

Prevention of anti-cancer induced nausea and vomiting

ID: 7 v.4 Under review

This document is an evidence based summary to complement treatment protocols and includes background and rationale for specific point of care actions. It is not intended to be a comprehensive literature review of all available evidence.

Related pages:

- [Management of radiation induced nausea and vomiting](#)

Key points

The purpose of this document is to provide guidance to minimise and, where possible, prevent treatment induced nausea and vomiting (CINV).

This document has been developed for the Australian clinical context using the most recent international guidelines including NCCN Clinical Practice Guidelines in Oncology - Antiemesis V.3 2018,¹ MASCC/ESMO Antiemetic Guidelines 2016 V1.2,² and ASCO Antiemetic Guidelines Update 2017³ and taking into account the availability of antiemetic drugs on the Australian Pharmaceutical Benefits Scheme (PBS).⁴

Recent changes to the national and international guidelines

There are a number of guidelines on the prevention and treatment of nausea and vomiting in cancer patients. However, there is no clear consensus between these guidelines for a number of cancer treatments. In 2016 to 2018 the MASCC/ESMO Antiemetic Guideline,² NCCN Antiemetic Guidelines¹ and ASCO Antiemetic Guidelines³ included some major updates with regards to antiemetic use for carboplatin, oxaliplatin and breast anthracycline and cyclophosphamide regimens, along with the addition of olanzapine as an antiemetic agent. A summary of the changes include:

- carboplatin is classified as moderately emetogenic regardless of the AUC dose in the MASCC/ESMO Antiemetic Guidelines² and ASCO Antiemetic Guidelines³. NCCN¹ classifies regimens with carboplatin dose AUC ≥ 4 as highly emetogenic and AUC < 4 as moderately emetogenic. NK1 receptor antagonists (in combination with a 5HT₃ receptor antagonist and dexamethasone) are now listed on the PBS for all carboplatin containing regimens, irrespective of the AUC dose.
- oxaliplatin regimens are still classified as moderately emetogenic in all guidelines however NCCN acknowledge that these regimens may be highly emetogenic. NK1 receptor antagonists (in combination with a 5HT₃ receptor antagonist and dexamethasone) are now listed on the PBS for all oxaliplatin regimens.
- breast anthracycline and cyclophosphamide regimens are classified as highly emetogenic by all guidelines. The MASCC/ESMO Antiemetic Guidelines and ASCO Antiemetic Guidelines recommend following the highly emetogenic guidelines on day 1, however no dexamethasone is required on days 2 or 3. The NCCN Guidelines recommend following the highly emetogenic regimen on day 1 with dexamethasone on days 2 to 4.
- olanzapine is recommended as part of the antiemetic treatment regimen for highly and moderately emetogenic risk agents as an effective antiemetic agent (note it is currently not TGA registered for this indication in Australia).^{1, 2, 3}

Based upon the above guidelines and clinical practice, eviQ have adopted the following guidelines:

- carboplatin regimens AUC ≥ 4 are classified as moderately emetogenic and follow the management for moderate emetogenic risk, however also include a NK1 receptor antagonist (as per PBS)
- carboplatin regimens AUC < 4 are classified as moderately emetogenic and follow the management for moderate emetogenic risk
- oxaliplatin regimens are still classified as moderately emetogenic and follow the management for moderate emetogenic risk, however also include a NK1 receptor antagonist (as per PBS)
- breast anthracycline and cyclophosphamide regimens are classified as highly emetogenic and follow the management for high emetogenic risk, including dexamethasone on days 2 to 4 with a note that these doses may not be required.

Background

Throughout this document 'chemotherapy' is used as an umbrella term and includes: anti-cancer drugs, hormonal agents, immune-system-modifying (immunomodifiers), biological and molecular targeted therapies.

Within the treatment protocols eviQ must include default antiemetics. The antiemetics chosen are based upon available evidence and clinical practice (which takes into consideration the efficacy, patient preference and availability on the PBS). These are only a default and may vary between institutions and can be substituted to reflect individual institutional policy.

Nausea and vomiting is one of the most frequently experienced side effects encountered by patients undergoing treatment with chemotherapy. Patients will often find the symptoms distressing and develop anxiety about the potential for such symptoms to recur with future cycles of chemotherapy.

Chemotherapy drugs vary in their ability to induce vomiting, and understanding the emetogenic potential of each chemotherapy drug and the overall treatment protocol is important in prescribing the appropriate prophylactic regimen.

Onset/duration

Chemotherapy induced nausea and vomiting (CINV) is generally classified into three phases: acute, delayed and anticipatory.

- **Acute emesis:** occurring within the first 24 hours following administration of chemotherapy, and generally peaking in the first 5-6 hours.
- **Delayed (or late) emesis:** occurring more than 24 hours following administration of chemotherapy, and may last up to 6 to 7 days.
- **Anticipatory emesis:** occurring prior to treatment as a conditioned response in patients who have developed significant nausea and vomiting during previous cycles of chemotherapy. This may be triggered by various stimuli (e.g. smell and sight of treatment room). The incidence of anticipatory nausea and/or vomiting ranges from 18 to 57%, and nausea is more common than vomiting.¹

Other categories include:

- **Breakthrough emesis:** development of nausea or vomiting, despite standard anti-emetic therapy; requires "rescue" with an additional agent.
- **Refractory emesis:** development of nausea or vomiting during subsequent treatment cycles when antiemetic prophylaxis and/or rescue have failed in earlier cycles.

It may be difficult to distinguish between acute and delayed phases when chemotherapy is given over a number of days or weeks. Optimal emetic control in the acute phase is essential to prevent nausea and vomiting in the delayed phase.

Radiation induced nausea and vomiting (RINV) is a common side effect of patients undergoing radiation therapy; it is related to radiation site, dose, volume irradiated and radiation therapy technique, and is generally milder than CINV. Read more about the [management of radiation induced nausea and vomiting](#).

Risk factors

Consideration should also be given to patient-related factors which may increase the risk of CINV, including:

- female sex,
- prior chemotherapy,
- younger age (<50 years),
- history of motion sickness, and/or nausea in pregnancy,
- poor performance status,
- previous episodes of chemotherapy-associated emesis, and
- no alcohol consumption.

A chronic high consumption of alcohol, substance misuse or smoking appears to protect against CINV.

Assessment

Signs and symptoms

Chemotherapy induced nausea and vomiting can include the following signs and symptoms:

- nausea
- vomiting
- pallor

- diaphoresis (increased perspiration)
- salivation
- anorexia (in advanced nausea and vomiting)
- signs/symptoms of dehydration:
 - postural hypotension (dizziness)
 - tachycardia (rapid heart rate)
 - low urine output
 - headaches.

Exclude:

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

- constipation
- bowel obstruction
- gastroparesis
- malignant ascites
- anxiety
- fluid and electrolyte imbalances (e.g. hypercalcaemia and renal failure)
- uraemia
- metastases or tumour site involving gastrointestinal tract, liver or central nervous system
- raised intracranial pressure
- peptic ulcer disease
- recent or concurrent radiation therapy
- vestibular dysfunction.

Investigations and diagnosis

The following should be included in an assessment of nausea and vomiting as part of a complete patient assessment:

- history and compliance with antiemetics
- the frequency (number of episodes in 24 hours), intensity, onset and duration of vomiting
- concomitant medications (e.g. opioids)
- hydration status
- nutritional intake +/- weight loss
- heartburn/dyspepsia
- [haematemesis](#)
- blood test:
 - full blood count (to assess for neutropenia and/or anaemia)
 - EUC + CMP (to assess for electrolyte imbalance).

Grading

Grade	Vomiting	Nausea
1	Intervention not indicated	Loss of appetite without alteration of eating habits
2	Outpatient IV hydration; medical intervention indicated	Oral intake decreased without significant weight loss, dehydration or malnutrition
3	Tube feeding, TPN or hospitalisation indicated	Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalisation indicated
4	Life-threatening consequences; urgent intervention indicated	-
5	Death	-

Common Terminology Criteria for Adverse Events Version (CTCAE) Version 5.0, 27 November, 2017

Management

Prevention and control of nausea and vomiting is of paramount importance, as when inadequately controlled, vomiting can result in serious metabolic imbalance, dehydration, anorexia, deterioration in physical and mental status, and withdrawal from potentially useful and/or curative treatment. Nausea and vomiting are among the most distressing and feared side effects for cancer patients and their families; prophylaxis when indicated and aggressive treatment are essential.

Antiemetic treatment for patients who receive combination chemotherapy should be determined according to the drug with the greatest emetic risk.

Optimal emetic control in the acute phase (the first 24 hours) is essential to prevent nausea and vomiting in the delayed phase (24 to 72 hours post chemotherapy).

For the purpose of this document, it is recommended that all oral and intravenous antiemetics are administered 60 minutes and 30 minutes respectively, before chemotherapy.

Please note that all eviQ chemotherapy treatment protocols state the specific emetogenic potential within the protocol document, and this should be the primary point of reference for prescribing anti-emetics.

The emetogenic risk of each agent is categorised below.

Management of high emetogenic risk (>90% risk of emesis)*

IV agents	
Carmustine	Cyclophosphamide with anthracycline in breast cancer
Cisplatin	Dacarbazine
Cyclophosphamide $\geq 1500 \text{ mg/m}^2$	Streptozocin
PO agents	
Busulfan $\geq 4 \text{ mg daily}$	Procarbazine

* percentage of patients who experience emesis in the absence of effective antiemetic prophylaxis

Recommended antiemetic regimen for highly emetogenic chemotherapy

For the purpose of this document, it is recommended that all oral and intravenous antiemetics are administered 60 minutes and 30 minutes respectively, before chemotherapy.

Acute emesis (day 1)

Neurokinin1 (NK1) receptor antagonist **PLUS**
 5HT₃ receptor antagonist **PLUS**
 Dexamethasone

Refer to tables below for the recommended agents and doses.

Recommended doses of neurokinin1 (NK1) receptor antagonists

NK1 RA	Intravenously		Orally
Aprepitant	NA	or	165 mg*
Fosaprepitant	150 mg	or	NA
Netupitant	NA	or	300 mg (fixed combination with 0.5 mg palonosetron)

* Aprepitant 165 mg as a single dose before chemotherapy (and none on days 2 and 3) is registered by TGA, but no randomised clinical trials have tested this dose schedule.

Recommended doses of 5HT₃ receptor antagonists

	Intravenously		Orally
Granisetron	3 mg	or	2 mg
Ondansetron	8 mg	or	16 mg (in divided doses)
Palonosetron	0.25 mg	or	0.5 mg (fixed combination with netupitant)

	Intravenously	Orally
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At equivalent doses for the prevention of acute emesis, 5HT₃ antagonists have equal efficacy.

ECG interval changes and cardiac arrhythmias:

- ECG interval changes are a class effect of the first generation 5HT₃ receptor antagonists, including ondansetron and granisetron; their use should be avoided in patients with congenital long QT syndrome
- *Ondansetron and QTc interval prolongation* - Read more about this effect in the [TGA Medicines Safety Update](#)
- QTc prolongation has not been described with palonosetron.⁵

Recommended doses of corticosteroids (dexamethasone)

Dexamethasone 20 mg PO or IV ONCE on day 1 (12 mg when used with (fos)aprepitant or netupitant)*

*The 12 mg dose of dexamethasone is the only one tested with (fos)aprepitant/netupitant in large, randomised trials

Delayed emesis (from day 2)

Dexamethasone 8 mg PO or IV ONCE daily for 3 days post chemotherapy (dexamethasone 8 mg PO or IV TWICE daily¹ for 3 days post chemotherapy when used without an NK1 receptor antagonist).

Practice points:

- New recommendation for anthracycline-cyclophosphamide chemotherapy for breast cancer:²
 - acute nausea: if an NK1 receptor antagonist is not available, palonosetron is the preferred 5HT₃ receptor antagonist. Clinical practice suggests that the full dose of dexamethasone on day 1 may not be required and may be reduced to 8mg at the clinicians discretion.¹
 - delayed nausea: if the NK1 receptor antagonist used on day 1 is fosaprepitant or netupitant then dexamethasone on days 2 and 3 is not required (i.e. only use dexamethasone for delayed emesis if aprepitant is given on day 1). *Note: this is per MASCC/ESMO Antiemetic Guidelines 2016 where aprepitant 125 mg is used on day 1, and unsure if this recommendation is based upon using aprepitant 165 mg or the 125/80/80 mg dosing schedule. evi has included dexamethasone on days 2 to 4 based on the NCCN Guideline and clinical practice.*
- Consider omitting dexamethasone in patients receiving chemotherapy for AML or MDS to reduce the risk of opportunistic infections. These patients may require a prolonged course of a 5HT₃ receptor antagonist, usually continuing until 2-3 days after highly emetogenic chemotherapy is completed.
- Omit dexamethasone when corticosteroids are included as part of the chemotherapy or premedication regimen, or when the patient is already on corticosteroids equivalent to the dose of dexamethasone that is required (dexamethasone 1 mg ~ hydrocortisone 27 mg ~ methylprednisolone 5 mg ~ prednisolone 7 mg).⁶
- Potential drug interactions between chemotherapy agents, antiemetic therapies and various other drugs should always be considered.¹
- Patients with dyspepsia may benefit from antacid therapy with a proton pump inhibitor or H₂ antagonist. Many patients have difficulty differentiating between nausea and dyspepsia.

Management of moderate emetogenic risk (30 to 90% risk of emesis)*

IV agents	
Aldesleukin > 12 to 15 million units/m ²	Doxorubicin
Alemtuzumab	Epirubicin
Amsacrine	Fotemustine
Arsenic trioxide	Idarubicin
Azacitidine	Ifosfamide
Bendamustine	Interferon alfa ≥ 10 million IU/m ²

* Percentage of patients who experience emesis in the absence of effective antiemetic prophylaxis.

** Daily use of antiemetics is not recommended based on clinical experience¹

*Although melphalan is generally regarded as being moderately emetogenic, when used in high doses as part of conditioning regimens for autologous bone marrow transplant, it is regarded as being highly emetogenic in clinical practice.

*NK1 receptor antagonists are included in protocols where carboplatin dose AUC ≥ 4. NK1 receptor antagonists are available on the PBS if required for carboplatin dose AUC < 4.

*Although oxaliplatin is regarded as being moderately emetogenic, in clinical practice it may be highly emetogenic. NK1 receptor antagonists are available on the PBS for primary prophylaxis.

Busulfan	Irinotecan
Carboplatin #	Melphalan ⁺
Clofarabine	Methotrexate $\geq 250 \text{ mg/m}^2$
Cyclophosphamide IV $< 1500 \text{ mg/m}^2$ <u>without</u> anthracycline	Oxaliplatin [^]
Cytarabine $> 1000 \text{ mg/m}^2$	Raltitrexed
Dactinomycin (actinomycin D)	Romidepsin
Daunorubicin	Vinflunine
PO agents	
Crizotinib	Midostaurin
Cyclophosphamide	Temozolomide
Imatinib**	Vinorelbine
Lomustine	

* Percentage of patients who experience emesis in the absence of effective antiemetic prophylaxis.

** Daily use of antiemetics is not recommended based on clinical experience¹

[^] Although melphalan is generally regarded as being moderately emetogenic, when used in high doses as part of conditioning regimens for autologous bone marrow transplant, it is regarded as being highly emetogenic in clinical practice.

[#] NK1 receptor antagonists are included in protocols where carboplatin dose $\text{AUC} \geq 4$. NK1 receptor antagonists are available on the PBS if required for carboplatin dose $\text{AUC} < 4$.

[^] Although oxaliplatin is regarded as being moderately emetogenic, in clinical practice it may be highly emetogenic. NK1 receptor antagonists are available on the PBS for primary prophylaxis.

Recommended antiemetic regimen for moderately emetogenic chemotherapy

For the purpose of this document, it is recommended that all oral and intravenous antiemetics are administered 60 minutes and 30 minutes respectively, before chemotherapy.

Acute emesis (day 1)

Palonosetron 0.25 mg IV* **PLUS**

Dexamethasone 8 mg PO or IV

* As per MASCC/ESMO Antiemetic Guidelines 2016 V1.2² palonosetron is the preferred 5HT₃ receptor antagonist in antiemetic regimens not containing an NK1 receptor antagonist.

Refer to the following table for other 5HT₃ receptor antagonists and their doses.

	Intravenously		Orally
Granisetron	3 mg	or	2 mg
Ondansetron	8 mg	or	16 mg (in divided doses)
Palonosetron	0.25 mg	or	0.5 mg (fixed combination with netupitant)

At equivalent doses for the prevention of acute emesis, 5HT₃ receptor antagonists have equal efficacy.

ECG interval changes and cardiac arrhythmias:

- ECG interval changes are a class effect of the first-generation 5HT₃ receptor antagonists, including ondansetron and granisetron; their use should be avoided in patients with congenital long QT syndrome
- *Ondansetron and QTc interval prolongation* - Read more about this effect in the [TGA Medicines Safety Update](#)
- QTc prolongation has not been described with palonosetron.⁵

Delayed emesis (from day 2)

Dexamethasone 8 mg PO or IV ONCE daily (or in divided doses) for 2 days post chemotherapy.

Practice points:

- Dexamethasone for delayed emesis may not be required for all patients and may be dose reduced or omitted at the clinicians discretion.
- Consider omitting dexamethasone in patients receiving chemotherapy for AML or MDS to reduce the risk of opportunistic infections. These patients may require a prolonged course of a 5HT₃ receptor antagonist, usually continuing until 2-3 days after highly emetic chemotherapy is completed.
- Omit dexamethasone when corticosteroids are included as part of the chemotherapy or premedication regimen, or when the patient is already on corticosteroids equivalent to the dose of dexamethasone that is required (dexamethasone 1 mg ~ hydrocortisone 27 mg ~ methylprednisolone 5 mg ~ prednisolone 7 mg).⁶
- Potential drug interactions between chemotherapy agents/antiemetic therapies and various other drugs should always be considered.¹
- Patients with dyspepsia may benefit from antacid therapy with a proton pump inhibitor or H₂ antagonist. Many patients have difficulty differentiating between nausea and dyspepsia.

Management of low emetogenic risk (10 to 30% risk of emesis)*

IV agents	
Aflibercept	Ipilimumab
Atezolizumab	Liposomal doxorubicin
Blinatumomab	Methotrexate < 250 mg/m ²
Brentuximab vedotin	Mitomycin
Bortezomib	Mitozantrone
Cabazitaxel	nab-Paclitaxel
Carfilzomib	Paclitaxel
Cetuximab	Panitumumab
Cytarabine ≤ 1000 mg/m ²	Pemetrexed
Docetaxel	Pertuzumab
Eribulin mesilate	Temsirolimus
Etoposide	Teniposide
Fluorouracil	Thiotepa
Gemcitabine	Topotecan
Interferon alfa > 5 to < 10 million IU/m ²	Trastuzumab emtansine
PO agents	
Abiraterone	Lenalidomide
Afatinib	Nilotinib
Alectinib	Olaparib
Axitinib	Osimertinib
Capecitabine	Pazopanib
Dabrafenib	Ponatinib
Dasatinib	Regorafenib
Etoposide	Sunitinib
Everolimus	Thalidomide
Fludarabine	Tretinoin
Ibrutinib	Vandetanib
Idelalisib	Venetoclax

Lapatinib	Vorinostat
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**percentage of patients who experience emesis in the absence of effective antiemetic prophylaxis*

Recommended antiemetic regimen for low emetogenic chemotherapy

For the purpose of this document, it is recommended that all oral and intravenous antiemetics are administered 60 minutes and 30 minutes respectively, before chemotherapy.

Acute emesis (day 1)

Dexamethasone 4 mg to 8 mg PO or IV **OR**

Metoclopramide 10 mg as required; maximum of 30 mg/24 hours **OR**

Prochlorperazine 10 mg PO as required

Delayed emesis (from day 2)

Antiemetics for delayed emesis are not routinely required.

Management of minimal emetogenic risk (<10% risk of emesis)*

IV agents	
Asparaginase - Colaspase®	Obinutuzumab
Bevacizumab	Ofatumumab
Bleomycin	Pembrolizumab
Cladribine	Rituximab
Daratumumab	Trastuzumab
Durvalumab	Vinorelbine
Fludarabine	Vincristine
Interferon alfa ≤ 5 million IU/m ²	Vindesine**
Nivolumab	Vinorelbine
PO agents	
Cabozantinib	Pomalidomide
Chlorambucil	Ribociclib
Erlotinib	Ruxolitinib
Gefitinib	Sorafenib
Hydroxyurea	Tioguanine
Melphalan	Trametinib
Mercaptopurine	Vemurafenib
Methotrexate	Vismodegib

**percentage of patients who experience emesis in the absence of effective antiemetic prophylaxis*

*** there is limited data on the emetogenic potential of vindesine and therefore its risk was extrapolated from the class effect of vinca alkaloids.*

No antiemetic should be routinely administered before chemotherapy in patients without a history of nausea and vomiting. If patients experience nausea and/or vomiting, consider using the [low antiemetic prophylaxis regimen](#).

Management of breakthrough emesis

Practice points:

NOTE: The literature on breakthrough emesis management is limited. These guidelines have been adapted directly from the NCCN Guidelines V.2 2017 ¹ and the product information for the individual drugs.

- Breakthrough nausea and vomiting poses a difficult scenario. It is generally far easier to prevent nausea and vomiting than it is to treat it.
- The principle of breakthrough treatment is to give an additional agent from a different drug class. The choice of agent should be based on assessment of the current prevention and strategies used. Some patients may require several agents with differing mechanisms of action.
- Consider regular around the clock administration rather than as required dosing.
- If nausea and vomiting is still not controlled consider changing the antiemetic therapy to a higher level e.g. from a low to a moderate regimen.
- Changing to a different 5HT₃ receptor antagonist may be efficacious in some patients, although there is limited anecdotal evidence.
- Potential drug interactions between chemotherapy agents/antiemetic therapies and various other drugs should always be considered.¹
- Patients with dyspepsia may benefit from antacid therapy with a proton pump inhibitor or H₂ antagonist. Many patients have difficulty differentiating between nausea and dyspepsia.

Commonly used drugs for breakthrough emesis

Drug class	Drug	Dose
Benzodiazepine	Lorazepam	0.5 mg to 2 mg <i>orally/sublingually/intravenously</i> every 6 hours
Corticosteroid	Dexamethasone	4 mg to 8 mg <i>orally</i> or <i>intravenously</i> TWICE daily
5HT ₃ receptor antagonists*	Granisetron	2 mg <i>orally</i> or 1 mg <i>intravenously</i> as a single dose (additional 1 mg IV doses may be given at intervals >10 minutes up to maximum of 9 mg/24 hours)
	Ondansetron	8 mg <i>orally</i> or <i>intravenously</i> TWICE daily (additional doses may be given up to maximum of 32 mg/24 hours)
	Tropisetron	5 mg <i>intravenously</i> ONCE daily
Dopamine receptor antagonists	Haloperidol	0.5 mg to 2 mg <i>orally/intravenously</i> every 4 to 6 hours
	Metoclopramide	10 mg <i>orally</i> or <i>intravenously</i> three time a day (maximum of 30 mg/24 hours, up to 5 days)
	Prochlorperazine	10 mg <i>orally</i> every 6 hours
	Promethazine	10 mg to 25 mg <i>orally</i> or 12.5 mg to 25 mg <i>intravenously</i> (<i>central line only</i>) ¹ every 4 to 6 hours

* ECG interval changes and cardiac arrhythmias:

- ECG interval changes are a class effect of the first-generation 5HT₃ receptor antagonists, including ondansetron and granisetron; their use should be avoided in patients with congenital long QT syndrome.
- *Ondansetron and QTc interval prolongation* - read more about this effect in the [TGA Medicines Safety Update](#).
- QTc prolongation has not been described with palonosetron.⁵

Management of anticipatory emesis

Practice points:

- The best management of anticipatory emesis is to ensure good control of acute and delayed emesis, starting from the initial chemotherapy cycle.
- Non-pharmacologic methods such as behavioural/psychological techniques may be useful.
- Benzodiazepines may be useful e.g. lorazepam.

Lorazepam 0.5 mg to 2 mg *orally* on the night before and the morning of treatment.

Practice points:

NOTE: The literature on antiemetic treatment for multi-day chemotherapy protocols is limited; therefore it is difficult to recommend a specific antiemetic regimen for multi-day chemotherapy protocols. Practical issues also need to be considered when prescribing the antiemetic regimen, taking into account the administration setting (e.g. inpatient vs. outpatient), preferred route of administration (IV vs. oral), duration of the 5HT₃ receptor antagonist and appropriate associated dosing intervals, tolerability of daily antiemetics (e.g. corticosteroids), and adherence/compliance issues.

The NCCN Guidelines V.2 2017,¹ MASCC/ESMO Antiemetic Guidelines 2016² and ASCO Antiemetic Guidelines Update 2017³ recommend:

- Antiemetics appropriate for the emetogenic risk class of the chemotherapy be administered for each day of the chemotherapy and for two days after, if appropriate.³ The period of risk for delayed emesis also depends on the specific regimen and the emetogenic potential of the last chemotherapy agent administered in the regimen.¹
- Dexamethasone dose may be modified or omitted when the chemotherapy regimen also includes a corticosteroid.
- The use of a steroid as an antiemetic is not recommended when using treatment regimens containing drugs that elicit an immune response such as interleukin-2 (IL-2, aldesleukin), interferon, ipilimumab, nivolumab or pembrolizumab¹.
- For patients receiving multi-day (three or more days) protocols that are moderately or highly emetogenic, it is recommended to use a daily dose of an oral 5HT₃ receptor antagonist plus daily dexamethasone, with the addition of an NK1 receptor antagonist for highly emetogenic regimens, starting on day 1 (*note that the frequency of repeated administration of the 5HT₃ receptor antagonist depends on the agent chosen*).
- Repeat dosing of IV palonosetron 0.25 mg is likely to be safe, based on available evidence. However, in terms of efficacy, limited data are available for multi-day dosing.⁷
- If oral aprepitant is given on day 1, limited data exists to support repeat administration of aprepitant on days 4 and 5 after multi-day chemotherapy.¹
- Studies investigating repeat dosing of fosaprepitant or netupitant are not available.¹

Special situations

- **Consecutive day therapy with highly emetogenic agents:** prophylaxis is more difficult; this may be due to anticipatory emesis on the subsequent treatment days and/or to the compounding of acute and delayed effects of treatment. ASCO Antiemetic Guidelines suggest that antiemetics appropriate for the emetogenic risk of the chemotherapy be administered for each day of the chemotherapy and for two days after, if appropriate.³
- **Fractionated chemotherapy (e.g. 5 day cisplatin):** patients will require the acute phase antiemetics to be administered on each day that chemotherapy is given (e.g. an oral 5HT₃ receptor antagonist plus dexamethasone, with the addition of aprepitant or fosaprepitant starting on day 1).³
- **Induction therapy for acute leukaemia:** High-dose cytarabine regimens (in which cytarabine is administered daily for five or seven days, often with an anthracycline) are the cornerstone of treatment for acute myeloid leukaemia (AML). Few studies have addressed the issue of CINV and optimal prophylaxis in this setting.^{8,9,10} Although data are lacking, a daily dose of a 5HT₃ receptor antagonist (e.g. ondansetron 16 mg daily or 8 mg BD) with or without dexamethasone appears to be a reasonable option in this setting.¹¹
- **High dose chemotherapy:** High dose chemotherapy is administered in association with blood and marrow transplant (BMT). Agents used as part of the conditioning therapy are often moderate to high emetogenic risk. Other factors can contribute to an increased incidence and severity of CINV in this setting e.g. combined radiation therapy, especially total body irradiation (TBI). The 2017 updated antiemetic guidelines from ASCO suggested a 5HT₃ receptor antagonist plus dexamethasone with consideration of aprepitant in this setting.³

Patient education

Educate patient:

- to report signs of dehydration:
 - reduced urine output
 - rapid heart rate
 - headaches
 - flushed, dry skin
 - coated tongue
 - irritability
 - confusion
 - dizziness
- to take antiemetics 30 minutes prior to meals

- on self care measures:
 - avoid eating or preparing food when they feel sick, and if possible have someone else do the cooking
 - avoid fried foods and foods with a strong smell
 - eat cold or warm food if the smell of hot food makes them feel sick
 - eat several small snacks and meals each day (rather than three large meals), and chew the food well
 - peppermints or peppermint tea may help with nausea
 - ginger may help with nausea, and to try ginger biscuits or ginger beer
 - sip drinks slowly
 - avoid drinking too much before a meal
 - avoid alcohol and high volumes of coffee.

Read more about [nausea and vomiting during cancer treatment](#) in the patient information. This patient information sheet is available in [several languages](#).

Read more about [food and cancer](#) on the Cancer Council website.

References

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History

Version 4

Date	Summary of changes
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30/05/2009	<ul style="list-style-type: none"> All approved antiemetic documents on CI-SCaT reviewed and collated. Updated with MASCC 2008 Antiemetic Guidelines and NCCN 2009 Antiemetic Guidelines. Breakthrough emesis and anticipatory emesis recommendations added. Transferred to eviQ.
08/10/2010	Everolimus added to low emetogenicity table (incidence of nausea and vomiting $\geq 10\%$ as per PI)
12/07/2011	PO etoposide and temsirolimus now added to low emetogenicity table, as per MASCC guidelines IV dose of prochlorperazine added as 12.5 mg
06/12/2011	Classification of sunitinib changed from minimal to low emetogenicity as per update in MASCC 2011 guidelines
19/04/2012	Phase 1 Review: protocol reviewed and updated as per updates in MASCC, ASCO and NCCN guidelines. Palonosetron added for moderate emetogenicity in combination with dexamethasone
19/06/2012	Phase 2 Review: title changed and classification of drug emetogenicity updated as per MASCC/ESMO, ASCO and NCCN guidelines. Access superseded version ID 7 eviQ Antiemetic regimens .
08/01/2013	Addition of abiraterone to table
15/03/2013	Addition of pazopanib and vemurafenib to table. Ondansetron and QTc interval prolongation - TGA Medicines Safety Update added
05/11/2013	Aprepitant 125/80/80 mg PO replaced with aprepitant 165 mg PO single dose on day 1. IV and rectal prochlorperazine removed
17/03/2015	<ul style="list-style-type: none"> Reformatted into new eviQ template. New sections added: background, onset/duration, assessment and patient education. Content updated in accordance with latest NCCN and MASCC/ESMO guidelines. TGA medicines safety update added re metoclopramide dosing (Read more about the TGA alert for metoclopramide). New drugs added to tables. Updated the multiday section.
16/10/2015	<p>New drugs added:</p> <ul style="list-style-type: none"> aflibercept bendamustine brentuximab ibrutinib nivolumab obinutuzumab pembrolizumab pomalidomide vinorelbine vinflunine
01/08/2016	<ul style="list-style-type: none"> Updated to align with MASCC/ESMO Antiemetic Guideline 2016 (V.1.1) and NCCN Version 2. 2016. Removed clinical alert regarding metoclopramide dosing as MASCC/ESMO now include restrictions on the dose of metoclopramide, as indicated by EMA. All relevant eviQ protocols have been updated with this information e.g. metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days). Inclusion of netupitant for highly emetogenic chemotherapy (netupitant is administered with palonosetron 0.5 mg (PO) as part of the fixed-dose oral combination agent NEPA). Dactinomycin moved from high to moderate emetogenic category (rationale: NCCN classify as moderate and PBS group with other moderately emetogenic agents, when using aprepitant if have prior episode of CINIV). In moderate section, included recommended antiemetics for patients receiving carboplatin, as per 2016 MASCC/ESMO guidelines. Changed from minimal to low: IV ipilimumab and pertuzumab; PO afatinib, dabrafenib, dasatinib, ibrutinib, nilotinib, pazopanib, regorafenib, sunitinib, vandetanib. Changed from low to minimal: PO pomalidomide, IV trastuzumab. Changed moderate to low: PO vandetanib. Added to low: PO carfilzomib, olaparib and ponatinib. Added to minimal: ruxolitinib and vismodegib.

Date	Summary of changes
	<ul style="list-style-type: none"> Breakthrough: benzodiazepine dose changed from every 4-6 hours to every 6 hours; added IV to haloperidol.
20/09/2016	<ul style="list-style-type: none"> Updated reference mark 1 to consistently display NCCN Version 2. 2016. Corrected first bullet reference in High Emetogenic Risk - Delayed Emesis - Practice Point to MASCC/ESMO (reference mark 2). Moved sentence below Moderate Emetogenic Risk title down into practice points and corrected it to state that for patients on some MEC with a prior episode of CIN V, aprepitant is the only NK1 antagonist available on the PBS, in combination with a 5HT3 antagonist and steroid. Corrected last sub-bullet in Moderate Emetogenic Risk - Practice Points to state that in Australia aprepitant is the only NK1 antagonist PBS reimbursed for carboplatin, and only if patients have had a prior episode of n & v. Updated sentence in Antiemetics for Multi-day Chemotherapy Protocols - practice points on why steroids should be avoided as antiemetics with certain treatments to give more context.
06/10/2016	<ul style="list-style-type: none"> Removed "and only if patients have had a prior episode of N & V." from last sub-bullet in Moderate Emetogenic Risk - Practice points, to reflect change in PBS criteria as of 01/10/2016.
30/08/2017	<p>Transferred to new eviQ website. Version number changed to V.3.</p> <p>Document reviewed.</p> <p>Antiemetic medications included as substitutable defaults were aligned with the national and international guidelines.</p> <ul style="list-style-type: none"> HIGH emetogenic risk: Day 1: netupitant 300 mg PO + palonosetron 0.5 mg PO and dexamethasone 12 mg PO Day 2 to 4 (or three days post highly emetogenic drug): dexamethasone 8 mg PO daily <ul style="list-style-type: none"> Carboplatin regimens with AUC ≥ 4 are considered highly emetogenic and follow the management for high emetogenic risk. Carboplatin AUC < 4 regimens are considered moderately emetogenic and follow the management for moderate emetogenic risk. Oxaliplatin regimens are still classified as moderately emetogenic, however it is recommended that the management for high emetogenic risk be followed. The breast anthracycline and cyclophosphamide regimens are classified as highly emetogenic and follow the management for high emetogenic risk, including dexamethasone on days 2 to 4. MODERATE emetogenic risk: Day 1: palonosetron 0.25 mg IV and dexamethasone 8mg PO Days 2 to 3 (or two days post moderately emetogenic drug): dexamethasone 8 mg PO daily
26/03/2018	Added daratumumab to 'Management of minimal emetogenic risk'.
24/04/2018	CTCAE information updated to v5.0 published November 27, 2017.
26/06/2018	<ul style="list-style-type: none"> Information updated in line with international guidelines including addition of NCCN Clinical Practice Guidelines in Oncology - Antiemesis - V.3.2018. Updated wording to dexamethasone in the treatment protocols. Information regarding the use of olanzapine being recommended internationally added. <p>Link to Notification: update to antiemetics for eviQ medical oncology protocols – June 2018 for further details.</p>
17/01/2019	<p>Document updated:</p> <ul style="list-style-type: none"> Carboplatin classification changed from high to moderate emetogenicity regardless of AUC, with the addition of a NK1 antagonist if AUC ≥ 4 as per MASCC/ESMO Antiemetic Guidelines 2016 V1.2, ASCO Antiemetic Guidelines Update 2017. Dexamethasone doses on day 2 and 3 may not be required and may be reduced or omitted at the clinician's discretion as per medical oncology reference committee consensus Oxaliplatin reworded to follow the management for moderate emetogenicity with the addition of a NK1 antagonist Added to moderate emetogenicity- romidepsin, midostaurin Added to low emetogenicity- atezolizumab, blinatumomab, osimertinib, venetoclax Added to minimal emetogenicity- durvalumab, alectinib, cabozantinib, ribociclib <p>Version number changed to V.4</p>

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