Northern Cancer Alliance

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

Adult Oncology & Haematology

Document Control

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Summary of Changes

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.
2.1	Added reference to Akynzeo® (netupitant and palonosetron) as alternative to palonsetron + aprepitant, reformatted and general updates
2.2	Changed summary table to localised Version of ASCO table, removed level 5 risk,
2.3	Typos corrected
2.4	Olanzapine added as a breakthrough option
2.5	carboplatin ≥ AUC4 added to high risk (3 drug combination) as option.

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

Summary – Standard Antiemetic Cover

Minimal Emetic Risk: 2-Chlorodeoxyadenosine, bevacizumab, bleomycin, busulfan, cetuximab, fludarabine, rituximab, vinblastine, vincristine, vinorelbine			
No antiemetic should be administered routinely before or after chemotherapy. However, normally supply metoclopramide as a rescue measure with first cycle			
Low Emetic Risk: fluorouracil, bortezomib, cabazitaxel, cytarabine <1000 mg/m2, docetaxel, doxorubicin HCL liposome injection, etoposide, gemcitabine, methotrexate, mitomycin, mitoxantrone, paclitaxel, panitumumab, pemetrexed, temsirolimus, topotecan, trastuzumab			
	Agent	**Dose on day of Chemotherapy**	**Dose(s) on Subsequent Days**
Corticosteroid	Dexamethasone	8mg oral or IV	No standard medication required. However, normally supply metoclopramide as a rescue measure with first cycle
Moderate Emetic Risk: azacitidine, alemtuzumab, bendamustine, carboplatin <AUC4, clofarabine, cyclophosphamide<1500 mg/m2, cytarabine>1000 mg/m2, daunorubicin, doxorubicin, epirubicin, idarubicin, ifosfamide, irinotecan, oxaliplatin			
5-HT3 Receptor Antagonist	Ondansetron ***or*** Palonosetron	8mg oral twice daily **OR** 8mg IV**	Ondansetron 8mg oral Twice Daily for 2 to 3 days Metoclopramide 10mg oral Twice Daily (for patients under 60kg) **OR** Three Times Daily (patients over 60kg) for 3 to 5 days when required
		0.5mg oral **OR** 0.25mg IV	Metoclopramide 10mg oral Twice Daily (for patients under 60kg) **OR** Three Times Daily (patients over 60kg) for 3 to 5 days when required
Corticosteroid	Dexamethasone	8mg oral or IV	4mg to 8mg oral for 2 to 3 days
High Emetic Risk: carboplatin ≥ AUC4*, carmustine, cisplatin, cyclophosphamide>1500 mg/m2, dacarbazine, dactinomycin, streptozocin, and combined anthracycline and cyclophosphamide regimens: All patients should be offered a three-drug combination of an NK1 receptor antagonist, a 5-HT3 receptor antagonist, and dexamethasone. The NK1 antagonist and 5-HT3 receptor antagonist may be given as a combination product			
	Agent	**Dose on day of Chemotherapy**	**Dose(s) on Subsequent Days**
NK1 Antagonist	Aprepitant ***or*** Fosaprepitant	125mg oral	80mg oral; days 2 and 3
		150mg IV	Day 1 only
5-HT3 Receptor Antagonist	Ondansetron ***or*** Palonosetron	8mg oral twice daily **OR** 8mg IV**	Ondansetron 8mg oral Twice Daily for 2 to 3 days Metoclopramide 10mg oral Twice Daily (for patients under 60kg) **OR** Three Times Daily (patients over 60kg) for 3 to 5 days when required
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Combined NK_1 antagonist and 5-HT_3 receptor antagonist	Netupitant-palonosetron	300mg netupitant / 0.5mg palonosetron oral	Metoclopramide 10mg oral Twice Daily (for patients under 60kg) **OR** Three Times Daily (patients over 60kg) for 3 to 5 days when required
Corticosteroid	Dexamethasone	8 mg oral or IV (can increase to 12mg if needed)	4mg to 8mg oral for 2 to 3 days
***3 drug combination for carbo >AUC4 if not adequately controlled with 2 drug regimen/ patient risk factors **Ondansetron IV must be infused over 15 minutes in patients over 65 years of age.**			

Contents

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

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 haemato-oncology patients receiving cytotoxic chemotherapy within the Northern Cancer Alliance.

Clinical Practice

These guidelines are intended to provide a framework to support clinical practice, they cannot 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 out-side of product licence.

There are now three alternate choices for NK1 inhibitors, the choice of product or combination of products should be made according to local Trust factors.

For all drugs the SmPC and BNF should be consulted prior to prescribing.

Causes of Nausea & Vomiting

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 and Age

Women are at increased risk of CINV than male.

Younger patients are more susceptible than older patients, with patients under 50 years old being at the greatest risk.

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
- Antimicrobials, including anti-fungals
- Ergot alkaloids
- Iron
- levodopa, carbidopa NSAIDs

Travel sickness

Patients who have a history of motion sickness are at increased risk of CINV

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 and Alcohol intake

Smoking reduces the risk of CINV. Patients with a long history of alcohol consumption are at reduced risk of CINV.

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 are 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 5)
- Constipation
- Bowel Obstruction
- Anxiety
- Metabolic Abnormalities
- Renal Failure
- Hypercalcaemia
- 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.

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

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. In **July 2013 The European Medicines Agency 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 exceeding total 30mg daily 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 (e.g. 4mg three times daily) 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

75years 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 15minutes in all patients over 65years 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 30minutes (Spector *et al* 1998) should be allowed to lapse between the oral dose and chemotherapy administration, peak plasma concentration is achieved after 90minutes. 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.

Transdermal Patch versions

Granisetron is available as transdermal patches, Sancuso®, that act for 7 days and releases 3.1 mg/24 hours. This product is currently not recommended in these guidelines as it is significantly more expensive than oral Granisetron.

Ondansetron is also available as a 'fast Melt' (dispersing oral dosage form).

Alternative 5HT3 antagonists

Tropisetron and Dolasetron 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 to other 5HT3 antagonists for the prevention of delayed emesis. Its 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 has no role to play in the rescue of patients with anti-emetic failure (i.e. treatment of breakthrough nausea / vomiting). Palonosetron is more expensive than generic ondansetron, though a cheaper generic version will be marketed in 2016. 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 $5HT_3$ antagonists *may not* be as pronounced with palonsetron.

NK-1 Antagonists: Aprepitant, Fosaprepitant & Akynzeo® (netupitant and palonosetron)

Aprepitant

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 requires a 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 NESCN would not use 20mg of dexamethasone as an anti-emetic, and therefore dose reduction of steroid is probably not necessary within NESCN 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

Fosaprepitant is a pro-drug of aprepitant that allows it to be given intravenously. A single 150mg IV dose can be used to replace the full oral schedule (day1: 125mg then 80mg on day 2

and day 3: 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 0.9%. 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 to 30 minutes should receive their fosaprepitant in a 250ml bag rather than a 100ml bag.

Clinical trials 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.

Akynzeo® (netupitant and palonosetron)

Netupitant is a novel potent and selective neurokinin-1 (NK1) receptor antagonist which blocks receptors located in the central nervous system and in the gastrointestinal tract wall. It appears to have a long duration (96 hours) when given as a single oral dose. The combination oral product Akynzeo® (netupitant 300mg and palonosetron 0.5mg) has been shown in three trials to be safe and effective for the prevention of acute and delayed phase CINV in patients receiving HEC and MEC when compared with palonosetron alone or palonosetron plus aprepitant. There is limited data on efficacy compared with ondansetron plus aprepitant.

Antiemetic cover with neurokinin 1 (NK1) receptor antagonists

ASCO 2017 antiemetic guidance recommends regimens containing carboplatin ≥ AUC4 should be classified as high risk of CINV and patients offered a three-drug combination of a neurokinin 1 (NK1) receptor antagonist, a serotonin (5-HT3) receptor antagonist and dexamethasone. Current practice in NCA is to start with a two drug regimen, serotonin (5-HT3) receptor antagonist and dexamethasone and add in a neurokinin 1 (NK1) receptor antagonist if CINV not adequately controlled. However if pre-assessment of patient identifies risk factors for CINV, units may wish to start with 3 drug combination.

Choice of NK1 antagonist should be based on local Trust factors, such as convenience of administration, local commissioning policy and relative costs of various combinations.

Notes

Licencing studies of both aprepitant and fosaprepitant have used 32mg of ondansetron on day one 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.

Olanzapine

Olanzapine is licenced as an anti-psychotic medication, however, it has been extensively trailed both for use in break-through and prophylaxis. It appears to have at least an additive effect when given alongside standard anti-emetics. Most studies have used 10mg once daily for 3 or 4 days. Weight gain is a concern with long term use of Olanzapine however this has not been observed in short term use. Fatigue is the most commonly reported side effect.

Four Drug Combination with Olzanapine for high risk patients

ASCO 2017 guidelines recommend 'patients who are treated with cisplatin and other high-emetic-risk single agents or anthracycline combined with cyclophosphamide should be offered a four-drug combination of a neurokinin 1 (NK1) receptor antagonist, a serotonin (5-HT3) receptor antagonist, dexamethasone, and olanzapine.'

Consensus in the NCA is that the four drug combination should be offered as 2nd line regimen if standard 1st line three drug therapy for high risk patient fails..

Levomepromazine (Nozinan)

Levomepromazine should be added after a dopamine agonist (e.g. metoclopramide), a glucocorticoid steroid (e.g. dexamethasone) and a $5HT_3$ antagonist (e.g. ondansetron).

Leveomepromazine 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 oral dose of 6.25mg – using ¼ of a 25mg tablet (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 orally 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.

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 an amnesic effect which may be useful in preventing conditioning behaviours 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.

Nabilone

Consider nabilone in patients refractory to all other treatments.

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

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 2011. 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 NESCN Chemotherapy Group.

Level 1: Minimal Risk (Less than 10%)		
Bevacizumab Bleomycin Busulphan Cladrabine Dasatinib Erlotinib	Fludarabine Gefitinib Nilotinib Rituximab Sorafenib	Vinblastine Vincristine Vindesine Vinflunine Vinorelbine (IV)
Level 2: Intermediate Risk (10 to 30%)		
Bortezomib Cetuximab Cabazitaxel* Cytarabine (≤1000mg/m²) Docetaxel* Etoposide Everolimus	Fluorouracil Gemcitabine Lapatinib Lenalidomide Methotrexate Mitomycin (IV) Mitoxantrone	Paclitaxel* Pemetrexed* Sunitinib Tegafur Uracil Temsirolimus Topotecan Trastuzumab
Level 3: Moderate Risk (30 to 90%)		
Azacitidine Bendamustine Carboplatin < AUC4 Clofarabine Cyclophosphamide (<1500mg/m²) Cytarabine > 1g/m² Daunorubicin Doxorubicin	Epirubicin Idarubicin Ifosfamide Imatinib Irinotecan Oxaliplatin Temozolomide Vinorelbine (Oral)	
Moderate risk chemotherapy covers a wide range of emetogenic risk. Consideration should specifically be given to other risk factors for nausea & vomiting (See Page 5)		
Level 4: High Risk (> 90%)		
Carmustine carboplatin ≥ AUC4 Cisplatin Cyclophosphamide (≥1500mg/m²) Dacarbazine	Dactinomycin Mechlorethamine Streptozocin	

*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

ABVD (Doxorubicin, Bleomycin, Vinblastine & Dacarbazine) – Level 4

AC or EC (Doxorubicin or Epirubicin & Cyclophosphamide) – Level 4

Carboplatin & Etoposide – Level 4

Carboplatin & Gemcitabine – Level 4

Carboplatin & Pemetrexed – Level 4

CHOP (Cyclophosphamide, Doxorubicin, Vincristine) – Level 4

Cisplatin & Etoposide – Level 4

Cisplatin & Gemcitabine – Level 4

Cisplatin & Pemetrexed – Level 4

Cisplatin & Topotecan - Level 4

Cisplatin & Vinorelbine (IV) – Level 4

CMF (Cyclophosphamide, Methotrexate & Fluorouracil) – Level 4

CVP (Cyclophosphamide & Vincristine) – Level 3

FC (Fludarabine & Cyclophosphamide) – Level 3

FEC-100 (Fluorouracil, Epirubicin & Cyclophosphamide) – Level 4

FMD (Fludarabine, Mitoxantrone & Dexamethasone) – Level 2

FOLFIRI (Irinotecan & Infusional Fluorouracil) – Level 4

FOLFOX (Oxaliplatin & Infusional Fluorouracil) – Level 4

Modified de Gramont (Infusional Fluorouracil) – Level 2

Paclitaxel & Gemcitabine – Level 3

R-CHOP (Rituximab & Cyclophosphamide, Doxorubicin, Vincristine) – Level 4

R-CVP (Rituximab & Cyclophosphamide & Vincristine) – Level 3

XELOX (Oxaliplatin & Capecitabine) – Level 4

Note this is not a comprehensive list, consultant drug SmPC and / or regimen protocols

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***3 drug combination for carbo >AUC4 if not adequately controlled with 2 drug regimen/patient risk factors **Ondansetron IV must be infused over 15 minutes in patients over 65 years of age.**			

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

Notes on Summary Sheet

5HT Antagonists

Ondansetron 8mg (oral or IV) can be substituted with:

- Granisetron 1mg (oral or IV)
- Palonosetron 250micrograms IV / 500 micrograms Oral (single dose)

Steroids

Patients with another steroid component in their chemotherapy regimen (e.g. 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 break through 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 oral 10mg every 4-6 hours as required *or* Cyclizine oral 50mg three times daily can be substituted.

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 (> 24hours 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
- Olanzapine

Failure of three drug combination for high risk patients

If the standard three drug (neurokinin 1 (NK1) receptor antagonist, a serotonin (5-HT3) receptor antagonist, dexamethasone) antiemetic cover is deemed to fail for patients on high risk drugs then they should be offered a four-drug combination of a neurokinin 1 (NK1) receptor antagonist, a serotonin (5-HT3) receptor antagonist, dexamethasone, and olanzapine.

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