North of England Cancer Network

Chemotherapy Induced Nausea and Vomiting (CINV) Anti-emetic Guidelines

Adult Oncology & Haematology

Quality and safety for every patient every time”

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See last page for Document Control
## Summary – Standard Anti emetic Cover

### Level 1: Minimal Risk (Less than 10%)

<table>
<thead>
<tr>
<th>Pre-medication:</th>
<th>Take Home Medication:</th>
</tr>
</thead>
<tbody>
<tr>
<td>No standard pre-medication normally required</td>
<td>No standard medication normally required. However, normally supply metoclopramide as a rescue measure with first cycle.</td>
</tr>
</tbody>
</table>

### Level 2: Intermediate Risk (10 to 30%)

<table>
<thead>
<tr>
<th>Pre-medication:</th>
<th>Take Home Medication:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone 8mg IV or Oral</td>
<td>No standard medication normally required. However, normally supply metoclopramide as a rescue measure with first cycle.</td>
</tr>
</tbody>
</table>

### Level 3: Moderate Risk (30 to 90%)

<table>
<thead>
<tr>
<th>Pre-medication:</th>
<th>Take Home Medication:</th>
</tr>
</thead>
</table>
| Dexamethasone 8mg IV or Oral  
Either Ondansetron 8mg IV / Oral  
Or Palonosetron** 0.25mg IV/ 0.5 mg Oral | Dexamethasone up to 8mg Daily* – Oral for 3 days  
Ondansetron 8mg Twice Daily – Oral for 2 to 3 days (not given if using IV Palonosetron)  
Metoclopramide 10mg Twice Daily (patients under 60kg) Three Times Daily (patients over 60kg) Oral for 3 to 5 days when required |

### Level 4: High Risk (> 90%)

<table>
<thead>
<tr>
<th>Pre-medication:</th>
<th>Take Home Medication:</th>
</tr>
</thead>
</table>
| Dexamethasone 12mg IV or Oral  
Aprepitant*** 125mg Oral ( with risk factors)  
Either Ondansetron 8mg IV / Oral  
Or Palonosetron** 0.25mg IV/ 0.5 mg Oral | Dexamethasone up to 8mg Daily* – Oral for 2 to 3 days  
Aprepitant*** 80mg Daily – Oral for 2 days†  
Ondansetron 8mg Twice Daily – Oral for 2 to 3 days (not given if using IV Palonosetron) |

* for patients receiving pre-medication doses before 12pm, they should take a divided evening dose at 4pm on the night of chemotherapy.

** consider palonosetron where there is concern, i.e. patient has risk factors overrisk of delayed nausea and vomiting

*** consider adding aprepitant where there is concern over risk of anti-emetic failure as identified by assessment of patient risk factorsAlternative Agents

† or fosaprepitant 150mg intravenously on day 1 only (See Page 15)

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**Ondansetron IV must be infused over 15minutes in patients over 65years of age."
**Breakthrough Management:**
If patients develop acute nausea / vomiting (within 24 hours of last chemotherapy dose), which is refractory to breakthrough medication already supplied, increase to the next treatment band.

If patients develop delayed nausea / vomiting (> 24 hours after last chemotherapy dose), which is refractory to breakthrough medication already supplied, add additional treatment from the following (using the next available agent on the list):

- Metoclopramide
- Dexamethasone
- Ondansetron (or another 5HT antagonist)
- Levomepromazine
- Cyclizine (?stop metoclopramide)
- Prochlorperazine
- Lorazepam
- Nabilone
- Haloperidol
## Contents

**Summary – Standard Antiemetic Cover** ................................................................. 2

**Breakthrough Management:** ............................................................................ 3

**Contents** ............................................................................................................. 4

**Introduction** ........................................................................................................ 6

**Causes of Nausea & Vomiting** ........................................................................... 8

**Pathophysiology** ................................................................................................ 8

**Acute** .................................................................................................................. 8

**Delayed** ................................................................................................................ 8

**Anticipatory** ......................................................................................................... 8

**Breakthrough** ...................................................................................................... 8

**Refractory** ............................................................................................................ 8

**Contributing Factors** .......................................................................................... 9

**Gender** .................................................................................................................. 9

**Age** ...................................................................................................................... 9

**Performance Status** ............................................................................................ 9

**Other Medication** ................................................................................................. 9

**Travel sickness** .................................................................................................... 9

**Morning sickness** ............................................................................................... 9

**Previous CINV** ..................................................................................................... 9

**Smoking** ................................................................................................................ 10

**Alcohol intake** ...................................................................................................... 10

**Drug use / misuse** ............................................................................................... 10

**Individual Drug Treatment** ................................................................................. 10

**Combination Treatments** .................................................................................... 10

**Concomitant Radiotherapy** ................................................................................ 10

**Management of anti-emetic failure** .................................................................... 11

**Exclusion of other causes** ................................................................................... 11

**Control / Treatment** ........................................................................................... 12

**Metoclopramide** .................................................................................................. 12

**Dexamethasone** .................................................................................................. 13

**Ondansetron / Granisetron** .................................................................................. 13

**Alternative 5HT₃ antagonists** ................................................................................. 14

**Aprepitant & Fosaprepitant** ................................................................................ 15

**Levomepromazine (Nozinan)** ............................................................................... 16

**Cyclizine** .............................................................................................................. 16

**Nabilone** .............................................................................................................. 16

**Benzodiazepines** ................................................................................................ 16
Introduction

Chemotherapy Induced Nausea and Vomiting (CINV) is one of the most frequently experienced side effects encountered by chemotherapy patients. Patients will often find the symptoms distressing, and develop anxiety about the potential for such symptoms to recur on future cycles of chemotherapy.

Modern drug treatment can successfully control CINV for the majority of patients.

Scope

These guidelines are intended to support health professionals in the management and prevention of chemotherapy induced nausea and vomiting. They are not intended to address radiotherapy induced nausea and vomiting or nausea and vomiting in palliative care. This guidance applies to Adults only.

Patient Group

These guidelines are intended to cover adult solid tumour and haematology patients receiving cytotoxic chemotherapy within the North of England Cancer Network.

Clinical Practice

These guidelines are intended to provide a framework to support clinical practice, they can not cover every clinical situation and good common clinical sense and clinical experience will be required when approaching the management of individual patients. Deviation from these guidelines will be necessary in some situations and this should be appropriately documented.

Drug Selection

These guidelines have purposefully chosen not to recommend one specific 5HT3 antagonist, as there is limited evidence to choose between ondansetron, granisetron and palonosetron for acute CINV. Palonosetron is more effective than other 5HT3 antagonist in preventing delayed CINV but is more expensive.

Dexamethasone is the backbone of many of the combinations recommended here. It should be
used with caution in patients with diabetes, and should not normally be used in regimens that contain high doses of alternative steroids such as prednisolone.

The dose of metoclopramide recommended here exceeds the licensed dose. Many of the individual drugs or combinations of anti-emetics described within this document are outside of product licence.

For all drugs the SmPC and BNF should be consulted prior to prescribing.
Causes of Nausea & Vomiting

Pathophysiology
CINV is most commonly grouped into three phases: anticipatory, acute and delayed. Successful management requires correct identification of the phase (or combination of phases) being treated. Two further terminologies have been adopted in this document – refractory and breakthrough.

Acute
Acute CINV is usually described as CINV presenting within the 24 hours immediately after administration of chemotherapy.

Delayed
Delayed CINV may present any time after the first 24 hours, and may continue for up to 6 or 7 days after chemotherapy.

Anticipatory
Occurs prior to administration of any chemotherapy (in this cycle). It is either a learned response following CINV on a previous cycle or an anxiety response. It is most common after 3 to 4 cycles of chemotherapy with very badly controlled acute or delayed symptoms.

Breakthrough
Development of symptoms (nausea or vomiting), despite standard anti-emetic therapy, which require treatment with an additional pharmacological agent

Refractory
Patients who have failed on both standard and rescue medication.
Contributing Factors

Gender
Women are at increased risk of CINV than males (1) (2).

Age
Younger patients are more susceptible than older patients, with patients under 50 years old being at the greatest risk (1) (2).

Performance Status
Poor performance status increases the risk of CINV

Other Medication
Various medications can cause nausea and vomiting and it has been proposed that when some of these are given in combination with chemotherapy that these increase the risk of CINV. Examples of these agents are listed below:

- Amifostine
- Anaesthetic Agents
- Anti-depressants
- Anti-microbials, including anti-fungals
- Ergot alakaloids
- Iron
- Lev and Carbo Dopa
- NSAIDs

Travel sickness
Patients who have a history of motion sickness are at increased risk of CINV (2)

Morning sickness
Morning sickness during pregnancy has been suggested as a predictive factor for CINV

Previous CINV
Previous exposure to chemotherapy which has resulted in CINV increases the risk of CINV with
future chemotherapy. In addition, the effectiveness of prophylactic treatment reduces with each cycle of chemotherapy.

Failure of prophylaxis in the acute setting increases the risk of failure in the delayed setting.

**Smoking**
Smoking reduces the risk of CINV.

**Alcohol intake**
Patients with a long history of alcohol consumption are at reduced risk of CINV. (3)

**Drug use / misuse**
Patients with a history of drug misuse are generally at a lower risk of CINV.

**Individual Drug Treatment**
Each individual chemotherapy drug will have a different risk factor for emetogenicity ranging from drugs such as vincristine with a risk of less than 10% emetogenicity without any prophylaxis to cisplatin with a nearly 100% risk without any prophylaxis.

**Combination Treatments**
When chemotherapy agents are combined, the effect of this may be additive or synergistic.

**Concomitant Radiotherapy**
When chemotherapy agents is given in combination with radiotherapy emetogenicity will increase.
Management of anti-emetic failure

Anti-emetic failure is described as:

- 4 hours of moderate to severe nausea
- or 2 or more episodes of vomiting and/or retching in 24 hours.

There are 3 key steps for successful management –
1. Exclusion of other causes,
2. Treatment,
3. Planning for the next cycle.

Exclusion of other causes

It is easy to assume that nausea and vomiting in a patient who has recently received chemotherapy is the result of their chemotherapy. However there are several other causes of nausea and vomiting many of which will commonly present in cancer patients and should therefore be excluded:

- Other medication (See Page 9)
- Constipation
- Bowel Obstruction
- Anxiety
- Metabolic Abnormalities (eg Renal Failure)
- Hyper-calcaemia
- Peptic Ulcer Disease
- Radiotherapy
- Raised Intra Cranial Pressure

If another cause is identified this should be corrected or treated rather than initiating treatment for CINV.
Control / Treatment
An additional anti-emetic should be added (from a different) therapeutic class. If necessary medication should be given rectally or parenterally to regain control.

If any medication was previously being given on a 'when required' basis this should be switched to a regular dosing schedule.

The use of multiple drugs may be necessary, and scheduling of treatment to avoid troughs of drug levels may be necessary.

Closely monitor hydration and electrolytes and correct any abnormalities if they present.

Metoclopramide
Metoclopramide should be considered the first line treatment to be added to existing therapy. 20mg may be required for some patients to achieve sufficient therapeutic levels to cross the blood brain barrier to treat acute CINV, and doses may need to be repeated 6 hourly rather than 8 hourly to maintain sufficient therapeutic levels in some patients in this setting. Metoclopramide can cause extra-pyramidal reactions in some patients and so should be used with caution in young adults and the elderly. The European Medicines Agency has recently (July 2013) reviewed the safety of metoclopramide and made a number of recommendations which are relevant to the use of metoclopramide in CINV:

- Use short courses – up to 5 days.
- Do not use for acute CINV, but is indicated for delayed CINV.
- Metoclopramide should not be a first line treatment in paediatrics, and should not be used in children under 1 year of age at all.
- Intravenous doses should be administered over at least 3 minutes.
- There are rare but known risks of QTc interval prolongation special care should be taken in at risk populations.
- The maximum daily dose for adults and children should be 0.5mg/kg/day and in adults the usual conventional dose for adults will be 10mg three times a day. Therefore patients under 60kg would require a lower dose.

Metoclopramide must not be given to patients with parkinson's disease. Domperidone may have similar efficacy, without causing extra-pyramidal reactions however the MHRA has recently highlighted (May 2013) that there is a cardiac risk associated with them, especially at doses over 30mg and in patients over 60 years of age.
Trusts choosing to ignore the EMA guidance and any subsequent guidance issued by the UK regulators should ensure they have discussed the matter at their appropriate governance forum.

**Dexamethasone**

Dexamethasone is the second line treatment of choice. It is a highly effective anti-emetic when given at doses ranging from 8 to 20mg daily. Published consensus guidance, ASCO, MASSC and NCCC all favour a dose of 8mg for prevention of acute emesis in moderate risk and 20mg for prevention of acute emesis in high risk. Note the 20mg dose is reduced to 12mg when given in combination with aprepitant as the AUC of dexamethasone is increased by aprepitant.

8mg Dexamethasone is used for prevention of acute emesis in low risk as a dose usually as 4mg in the morning and at 4pm. Lower doses (4mg or 6mg) are also sometimes effective. It should not be given to patients who are already receiving another steroid as part of their chemotherapy regimen (e.g. CHOP) and should be used in care in patients who have diabetes. Doses after 6pm are likely to cause sleep disturbance.

**Ondansetron / Granisetron**

5HT3 antagonists (ondansetron or granisetron) should be considered third line, for any patient who has not already been prescribed them who is unable to be prescribed a steroid or in whom steroid treatment is inadequate.

Ondansetron - 8mg twice daily (or 16mg once daily rectally) should be the normal dose prescribed. Common surgical prophylaxis schedules (eg 4mg TDS) are unlikely to be adequate. Doses of up to 32mg of ondansetron per day can be given however there is little evidence that higher doses produce additional therapeutic effect for most patients and they are more likely to cause side effects such as headache and constipation, or more serious cardiac complications in some patients. Single doses must not exceed 16mg (8mg in patients over 75 years of age) and doses must not be repeated for at least 4 hours.

Following recent Intravenous ondansetron must be infused in 50-100ml Sodium Chloride 0.9% over 15 minutes in all patients over 65 years of age. Ondansetron can be infused in younger patients and some trusts have adopted a policy to infuse all ondansetron to prevent risk of confusion. Alternatively use of oral ondansetron is appropriate provided the patient is not vomiting. Where oral ondansetron is used as a pre-med’ before chemotherapy at least 30 minutes (Spector *et al* 1998) should be allowed to lapse between the oral dose and...
chemotherapy administration, peak plasma concentration is achieved after 90 minutes. Trusts should consider how this can be achieved without adding extra inconvenience to patients.

Granisetron – 1mg twice daily (or 3mg once daily) is usually considered equivalent to 8mg twice daily of ondansetron. There is no head to head comparison of cardiac risk with granisetron versus ondansetron. Caution is still required for patients with additional cardiac risk factors for granisetron.

**Alternative 5HT₃ antagonists**

- Tropisetron and Dolasteron are no longer commercially available in the UK

**Palonosetron**

Palonosetron is given as a single 0.25mg IV or 0.5mg oral dose prior to chemotherapy. It is at least as effective as ondansetron, and has been shown to be superior than other 5HT₃ antagonists for the prevention of delayed emesis. It’s extensive half life means there is no requirement to repeat the dose which may be useful in patients where compliance is a particular concern. It is more effective than standard 5HT₃ antagonists at preventing delayed CINV. However, it has no role to play in the rescue of patients with anti-emetic failure (i.e. treatment of breakthrough nausea / vomiting). Palonosetron is significantly more expensive than generic ondansetron. The 2010 MASSC Guidelines recommended palonosetron as the preferred 5-HT₃ receptor antagonist in Moderately Emetogenic Chemotherapy (excluding the AC regimen)

Cardiac risks associated with other 5HT₃ antagonists *may not* be as pronounced with palonosetron.
**Aprepitant & Fosaprepitant**

Aprepitant is a NK-1 receptor antagonist that has been shown to be effective for the management of delayed chemotherapy induced nausea and vomiting. Aprepitant has a known interaction with dexamethasone which may require dose reduction of dexamethasone. In clinical trials 20mg of dexamethasone was used in the control arm and 12mg in the aprepitant arm. Conventional practice within NECN would not use 20mg of dexamethasone as an anti-emetic, and therefore dose reduction of steroid is probably not necessary within NECN anti-emetic combinations. 125mg is given orally on day 1 an hour before treatment and 80mg on day 2 and 3, a combination pack is provided with all three doses included.

Fosaprepitant is a pro-drug of aprepitant that allows it to be given intravenously. Recent data has shown that a single 150mg IV dose can be used to replace the full oral schedule (d1: 125mg and d2+3: 80mg). The SmPC recommends this is given as a 1mg/ml solution over 20 minutes, 30 minutes before chemotherapy. This is difficult to administer clinically given the size of IV infusion bags commercially available. MSD has data from clinical trials which demonstrate that the drug can be mixed in volumes from 100 to 250ml of Sodium Chloride. Where the concentration is stronger than 1mg/ml there appears to be a slightly increased risk of venous irritation therefore patients who can handle 250ml of fluid in 20-30 minutes should receive their fosaprepitant in a 250ml bag rather than a 100ml bag.

Clinical trails of fosaprepitant gave dexamethasone orally in doses of 12mg daily, 8mg daily, 8mg twice daily on days 1, 2, 3&4 respectively. Consideration to giving higher doses of dexamethasone should be given.

Licencing studies of both aprepitant and fosaprepitant have used 32mg of ondansetron on day 1 with no other ondansetron. A single European study has used a granisetron schedule which is similar to the ondansetron schedule used in the UK.

No robust data exists to confirm if aprepitant duration should be extended if chemotherapy lasts more than 1 day. In view of the cost and lack of evidence aprepitant should not be used to rescue patients with anti-emetic failure.
Levomepromazine (Nozinan)
Levomepromazine should be added after a dopamine agonist (eg metoclopramide), a glucocorticoid steroid (eg dexamethasone) and a 5HT\textsubscript{3} antagonist (eg ondansetron). Levomepromazine has a significant sedating effect which may be beneficial in achieving its antiemetic effect, however, care should be taken to avoid over sedating patients. A starting dose of 6.25mg – using $\frac{1}{4}$ of a 25mg tablet (or a 6mg tablet is available but is not currently licenced) should be used, with doses repeated every 8 to 12 hours unless nausea returns sooner.

Cyclizine
If levomepromazine is not felt adequate, cyclizine (50mg three times a day) should be considered. However cyclizine, theoretically, inhibits the gastro-intestinal motility stimulating actions of metoclopramide. Although, in clinical practice many patients find cyclizine plus metoclopramide more effective than either alone, a small number of patients will find the combination worse than either agent alone.

Patients who have reached this level of “refractoryness” to treatment should be considered for addition of aprepitant to the next cycle of chemotherapy. Aprepitant does not currently have any evidence to support its use in the acute management of antiemetic failure.

Nabilone
Consider nabilone in patients refractory to all other treatments.

Benzodiazepines
While benzodiazepines have limited anti-emetic properties their anxiolytic properties mean they can be a useful adjunct. They should be considered at any stage when anxiety is felt to be contributing factor to CINV. Some benzodiazepines also have a amnesiac effect which may be useful in preventing conditioning behaviors for the following cycle. Lorazepam 0.5-1mg orally (or sub-lingually) up to 12 hourly is usually sufficient. Consider staring the night before treatment, continuing on the morning of treatment.

Haloperidol
Haloperidol is considered useful as an anti-emetic in palliative care, and due to its anxiolytic properties may have additional roles outside of palliative care. While not used frequently in CINV, it may have a role in the management of patients who are refractory to other treatments.

Plan for next cycle
Once adequate control has been achieved, focus can switch to careful planning for the next cycle of chemotherapy. This should include:

- Avoiding 'as required' scheduling
- Providing the most effective combination used to achieve control
- A rescue medication strategy in case loss of control occurs
## Emetogenicity of Chemotherapy

### Single Agent Chemotherapy

The individual emetogenicity of chemotherapy agents has been derived from Kris *et al* American Society of Clinical Oncology Guideline for Antiemetics in Oncology: Update 2006. Percentages refer to the level of risk if no anti-emetic cover is given at all. Carboplatin has been increased in emetogenicity on a consensus opinion of oncologists at the North of England Cancer Network Chemotherapy Group.

*Patients receiving taxanes or pemetrexed should receive steroid cover for hypersensitivity reaction.*

### Level 1: Minimal Risk (Less than 10%)

<table>
<thead>
<tr>
<th>Bevacizumab</th>
<th>Fludarabine</th>
<th>Vinblastine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleomycin</td>
<td>Gefitinib</td>
<td>Vincristine</td>
</tr>
<tr>
<td>Busulphan</td>
<td>Nilotinib</td>
<td>Vindesine</td>
</tr>
<tr>
<td>Cladribine</td>
<td>Rituximab</td>
<td>Vinflunine</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>Sorafenib</td>
<td>Vinorelbine (IV)</td>
</tr>
<tr>
<td>Erlotinib</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Level 2: Intermediate Risk (10 to 30%)

<table>
<thead>
<tr>
<th>Bortezomib</th>
<th>Fluorouracil</th>
<th>Paclitaxel*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetuximab*</td>
<td>Gemcitabine</td>
<td>Pemetrexed* Sunitinib</td>
</tr>
<tr>
<td>Cabazitaxel*</td>
<td>Lenalidomide Methotrexate</td>
<td>Tegafur Uracil</td>
</tr>
<tr>
<td>Cytarabine (≤1000mg/m²)</td>
<td>Lapatinib</td>
<td>Temsirolimus</td>
</tr>
<tr>
<td>Docetaxel*</td>
<td>Mitomycin (IV)</td>
<td>Topotecan</td>
</tr>
<tr>
<td>Etoposide</td>
<td>Mitoxantrone</td>
<td>Trastuzumab</td>
</tr>
<tr>
<td>Everolimus</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Level 3: Moderate Risk (30 to 90%)

<table>
<thead>
<tr>
<th>Azacitidine</th>
<th>Epirubicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bendamustine</td>
<td>Idarubicin</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>Ifosfamide</td>
</tr>
<tr>
<td>Clofarabine</td>
<td>Imatinib</td>
</tr>
<tr>
<td>Cyclophosphamide (&lt;1500mg/m²)</td>
<td>Irinotecan</td>
</tr>
<tr>
<td>Cytarabine &gt; 1g/m²</td>
<td>Oxaliplatin</td>
</tr>
<tr>
<td>Daunorubicin</td>
<td>Temozolomide</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>Vinorelbine (oral)</td>
</tr>
</tbody>
</table>

*Moderate risk chemotherapy covers a wide range of emetogenic risk. Consideration should specifically be given to other risk factors for nausea & vomiting (See Page 9)*

### Level 4: High Risk (> 90%)

<table>
<thead>
<tr>
<th>Carmustine</th>
<th>Dactinomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>Mechlorethamine</td>
</tr>
<tr>
<td>Cyclophosphamide (≥1500mg/m²)</td>
<td>Streptozocin</td>
</tr>
<tr>
<td>Dacarbazine</td>
<td></td>
</tr>
</tbody>
</table>

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*Level 1: Minimal Risk (Less than 10%)

- Bevacizumab
- Bleomycin
- Busulphan
- Cladribine
- Dasatinib
- Erlotinib

*Level 2: Intermediate Risk (10 to 30%)

- Bortezomib
- Cetuximab
- Cabazitaxel*
- Cytarabine (≤1000mg/m²)
- Docetaxel*
- Etoposide
- Everolimus

*Level 3: Moderate Risk (30 to 90%)

- Azacitidine
- Bendamustine
- Carboplatin
- Clofarabine
- Cyclophosphamide (<1500mg/m²)
- Cytarabine > 1g/m²
- Daunorubicin
- Doxorubicin

*Level 4: High Risk (> 90%)

- Carmustine
- Cisplatin
- Cyclophosphamide (≥1500mg/m²)
- Dacarbazine

*Patients receiving taxanes or pemetrexed should receive steroid cover for hypersensitivity reaction.*
Combination Chemotherapy
When assessing the emetogenicity of combination chemotherapy:

1. Identify the most emetogenic agent in the combination
2. For each drug with an emetogenic risk > 30% increase the emetogenicity by one level per drug
3. For all the drugs with an emetogenicity 10-30% the emetogenicity should be increased one level
4. For drugs with an emetogenicity < 10% no adjustment is necessary.

Common Combinations – Emetogenicity

<table>
<thead>
<tr>
<th>Combination</th>
<th>Emetogenicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABVD (Doxorubicin, Bleomycin, Vinblastine &amp; Dacarbazine)</td>
<td>Level 5</td>
</tr>
<tr>
<td>AC or EC (Doxorubicin or Epirubicin &amp; Cyclophosphamide)</td>
<td>Level 4</td>
</tr>
<tr>
<td>Carboplatin &amp; Etoposide</td>
<td>Level 4</td>
</tr>
<tr>
<td>Carboplatin &amp; Gemcitabine</td>
<td>Level 4</td>
</tr>
<tr>
<td>Carboplatin &amp; Pemetrexed</td>
<td>Level 4</td>
</tr>
<tr>
<td>CHOP (Cyclophosphamide, Doxorubicin, Vincristine)</td>
<td>Level 4</td>
</tr>
<tr>
<td>Cisplatin &amp; Etoposide</td>
<td>Level 5</td>
</tr>
<tr>
<td>Cisplatin &amp; Gemcitabine</td>
<td>Level 4</td>
</tr>
<tr>
<td>Cisplatin &amp; Pemetrexed</td>
<td>Level 4</td>
</tr>
<tr>
<td>Cisplatin &amp; Topotecan</td>
<td>Level 5</td>
</tr>
<tr>
<td>Cisplatin &amp; Vinorelbine (IV)</td>
<td>Level 4</td>
</tr>
<tr>
<td>CMF (Cyclophosphamide, Methotrexet &amp; Fluorouracil)</td>
<td>Level 4</td>
</tr>
<tr>
<td>CVP (Cyclophosphamide &amp; Vincristine)</td>
<td>Level 3</td>
</tr>
<tr>
<td>FC (Fludarabine &amp; Cyclophosphamide)</td>
<td>Level 3</td>
</tr>
<tr>
<td>FEC-100 (Fluorouracil, Epirubicin &amp; Cyclophosphamide)</td>
<td>Level 4</td>
</tr>
<tr>
<td>FMD (Fludarabine, Mitoxantrone &amp; Dexamethasone)</td>
<td>Level 2</td>
</tr>
<tr>
<td>FOLFIRI (Irinotecan &amp; Infusional Fluorouracil)</td>
<td>Level 4</td>
</tr>
<tr>
<td>FOLFOX (Oxaliplatin &amp; Infusional Fluorouracil)</td>
<td>Level 4</td>
</tr>
<tr>
<td>Modified de Grammont (Infusional Fluorouracil)</td>
<td>Level 2</td>
</tr>
<tr>
<td>Paclitaxel &amp; Gemcitabine</td>
<td>Level 3</td>
</tr>
<tr>
<td>R-CHOP (Rituximab &amp; Cyclophosphamide, Doxorubicin, Vincristine)</td>
<td>Level 4</td>
</tr>
<tr>
<td>R-CVP (Rituximab &amp; Cyclophosphamide &amp; Vincristine)</td>
<td>Level 3</td>
</tr>
<tr>
<td>XELOX (Oxaliplatin &amp; Capecitabine)</td>
<td>Level 4</td>
</tr>
</tbody>
</table>
### Suggested standard anti-emetics according to emetogenic risk.

<table>
<thead>
<tr>
<th>Level 1: Minimal Risk (Less than 10%)</th>
<th>Pre-medication:</th>
<th>Take Home Medication:</th>
</tr>
</thead>
<tbody>
<tr>
<td>No standard pre-medication normally required</td>
<td>No standard medication normally required. However, normally supply metoclopramide as a rescue measure with first cycle.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level 2: Intermediate Risk (10 to 30%)</th>
<th>Pre-medication:</th>
<th>Take Home Medication:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone 8mg IV or Oral</td>
<td>No standard medication normally required. However, normally supply metoclopramide as a rescue measure with first cycle.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level 3: Moderate Risk (30 to 90%)</th>
<th>Pre-medication:</th>
<th>Take Home Medication:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone 8mg IV or Oral</td>
<td>Dexamethasone up to 8mg Daily* – Oral for 3 days</td>
<td></td>
</tr>
<tr>
<td>Either Ondansetron 8mg IV / Oral</td>
<td>Ondansetron 8mg Twice Daily – Oral for 2 to 3 days (not given if using IV Palonosetron)</td>
<td></td>
</tr>
<tr>
<td>Or Palonosetron** 0.25mg IV/ 0.5 mg Oral</td>
<td>Metoclopramide 10mg Twice Daily (patients under 60kg) Three Times Daily (patients over 60kg) Oral for 3 to 5 days when required</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level 4: High Risk (&gt; 90%)</th>
<th>Pre-medication:</th>
<th>Take Home Medication:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone 12mg IV or Oral</td>
<td>Dexamethasone up to 8mg Daily* – Oral for 2 to 3 days</td>
<td></td>
</tr>
<tr>
<td>Aprepitant*** 125mg Oral ( with risk factors)</td>
<td>Aprepitant*** 80mg Daily – Oral for 2 days†</td>
<td></td>
</tr>
<tr>
<td>Either Ondansetron 8mg IV / Oral</td>
<td>Ondansetron 8mg Twice Daily – Oral for 2 to 3 days (not given if using IV Palonosetron)</td>
<td></td>
</tr>
<tr>
<td>Or Palonosetron** 0.25mg IV/ 0.5 mg Oral</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* for patients receiving pre-medication doses before 12pm, they should take a divided evening dose at 4pm on the night of chemotherapy.

** consider palonosetron where there is concern, i.e. patient has risk factors of overrisk of delayed nausea and vomiting

*** consider adding aprepitant where there is concern over risk of anti-emetic failure as identified by assessment of patient risk factors

Alternative Agents

† or fosaprepitant 150mg intravenously on day 1 only (See Page 15)

Ondansetron IV must be infused over 15 minutes in patients over 65 years of age.
5HT Antagonists

Ondansetron 8mg (oral or IV) can be substituted with:
- Granisetron 1mg (oral or IV)
- Polanosteron 250 micrograms IV / 500 micrograms Oral (single dose)

Steroids

Patients with another steroid component in their chemotherapy regimen (eg CHOP) should not normally receive additional dexamethasone. However, as most other steroids are less effective at crossing the blood brain barrier, an alternative anti-emetic agent (as for managing breakthrough emesis: Page 8) should be added as a substitute. The same applies for patients where use of a steroid is undesirable – e.g. patients with diabetes.

Metoclopramide

Prochlorperazine 10mg every 4-6 hours as required or Cyclizine 50mg TDS can be substituted.
Credits & Acknowledgments

This document has been developed after consultation of the following guidelines:


In addition, thanks are due to Denise Blake, Paediatric Oncology Pharmacist – Newcastle Hospitals Foundation NHS Trust, upon who's paediatric guidelines some of this content has been derived.
References


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<td><strong>Document No:</strong></td>
<td>CHEMO 001</td>
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<td>Calum Polwart, Network Pharmacist</td>
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<tr>
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<tr>
<td><strong>Approved by:</strong></td>
<td>Chemotherapy Group</td>
</tr>
<tr>
<td><strong>Date Approved:</strong></td>
<td>18.09.13</td>
</tr>
<tr>
<td><strong>Due for Review:</strong></td>
<td>Sept 2015</td>
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**Summary of Changes**

1.1a Minor amendments per chemo group.

1.2a Added missing cross references. Added radiotherapy increased emetogenicity & reduced emetogenicity of carboplatin.

1.3 Updated guidance to reflect agreed changes to policy regarding dose of dexamethasone and NECDAG approval of aprepitant and palonosetron to match MASCC, ASCO and NCCN guidelines. Added antiemetic ladder as an appendix.

1.4 Updated format, added fosaprepitant and reference to MASSC 2010 guidelines updated table of emetogenicity

1.5 Added reference to oral formulation of palonsetron

2.0 Updated to reference infusion of ondansetron and revised dose schedule. Plus metoclopramide EMA recommendations.
Appendix One Antiemetic Ladder

This can be used as a quick visual guide to support the guidance and indicates how patients can progress through the levels.

Regimens with low risk of emesis

No Anti-emetics pre chemo
Metoclopramide as take home

IV Dexamethasone pre chemo
Ondansetron as take home
Dexamethasone as take home
Metoclopramide as take home

Regimens with moderate risk of emesis

IV Ondansetron pre chemo
IV Dexamethasone pre chemo
Ondansetron as take home
Dexamethasone as take home
Metoclopramide as take home

Regimens with high risk of emesis

As previous step with both Aprepitant and Palonosetron in place of Ondansetron IV and oral

As previous step with either Aprepitant in addition or Palonosetron in place of Ondansetron (IV and oral)