.

3.3 These three areas of nausea and vomiting are interrelated. If the acute phase is poorly controlled then the patient is more susceptible to delayed symptoms. If acute and delayed symptoms are poorly controlled then the patient is at high risk of anticipatory symptoms.

3.4 Risk factors that make some patients more susceptible to nausea and vomiting include females, younger patients, previous history of vomiting whilst receIVing chemotherapy, high levels of anxiety, other disease, symptoms of disease or side effects of other treatments such as radiotherapy.

3.5 Anti emetics should be given before moderate to highly emetic chemotherapy. Oral anti emetic medication needs to be given at least 30 minutes before treatment. Generally there is no significant benefit for using intravenous anti emetics over oral medication.

3.6 The following tables identify the recommended anti emetic regimen and the options for breakthrough nausea and vomiting. The tables in the appendix one identify the emetogenic potential of a number of cytotoxic agents and doses where appropriate. With combination chemotherapy use the recommended treatment for the agent with the highest emetogenic potential.

4. Table of Recommended Anti Emetic Regimens

4.1 Daycase Regimens:

Emetogenic potential	Treatment
None	**None required**
Mild	**Pre-medication (to be administered 30-60 minutes prior to cytotoxic drug administration)** Domperidone 10-20mg po stat or Metoclopramide 10-20mg po/IV stat **TTO's** Domperidone 10-20mg po qds or Metoclopramide 10-20mg tds as required (prn) for 3-5 days post chemotherapy
Moderate	**Pre-medication (to be administered 30-60 minutes prior to cytotoxic drug administration)** 5-HT3 antagonist po/IV stat Dexamethasone 4-8mg po/IV stat (Oncology only)* **NB for regimens containing paclitaxel, dexamethasone dose is 20mg IV stat and regimen with Docetaxel should use Dexamethasone po 8mg bd starting the day before chemotherapy** **TTO's** Domperidone 10-20mg po qds or Metoclopramide 10-20mg tds for 3-5 days post chemotherapy then prn Dexamethasone 2-4mg po bd – tds for 3 days post chemotherapy
High	**Pre-medication (to be administered 30-60 minutes prior to cytotoxic drug administration)** 5HT3 antagonist po/IV stat Dexamethasone 8mg po/IV stat* **NB for regimens containing paclitaxel, dexamethasone dose is 20mg IV stat** **TTO's** 5HT3 antagonist po for 2 days post chemotherapy Dexamethasone 4mg po tds for 3 days (Oncology only)* Domperidone 10-20mg po qds or Metoclopramide 10-20mg tds for 3-5 days then prn post chemotherapy

Very High	**Pre-medication (to be administered 30-60 minutes prior to cytotoxic drug administration)** 5HT3 antagonist IV stat Dexamethasone 8-20mg IV stat* **TTO's** 5HT3 antagonist po for 2 days post chemotherapy Dexamethasone 4mg po tds for 3 days (Oncology only)* Domperidone 10-20mg po qds or Metoclopramide 10-20mg tds for 3-5 days then prn post chemotherapy **<u>Regimens with Cisplatin in patients at increased risk of nausea and vomiting (such as younger patients)</u>** Aprepitant 125mg 1 hour before chemotherapy then 80mg daily for the next 2 days 5HT3 antagonist po/IV stat then po for 2 days post chemotherapy Dexamethasone 4mg po/IV stat* then 2-4mg po bd for 3 days Domperidone 10-20mg po qds or Metoclopramide 10-20mg tds for 3-5 days then prn post chemotherapy

Notes:

- For **haematology** patients avoid dexamethasone where possible and only use with highly emetic regimen or where previous anti emetic regimens have failed.
- Consider the benefit versus risk of using steroid in patients with **diabetes** and/or **hypertension.**
- Omit dexamethasone in regimens where other steroids are prescribed such as prednisolone with CHOP and PMitCEBO.
- For weekly regimens with agents with moderate or higher emetogenic potential consider reducing the dose or decreasing the number of the days of the dexamethasone treatment.

4.2 Multiple Day Regimens:

4.2.1 Patients receiving chemotherapy as an in-patient should have regular prophylactic anti emetics prescribed for the duration of treatment (see below).

4.2.2 Select the appropriate pre chemotherapy prophylaxis for the first day of the multi-day regimen and on discharge choose the take home anti emetics for the agent with the highest emetogenic potential.

4.2.3 Pre chemotherapy anti emetic should be described with the chemotherapy as discussed in the table above.

Emetogenic Potential	Continuous Prophylaxis anti emetics for in-patient chemotherapy regimens
Mild	Domperidone 10-20mg po qds prn or Metoclopramide 10-20mg tds prn
Moderate	Domperidone 20mg po qds or Metoclopramide 10-20mg tds x 3-5 days then prn Dexamethasone 2-4mg po bd –tds 3days
High	5HT3 antagonist 24 hour post chemotherapy Dexamethasone 4-8mg po bd – tds * Domperidone 10-20mg po qds or Metoclopramide 10-20mg tds
Very High	5HT3 antagonist 12 and 24 hour post chemotherapy Dexamethasone 4-8mg po tds* Domperidone 10-20mg po qds or Metoclopramide 10-20mg tds **Regimens with Cisplatin in patients at increased risk of nausea and vomiting (such as younger patients)** Aprepitant 125mg 1 hour before chemotherapy then 80mg daily for next 2 days 5HT3 antagonist po/IV stat then po for 2 days post chemotherapy Dexamethasone 4mg po/IV stat* then 2-4mg po bd for 3 days Domperidone 10-20mg po qds or Metoclopramide 10-20mg tds for 3-5 days then prn post chemotherapy

Notes:

- For **haematology** patients avoid dexamethasone where possible and only use with highly emetic regimen or where previous anti emetic regimens have failed. Consider the benefit versus risk of using steroid in patients with **diabetes** and **hypertension**.

5. ANTI EMETIC FAILURE:

Failure of first line anti emetics is defined as:

a) Single episode of vomiting
b) Two episodes of retching
c) Prolonged or distressing nausea

5.1 Failure of first line anti emetics should be dealt with swiftly. The next course of treatment should be commenced with anti emetics for the next level of emetogenicity (e.g. move from moderate to high or from high to very high).

Emetogenic Potential	Anti emetic protocol for failure of first line therapy
Mild	Proceed to recommendations for group 2
Moderate	Proceed to recommendations for group 3 **NB Consider IV drugs if orals not tolerated**
High	Extend use of 5HT3 antagonist or consider: • Lorazepam 1-2mg po 1 hour prior to treatment and PRN (especially for anticipatory emesis). • Change Domperidone/ Metoclopramide to Cyclizine 50mg tds. • Methotrimeprazine 6.25mg po tds or 6.25 – 12.5mg IV or via subcutaneous pump over 24 hours. • It is proposed that aprepitant is used for secondary prophylaxis of nausea and vomiting in those patients receiving cisplatin who fail first-line anti emetics. **NB Consider IV drugs if orals not tolerated. Suppositories may be an option for discharged patients who cannot take oral anti emetics.**

5.2 The reason for anti emetic failure should be considered carefully to ensure appropriate treatment intervention.

5.2.1 **Acute emesis**- if adequate time was given between the administration of the pre medication and commencing chemotherapy consider changing the pre medication to include 5HT3 antagonist, Lorazepam or Cyclizine.

5.2.2 **Delayed emesis** (i.e. that which occurs >24 hours post chemotherapy) - Most common with cisplatin and ifosfamide but may occur with any regimen if acute emesis is not controlled effectively.

- If anti emetics fail in the first 24 hours and the patient is already receiving 5HT3 antagonist, consider adding or increasing the Dexamethasone, or Cyclizine 50mg tds.
- If anti emetics fail on stopping the 5HT3 antagonist, prolong use of 5HT3 antagonist for further two days.

5.2.3 **Anticipatory nausea and vomiting** (that is vomiting that commences up to 24 hours prior to commencing chemotherapy). Consider the use of Haloperidol 3mg po the evening before treatment or Lorazepam 1mg the evening before and morning of treatment.

NB: Patients must be informed that these drugs may make them drowsy and advised not to drive to the hospital for their appointment.

5.2.4 **Nabilone:** A synthetic cannabinoid with anti emetic properties. It may benefit patients whose nausea and vomiting is unresponsive to conventional anti emetics (such as patients receiving cisplatin or ifosfamide). Initially 1 mg twice daily increased if necessary to 2mg twice daily throughout cytotoxic therapy and for up to 48 hours after the last dose of chemotherapy. The first dose

should be given the night before and the second dose 1 - 3 hours before the initiation of chemotherapy.

6. SIDE-EFFECTS OF COMMONLY USED ANTI EMETICS:

6.1 **Metoclopramide** can cause agitation or the development of extra pyramidal symptoms, which can occur up to 24 hours after a dose. These symptoms may require treatment with procyclidine 10mg or diazepam 10mg. Metoclopramide is best avoided in patients with Parkinson's disease and only used with caution in patients under 20 years of age. If there is need to substitute use Cyclizine 50mg tds.

6.2 **Domperidone** is generally well tolerated but like metoclopramide can cause diarrhoea due to increased gut motility.

6.3 **5HT3 antagonists** can induce constipation in a high proportion of patients. Some patients also complain of headaches.

a) For constipation - prescribe laxatives if no contraindications
b) For headache - advise simple analgesia e.g. Paracetamol 1g up to qds if no contra-indications
d) If side effects are severe either try an alternate 5HT3 or a separate class of anti emetics.

6.4 **Dexamethasone** can cause activation and increased appetite which may be used to the advantage of certain patients. Other side effects include fluid retension, dyspepsia. It should be noted that some patients experience perineal discomfort if drug is given by fast IV bolus. IV doses should be given slowly and preferably by infusion.

6.4.1 **Contraindications for use of dexamethasone as an anti emetic:**

a) Diabetes, unless arrangements are made to monitor the patient closely.
b) Steroid induced side effects such as myopathy, gross weight gain, gastro-intestinal effects, or psychosis with previous course.
c) Patients already receiving high dose steroids e.g. prednisolone with CHOP chemotherapy.
d) Patient is already receiving dexamethasone as part of their treatment protocol.

6.5 **Cyclizine** can cause urticaria, drug rash, drowsiness, headache, dryness of the mouth, nose and throat, blurred vision, urinary retention, constipation, restlessness. It should be used with caution in patients with glaucoma, obstructive disease of the GI tract, hepatic disease, epilepsy. Cyclizine may cause an increase in heart rate and a decrease in cardiac output in patients with severe heart failure.

6.6 **Aprepitants** common side effects include hiccups, dyspepsia, diarrhoea, constipation, anorexia, asthenia, headache and dizziness. Less common side effects include dry mouth, flatulence and abdominal pain. Treat symptomatically and try alternative anti emetics where necessary. The usual oral dexamethasone dose should be reduced by approximately 50% when co administered with Aprepitant 125 mg/80 mg regimen.

6.7 **Lorazepam** causes drowsiness, light headedness, confusion and ataxia that can affect performance of skilled tasks and concentration difficulties
NB: Patients must be informed that it may make them drowsy and advised not to drive to the hospital for their appointment.
Dependence should not become an issue if the patient only uses a few doses each cycle. Occasionally the patient may experience headache, vertigo, hypotension and visual disturbances.

6.8 **Methotrimeprazine (Levomepromazine)** causes drowsiness that can affect performance of skilled tasks, and concentration difficulties
NB: Patients must be informed that it may make them drowsy and advised not to drive to the hospital for their appointment.
Other side effects include apathy, agitation, dizziness and headache. Extrapyramidal symptoms may occur but are less common.

6.9 **Nabilone** causes drowsiness that can affect performance of skilled tasks, and concentration difficulties. It enhances the effects of alcohol and can cause sleep disturbances. Patients may experience dry mouth, ataxia, visual disturbances and should be advised that they may experience changes in mood such as euphoria and dysphoria.

7. ABBREVIATIONS:

po:	orally
IV:	intravenous
bd:	twice daily
tds:	three times daily
qds:	four times daily
prn:	as required
mg:	milligrams

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Monitoring of the Guidance

Compliance with the guidance will be considered as a topic for audit by the NSSG in 2011/2012.

Approval Date of Network Site Specific Group: **Date: 22.12.08**
Date of Approval by the Governance Committee: **Date: 21.01.09**

Approval Signatures

Pan Birmingham Cancer Network Governance Committee Chair
Name: Doug Wulff

Signature: Date: 21 January 2009

Pan Birmingham Cancer Network Manager
Name: Karen Metcalf

Signature: Date: 21 January 2009

Network Site Specific Group Chair
Name: Harriet Launders

Signature: Date: 22 December 2008

Appendix 1: Emetogenic Potential of Individual Anti Cancer Drugs

These tables give a guide as to the emetogenic potential of agents but some patients experience higher levels of emesis due to their disease, other treatments such as radiotherapy and such factors should also be considered when prescribing antiemetics.

Table 1 Table of Low Emetogenic Agents

Individual drugs	Comments
Alemtuzumab	
Asparaginase	
Bleomycin	
Bortezomib	
Busulfan	Doses <10mg
Capecitabine	
Cetuximab	
Chlorambucil	
Cladrabine	
Ertot	
Etoposide	Standard dose (Oral and IV)
Fludarabine	
Fluorouracil	
Gefitnib	
Gemtuzumab	
Hydroxyurea	
Imatinib	
Liposomal Daunorubicin	
Liposomal Doxorubicin	
Melphalan	Oral
Mercaptopurine	
Methotrexate	Doses ≤50mg/m^2
Pentostatin	
Rituximab	
Sunit	
Thioguanine	
Trastuzumab	
Vinblastine	
Vincristine	
Vindesine	
Vinorelbine	IV

Table 2 Table of Moderate Emetogenic Agents

Individual drugs	Comments
Arsenic	
Carmustine	<100mg/m^2
Cyclophosphamide	≤750mg/m^2
Cytarabine	<900mg/m^2
Daunorubicin	<50mg/m^2
Docetaxel	
Doxorubicin	>20mg or <60mg/m^2
Gemcitabine	
Methotrexate	>250mg to ≤1g/m^2
Mitomycin C	
Mitoxantrone	
Paclitaxel	
Procarbazine	
Temozolomide	
Topotecan	
Vinorelbine	oral

Table 3 Table of Highly Emetogenic Agents

Individual drugs	Comments
Altretamine	Treat only using 5-HT$_3$ antagonist not steroid
Amsacrine	
Carboplatin	
Carmustine	>100mg/m^2
Cisplatin	<50mg/m^2
Cyclophosphamide	Doses >750mg/m^2 to ≤1500mg/m^2
Cytarabine	Doses >900mg/m^2
Dactinomycin	
Daunorubicin	>50mg/m^2
Doxorubicin	≥60mg
Epirubicin	
Estramustine	
Idarubicin	
Ifosfamide	<3g/m^2
Irinotecan	
Lomustine	
Melphalan	Doses IV >100mg/m^2
Methotrexate	Doses > 1000mg/m^2
Oxaliplatin	
Streptozocin	

Table 4 Table of Very Highly Emetogenic Agents

Individual drugs	Comments
Busulfan	Conditioning doses
Carmustine	≥250mg/m^2
Cisplatin	≥50mg/m^2
Cyclophosphamide	>1500mg/m^2
Dacarbazine	
Ifosfamide	≥3g/m^2/day

Table 5 Emetic Potential of Chemotherapy Regimens

Low Incidence < 30%	Moderate Incidence 30 – 60%	High Incidence 60 – 90 %	Very High Incidence > 90%
5Fluorouracil/Folinic Acid	CDT	AC	ABVD
Modified DeGramont	ChIVPP	ADE (High D1-5, otherwise moderate)	BEAM (treat as moderate on D2-5)
VAD	ChIVPP/PABLOE	CAF	BEP 3/7
VAMP	CVP	CAP	BEP 5/7
Vinc/bleo	Cyclo-dex	CAV-PE	Carboplatin/ etoposide
	FAD	CHOP	Dox/Cis(PAM)
	Flu/Cyclo	CMF	Dox/Ifos
	FMD	CODOX-M (High D1, otherwise moderate)	EC90
	Mitomycin/FU (low on FU days)	C-VAMP (Moderate D2-4)	ESHAP (High D2-5)
	MM	C-Z-dex	FEC
	MMM	DA (High D1,3,5 otherwise moderate)	FLAG-Ida
	PABLOE	EC	FU/Cisplatin
		ECF	Gem/Cisplatin
		FAC	High dose MTX
		ICE	IVAC
		IVE	MAP
		MACE	PE
		MidAC (Moderate D4-5)	VAC
		Mini-BEAM (treat as moderate D2-5)	VAI
		MVP	VIDE
		PCV	
		PMitCeBo	
		POMB- ACE	
		Z-dex	

The tables are not an exclusive list. Antiemetics for regimens not listed in this table should be based on the agent in the regimen with the highest emetogenic potential. In the Paclitaxel Gemcitabine regimen Paclitaxel has the higher emetogenic potential and the patients should be given anti emetics for a moderate emetogenic regimen.

In this table ‘incidence’ refers to the proportion of patients that experience emesis. It does not refer to the severity of the symptoms. Some agents can cause delayed nausea and vomiting for several days such as cyclophosphamide.