MASCC/ESMO ANTIEMETIC GUIDELINE 2016

Organizing and Overall Meeting Chairs:
Matti Aapro, MD
Richard J. Gralla, MD
Jørn Herrstedt, MD, DMSli
Alex Molassiotis, RN, PhD
Fausto Roila, MD

© Multinational Association of Supportive Care in Cancer™ All rights reserved worldwide.
These slides are provided to all by the Multinational Association of Supportive Care in Cancer and can be used freely, provided no changes are made and the MASCC and ESMO logos, as well as date of the information are retained.

For questions please contact:
Matti Aapro at maapro@genolier.net
Chair, MASCC Antiemetic Study Group
or Alex Molassiotis at alex.molasiotis@polyu.edu.hk
Past Chair, MASCC Antiemetic Study Group
Consensus

A few comments on this guideline set:

• This set of guideline slides represents the latest edition of the guideline process.

• This set of slides has been endorsed by the MASCC Antiemetic Guideline Committee and ESMO Guideline Committee.

• The guidelines are based on the votes of the panel at the Copenhagen Consensus Conference on Antiemetic Therapy, June 2015.

• Latest update: March 2016.
2016 V.1.2 Changes from 2016 V.1.0

The Steering Committee has clarified some points:

• A footnote clarified that aprepitant 165 mg is approved by regulatory authorities in some parts of the world (although no randomised clinical trial has investigated this dose). Thus use of aprepitant 80 mg in the delayed phase is only for those cases where aprepitant 125 mg is used on day 1.

• Slide 12 has been corrected

• A probable modification in pediatric guidelines based on the recent Cochrane meta-analysis is indicated.

• The need to modify the dose of dexamethasone has been clarified to include all NK\textsubscript{1} RAs that have a CYP3A4 interaction.

• Restrictions on the dose of metoclopramide, as indicated by EMA, are highlighted as a footnote.
2015 Copenhagen Antiemetic Guideline Committee Participants

- Matti Aapro, MD
- Enzo Ballatori, PhD
- Mary Jacqueline Brames, RN, BSN
- Eduardo Bruera, MD
- Luigi Celio, MD
- Alex Chan, PharmD
- Rebecca Clark-Snow, RN, BSN
- Andrew Davies, MD
- Mellar Davis, MD
- Kristopher Dennis, MD
- L. Lee Dupuis, RPh, PhD
- Lawrence Einhorn, MD
- Petra Feyer, MD
- Richard Gralla, MD
- Jørn Herrstedt, MD, DMSci
- Paul Hesketh, MD
- Regine Deniel Ihlen (patient advocate)
- Franziska Jahn, MD
- Karin Jordan, MD
- Ernesto Maranzano, MD
- Alexander Molassiotis, RN, PhD
- Rudolph Navari, MD, PhD
- Ian Olver, MD, PhD
- Andrea Orsey, MD
- Bernardo Rapoport, MD
- Cynthia Rittenberg, RN, MN
- Carla Ripamonti, MD
- Joseph Roscoe, PhD
- Fausto Roila, MD
- Christina Ruhlmann, MD, PhD
- Wim Tissing, MD
- Mitsue Saito, MD
- Lee Schwartzberg, MD
- Lillian Sung, MD, PhD
- Declan Walsh, MD
- David Warr, MD
- Marianne van de Wetering, PhD
- Theresa Zanatta (patient advocate)
- Li Zhang, MD
Disclosures  (Receipt of honoraria or research funding; stocks; employment; conflicting leadership positions; expert testimony; other remuneration: in past 3 years)

- Matti Aapro: Helsinn; Tesaro; MSD Merck; Roche
- Enzo Ballatori: None declared
- Mary Jacqueline Brames: None declared
- Eduardo Bruera: None declared
- Luigi Celio: Helsinn
- Alex Chan: MSD Merck; Mundipharma; Lexicomp; GSK
- Rebecca Clark-Snow: None declared
- Andrew Davies: None declared
- Mellar Davis: None declared
- Kristopher Dennis: None declared
- L. Lee Dupuis: Sea-Band Ltd
- Lawrence Einhorn: Celgene; Ziopharm; Amgen
- Petra Feyer: MSD Merck; Riemser
- Richard Gralla: Helsinn; MSD Merck; Tesaro; Eisai
- Jørn Herrstedt: Tesaro; Swedish Orphan Biovitrum
- Paul Hesketh: None declared
- Regine Deniel Ihlen (patient advocate): None declared
- Franziska Jahn: Helsinn; MSD Merck; Tesaro
- Karin Jordan: Helsinn; MSD Merck; Tesaro
- Ernesto Maranzano: None declared

- Alexander Molassiotis: MSD Merck; Helsinn; Tesaro; Norgine; Acacia Pharma
- Rudolph Navari: None declared
- Ian Olver: Tesaro
- Andrea Orsey: Pfizer
- Bernardo Rapoport: Helsinn; MSD Merck; Tesaro
- Carla I. Ripamonti: Teva; Norgine; Otsuka; Amgen
- Cynthia Rittenberg: None declared
- Joseph Roscoe: None declared
- Fausto Roila: None declared
- Christina Ruhlmann: Swedish Orphan Biovitrum
- Mitsue Saito: None declared
- Lee Schwartzberg: Helsinn, Tesaro, MSD Merck, Eisai
- Lillian Sung: None declared
- Wim Tissing: None declared
- Declan Walsh: Nualtra Ltd
- David Warr: Helsinn, MSD Merck; Tesaro
- Marianne van de Wetering: None declared
- Theresa Zanatta (patient advocate): None declared
- Li Zhang: None declared
## Continents and Countries Represented in the Antiemetic Guideline Process

<table>
<thead>
<tr>
<th>Continent</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>Japan, China, Hong Kong SAR, Singapore</td>
</tr>
<tr>
<td>Africa</td>
<td>South Africa</td>
</tr>
<tr>
<td>Australia/Oceania</td>
<td>Australia</td>
</tr>
<tr>
<td>Europe</td>
<td>Denmark, Germany, Italy, The Netherlands, Norway, Switzerland, United Kingdom</td>
</tr>
<tr>
<td>North America</td>
<td>Canada, United States of America</td>
</tr>
</tbody>
</table>
Process

• Presentation of findings at Copenhagen meeting
• Committee work prior to Copenhagen meeting
  ➢ Systematic literature review
  ➢ Level of evidence / confidence ratings
• Group discussion and consensus
• Post-meeting follow-up if necessary
  ➢ Recommendations
  ➢ Second voting

Consensus Criteria Required to Change Guideline

• Degree of agreement: 67% or greater
• Basis of evidence: well-conducted trials • comparator consistent with guidelines and best practice • at least 10% difference in degree of benefit
Committees and Areas of Expertise

I. Emetic Classification of Antineoplastic Agents
II. Highly Emetic Chemotherapy
III. Moderately Emetic Chemotherapy
IV. Low or Minimally Emetic Chemotherapy
V. Other Issues: Multiple-day and high-dose chemotherapy, refractory and breakthrough nausea and vomiting
VI. Anticipatory Nausea and Vomiting
VII. Radiotherapy-Induced Nausea and Vomiting
VIII. Nausea and Vomiting in Children Receiving Chemotherapy
IX. Nausea and Vomiting in Advanced Cancer
X. Future Considerations: research directions, study design, economic considerations
Process for the Future: Keeping the Guidelines Accurate, Up-to-Date, and Valid

• Permanent committees

• Each chair to query committee every 6 months regarding any new information that might affect the guideline

• Steering committee to query chairs for suggestions

• If evidence appears compelling, all group members asked for opinions

• If consensus is achieved, Guideline is updated on MASCC website
## ACUTE Nausea and Vomiting: SUMMARY

<table>
<thead>
<tr>
<th>EMETIC RISK GROUP</th>
<th>ANTIEMETICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Non-AC</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; + DEX + NK&lt;sub&gt;1&lt;/sub&gt;</td>
</tr>
<tr>
<td>High AC</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; + DEX + NK&lt;sub&gt;1&lt;/sub&gt;</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; + DEX + NK&lt;sub&gt;1&lt;/sub&gt;</td>
</tr>
<tr>
<td>Moderate (other than carboplatin)</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; + DEX</td>
</tr>
<tr>
<td>Low</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; or DEX or DOP</td>
</tr>
<tr>
<td>Minimal</td>
<td>No routine prophylaxis</td>
</tr>
</tbody>
</table>

**NOTE:** If the NK<sub>1</sub> receptor antagonist is not available for AC chemotherapy, palonosetron is the preferred 5-HT<sub>3</sub> receptor antagonist.

**5-HT<sub>3</sub>** = serotonin<sub>3</sub> receptor antagonist  
**DEX** = Dexamethasone  
**NK<sub>1</sub>** = neurokinin<sub>1</sub> receptor antagonist such as Aprepitant or Fosaprepitant or Rolapitant or Nepa (combination of netupitant and palonosetron)  
**DOP** = dopamine receptor antagonist
### DELAYED Nausea and Vomiting: SUMMARY

<table>
<thead>
<tr>
<th>Emetic Risk Group</th>
<th>Antiemetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Non-AC</td>
<td>DEX or (if APR 125mg for acute: (MCP + DEX) or (APR + DEX))</td>
</tr>
<tr>
<td>High AC</td>
<td>None or (if APR 125mg for acute: DEX or APR)</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>None or (if APR 125mg for acute: APR)</td>
</tr>
<tr>
<td>Oxaliplatin, or anthracycline, or cyclophosphamide</td>
<td>DEX can be considered</td>
</tr>
<tr>
<td>Moderate (other)</td>
<td>No routine prophylaxis</td>
</tr>
<tr>
<td>Low and Minimal</td>
<td>No routine prophylaxis</td>
</tr>
</tbody>
</table>

**Notes:**

- **DEX** = Dexamethasone
- **MCP** = Metoclopramide
- **APR** = Aprepitant
## Committee I (1/5): The Four Emetic Risk Groups

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH</td>
<td>Risk in nearly all patients (&gt; 90%)</td>
</tr>
<tr>
<td>MODERATE</td>
<td>Risk in 30% to 90% of patients</td>
</tr>
<tr>
<td>LOW</td>
<td>Risk in 10% to 30% of patients</td>
</tr>
<tr>
<td>MINIMAL</td>
<td>Fewer than 10% at risk</td>
</tr>
</tbody>
</table>
### Committee I (2/5): Emetic Risk Groups – Adults – Single IV Agents

<table>
<thead>
<tr>
<th>HIGH</th>
<th>MODERATE</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthracycline/cyclophosphamide combination*</td>
<td>Alemtuzumab</td>
<td>Daunorubicin</td>
</tr>
<tr>
<td>Carmustine</td>
<td>Azacitidine</td>
<td>Doxorubicin</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Bendamustine</td>
<td>Epirubicin</td>
</tr>
<tr>
<td>Cyclophosphamide &gt; 1500 mg/m²</td>
<td>Carboplatin</td>
<td>Idarubicin</td>
</tr>
<tr>
<td>Dacarbazine</td>
<td>Clofarabine</td>
<td>Ifosfamide</td>
</tr>
<tr>
<td>Mechlorethamine</td>
<td>Cyclophosphamide &lt; 1500 mg/m²</td>
<td>Irinotecan</td>
</tr>
<tr>
<td>Streptozocin</td>
<td>Cytarabine &gt; 1000 mg/m²</td>
<td></td>
</tr>
</tbody>
</table>

* The combination of an anthracycline and cyclophosphamide in patients with breast cancer should be considered highly emetogenic.

** No direct evidence found for temozolomide IV. Classification is based on oral temozolomide, since all sources indicate a similar safety profile.
## Committee I (3/5): Emetic Risk Groups – Adults – Single IV Agents

| LOW | Aflibercept | Belinostat | Blinatumomab | Bortezomib | Brentuximab | Cabazitaxel | Carfilzomib | Catumaxumab | Cetuximab | Cytarabine ≤ 1000 mg/m² | Docetaxel | Eribulin | Etoposide | 5-Fluorouracil | Gemcitabine | Ipilimumab | Ixabepilone | Methotrexate | Mitomycin | Mitoxantrone | Nab-paclitaxel | Paclitaxel | Panitumumab | Pemetrexed | Pegylated liposomal doxorubicin | Pertuzumab | Temsirolimus | Topotecan | Trastuzumab-emtansine | Vinflunine |
|-----|-------------|------------|--------------|------------|-------------|-------------|-------------|-------------|-----------|----------------|-----------|-----------|-----------|----------------|-------------|-----------|-------------|-------------|-----------|-------------|---------------|-----------|----------------|-----------|----------------|---------|----------------|---------|---------------|---------|----------------|---------|

> 2016 V.1.2

**Multinational Association of Supportive Care in Cancer**

Supportive Care Makes Excellent Cancer Care Possible
### Committee I (4/5): Emetic Risk Groups – Adults – Single IV Agents

<table>
<thead>
<tr>
<th>MINIMAL</th>
<th>Bevacizumab</th>
<th>Pembrolizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bleomycin</td>
<td>Pembrolizumab</td>
</tr>
<tr>
<td></td>
<td>Busulfan</td>
<td>Pembrolizumab</td>
</tr>
<tr>
<td></td>
<td>2-Chlorodeoxyadenosine</td>
<td>Pembrolizumab</td>
</tr>
<tr>
<td></td>
<td>Cladribine</td>
<td>Pembrolizumab</td>
</tr>
<tr>
<td></td>
<td>Fludarabine</td>
<td>Pembrolizumab</td>
</tr>
<tr>
<td></td>
<td>Nivolumab</td>
<td>Pembrolizumab</td>
</tr>
<tr>
<td></td>
<td>Ofatumumab</td>
<td>Pembrolizumab</td>
</tr>
<tr>
<td></td>
<td>Vinorelbine</td>
<td>Pembrolizumab</td>
</tr>
</tbody>
</table>

### Additional Agents
- Pembrolizumab
- Pembrolizumab
- Pembrolizumab
- Pembrolizumab
- Pembrolizumab
- Pembrolizumab
- Pembrolizumab
- Pembrolizumab
- Pembrolizumab
- Pembrolizumab
- Pembrolizumab
- Pembrolizumab
- Pembrolizumab
- Pembrolizumab
- Pembrolizumab
Committee I (5/5): Emetic Risk Groups – Adults – Single Oral Agents

<table>
<thead>
<tr>
<th>Emetic Risk Group</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIGH</strong></td>
<td>Hexamethylmelamine, Procarbazine</td>
</tr>
<tr>
<td><strong>MODERATE</strong></td>
<td>Bosutinib, Ceritinib, Crizotinib, Cyclophosphamide, Imatinib, Temozolomide, Vinorelbine</td>
</tr>
<tr>
<td><strong>LOW</strong></td>
<td>Afatinib, Axatinib, Capecitabine, Dabrafenib, Dasatinib, Everolimus, Etoposide, Fludarabine, Ibrutinib, Idelalisib, Lapatinib, Lenalidomide, Olaparib, Nilotinib, Pazopanib, Ponatinib, Regorafenib, Sunitinib, Tegafur Uracil, Thalidomide, Vandetanib, Vorinostat</td>
</tr>
<tr>
<td><strong>MINIMAL</strong></td>
<td>Chlorambucil, Erlotinib, Gefitinib, Hydroxyurea, Melphalan, Methotrexate, L-Phenylalanine mustard, Pomalidomide, Ruxolitinib, Sorafenib, 6-Thioguanine, Vemurafenib, Vismodegib</td>
</tr>
</tbody>
</table>
**COMMITTEE II (1/5):**

Prevention of Acute Nausea and Vomiting Following Non-AC Chemotherapy of High Emetic Risk

A three-drug regimen including single doses of a 5-HT₃ receptor antagonist, dexamethasone, and an NK₁ receptor antagonist (aprepitant, fosaprepitant, netupitant* or rolapitant), given before chemotherapy is recommended.

MASCC Level of Confidence: High
MASCC Level of Consensus: High
ESMO Level of Evidence: I
ESMO Grade of Recommendation: A

* Netupitant is administered with palonosetron as part of the fixed-dose oral combination agent NEPA
COMMITTEE II (2/5):

Prevention of Delayed Nausea and Vomiting Following Non-AC Chemotherapy of High Emetic Risk

In patients receiving non-AC highly emetogenic chemotherapy treated with a combination of an NK$_1$ receptor antagonist*, a 5-HT$_3$ receptor antagonist, and dexamethasone to prevent acute nausea and vomiting, dexamethasone on days 2 to 4 is suggested to prevent delayed nausea and vomiting.

MASCC Level of Confidence: High
MASCC Level of Consensus: Moderate
ESMO Level of Evidence: I
ESMO Grade of Recommendation: B

* If aprepitant 125 mg is used in day 1, then dexamethasone 8 mg x 1 (days 2-4) + aprepitant 80 mg x 1 (days 2-3) OR dexamethasone 8 mg x 2 (days 2-4) + metoclopramide 20 mg x 4 (days 2-4). Please note that this dosage of metoclopramide derives from a phase III study and some regulatory authorities like EMA now recommend a maximum 0.5 mg/kg total daily dose.
COMMITTEE II (3/5):

Prevention of Acute Nausea and Vomiting Following Anthracycline-Cyclophosphamide-Based Chemotherapy of High Emetic Risk

In women with breast cancer, a three-drug regimen including single doses of a 5-HT\textsubscript{3} receptor antagonist, dexamethasone, and an NK\textsubscript{1} receptor antagonist (aprepitant, fosaprepitant, netupitant* or rolapitant), given before chemotherapy is recommended.

MASCC Level of Confidence: High
MASCC Level of Consensus: High
ESMO Level of Evidence: I
ESMO Grade of Recommendation: A

* Netupitant administered with palonosetron as part of the fixed-dose oral combination agent NEPA

NOTE: If a NK1 receptor antagonist is not available for AC chemotherapy, palonosetron is the preferred 5-HT3 receptor antagonist.
COMMITTEE II (4/5):

Prevention of Delayed Nausea and Vomiting Following Anthracycline-Cyclophosphamide-Based Chemotherapy of High Emetic Risk

In women with breast cancer treated with a combination of a $5\text{-HT}_3$ receptor antagonist, dexamethasone and a $\text{NK}_1$ receptor antagonist to prevent acute nausea and vomiting, aprepitant or dexamethasone should be used on days 2 and 3 or none if fosaprepitant, netupitant or rolapitant has been used in day 1.

MASCC Level of Confidence: Moderate
MASCC Level of Consensus: Moderate
ESMO Level of Evidence: II
ESMO Grade of Recommendation: B

If aprepitant 125 mg is used on day 1, then aprepitant 80 mg x 1 (days 2-3) OR dexamethasone 4 mg x 2 (days 2-3).
The MASCC/ESMO Antiemetics Guidelines Committee has discussed the presently available published data about olanzapine, which suggest that it is an effective antiemetic agent.

Olanzapine may be considered with a 5-HT$_3$ receptor antagonist plus dexamethasone, particularly when nausea is an issue.

(Note: Patient sedation may be a concern for the 10 mg dose.)

MASCC Level of Confidence: Low
MASCC Level of Consensus: Low
ESMO Level of Evidence: II
ESMO Grade of Recommendation: B
COMMITTEE III (1/3):

Prevention of Acute Nausea and Vomiting in Moderately Emetogenic Chemotherapy

For the prevention of acute nausea and vomiting in moderately emetogenic chemotherapy-treated patients, a 5-HT$_3$ receptor antagonist plus dexamethasone is recommended.*

MASCC Level of Confidence: Moderate
MASCC Level of Consensus: Moderate
ESMO Level of Evidence: II
ESMO Grade of Recommendation: B

* See specific slides for carboplatin recommendation.
COMMITTEE III (2a/3):

Prevention of Delayed Nausea and Vomiting in Moderately Emetogenic Chemotherapy

In patients receiving moderately emetogenic chemotherapy with known potential for delayed nausea and vomiting (e.g., oxaliplatin, anthracycline, cyclophosphamide), the use of dexamethasone for days 2 to 3 can be considered.*

MASCC Level of Confidence: Low
MATCC Level of Consensus: Moderate
ESMO Level of Evidence: III
ESMO Grade of Recommendation: C

* See specific slides for carboplatin recommendation.
COMMITTEE III (2b/3):

Prevention of Delayed Nausea and Vomiting in Moderately Emetogenic Chemotherapy

No routine prophylaxis for delayed nausea and vomiting can be recommended for all other patients receiving moderately emetogenic chemotherapy.

MASCC Level of Confidence: No Confidence Possible
MASCC Level of Consensus: High
ESMO Level of Evidence: IV
ESMO Grade of Recommendation: D

* See specific slides for carboplatin recommendation.
COMMITTEE III (3a/3):

Prevention of Acute Nausea and Vomiting in Patients Receiving Carboplatin-Based Chemotherapy

A combination of an NK\textsubscript{1} receptor antagonist, 5-HT\textsubscript{3} receptor antagonist, and dexamethasone is recommended for the prophylaxis of nausea and vomiting induced by carboplatin-based chemotherapy.

MASCC Level of Confidence:  Moderate
MASCC Level of Consensus:  Moderate
ESMO Level of Evidence:  II
ESMO Grade of Recommendation:  B
COMMITTEE III (3b/3):

Prevention of Delayed Nausea and Vomiting in Patients Receiving Carboplatin-Based Chemotherapy

If aprepitant 125 mg is used on day 1, aprepitant 80 mg on days 2 to 3 is recommended for the prevention of delayed nausea and vomiting. If other NK₁ receptor antagonists are used on day 1, no additional prophylaxis for delayed nausea and vomiting prevention is suggested.

MASCC Level of Confidence:  Moderate
MASCC Level of Consensus:  Moderate
ESMO Level of Evidence:  II
ESMO Grade of Recommendation:  B
### Recommended Doses of Serotonin Receptor (5-HT<sub>3</sub>) Antagonists for Acute Nausea and Vomiting

<table>
<thead>
<tr>
<th>AGENT</th>
<th>ROUTE</th>
<th>ANTIEMETICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ondansetron</td>
<td>IV</td>
<td>8 mg or 0.15 mg/Kg</td>
</tr>
<tr>
<td></td>
<td>Oral</td>
<td>16 mg*</td>
</tr>
<tr>
<td>Granisetron</td>
<td>IV</td>
<td>1 mg or 0.01 mg/Kg</td>
</tr>
<tr>
<td></td>
<td>Oral</td>
<td>2 mg (or 1 mg**)</td>
</tr>
<tr>
<td>Dolasetron</td>
<td>Oral</td>
<td>100 mg</td>
</tr>
<tr>
<td>Tropisetron</td>
<td>IV</td>
<td>5 mg</td>
</tr>
<tr>
<td></td>
<td>Oral</td>
<td>5 mg</td>
</tr>
<tr>
<td>Palonosetron</td>
<td>IV</td>
<td>0.25 mg</td>
</tr>
<tr>
<td></td>
<td>Oral</td>
<td>0.5 mg</td>
</tr>
</tbody>
</table>

* Randomized studies have tested the 8 mg twice daily schedule.
** The 1 mg dose is preferred by some panelists.
## Recommended Corticosteroid* (Dexamethasone) Dosing

<table>
<thead>
<tr>
<th>DEXAMETHASONE</th>
<th>Dose and Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High Risk</strong></td>
<td></td>
</tr>
<tr>
<td>- Acute Emesis</td>
<td>20 mg once</td>
</tr>
<tr>
<td>- Delayed Emesis</td>
<td>8 mg bid for 3 - 4 days</td>
</tr>
<tr>
<td></td>
<td>(12 mg when used with (fos)aprepitant or netupitant)**</td>
</tr>
<tr>
<td><strong>Moderate Risk</strong></td>
<td></td>
</tr>
<tr>
<td>- Acute Emesis</td>
<td>8 mg once</td>
</tr>
<tr>
<td>- Delayed Emesis</td>
<td>8 mg daily for 2 - 3 days</td>
</tr>
<tr>
<td></td>
<td>(many panelists give the dose as 4 mg bid)</td>
</tr>
<tr>
<td><strong>Low Risk</strong></td>
<td></td>
</tr>
<tr>
<td>- Acute Emesis</td>
<td>4 - 8 mg once</td>
</tr>
</tbody>
</table>

* While corticosteroids other than dexamethasone are effective antiemetics, the dose and schedule of dexamethasone coupled with its wide availability in various dose forms established it as the guideline agent of choice.

** The 12 mg dose of dexamethasone is the only one tested with (fos)aprepitant/netupitant in large randomized trials.
# Recommended NK₁ Receptor Antagonist Dosing

<table>
<thead>
<tr>
<th>NK₁ Receptor Antagonist</th>
<th>Dose and Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>APREPITANT</strong> and <strong>FOSAPREPITANT</strong></td>
<td><strong>Acute Emesis</strong></td>
</tr>
<tr>
<td></td>
<td>Aprepitant: 125 mg once on the day of chemotherapy*</td>
</tr>
<tr>
<td></td>
<td>- or -</td>
</tr>
<tr>
<td></td>
<td>Fosaprepitant: 150 mg IV, once on the day of chemotherapy</td>
</tr>
<tr>
<td><strong>APREPITANT</strong> and <strong>FOSAPREPITANT</strong></td>
<td><strong>Delayed Emesis</strong></td>
</tr>
<tr>
<td></td>
<td>Aprepitant 80 mg orally, once daily for the 2 days after chemotherapy; or none if</td>
</tr>
<tr>
<td></td>
<td>Fosaprepitant is used</td>
</tr>
<tr>
<td><strong>ROLAPITANT</strong></td>
<td>180 mg orally once on the day of chemotherapy</td>
</tr>
<tr>
<td><strong>NETUPITANT</strong></td>
<td>300 mg netupitant/0.5 mg palonosetron orally once on the day of chemotherapy</td>
</tr>
</tbody>
</table>

* aprepitant 165 mg as a single dose before chemotherapy (and none day 2-3) is registered by EMA and other authorities
COMMITTEE IV (1/3):

Prevention of Acute Nausea and Vomiting in Patients Receiving Low Emetogenic Chemotherapy

A single antiemetic agent, such as dexamethasone, a 5-HT$_3$ receptor antagonist, or a dopamine receptor antagonist, such as metoclopramide, may be considered for prophylaxis in patients receiving chemotherapy of low emetic risk.

MASCC Level of Confidence: Low
MASCC Level of Consensus: Moderate
ESMO Level of Evidence: II
ESMO Grade of Recommendation: B
COMMITTEE IV (2/3):

Prevention of Acute Nausea and Vomiting in Patients Receiving Minimally Emetogenic Chemotherapy*

No antiemetic should be routinely administered before chemotherapy to patients without a history of nausea and vomiting.

MASCC Level of Confidence: No Confidence Possible
MASCC Level of Consensus: High
ESMO Level of Evidence: IV
ESMO Grade of Recommendation: D

* While unusual at this emetic level, if a patient experiences nausea or vomiting, it is advised that, with subsequent chemotherapy treatments, the regimen for the next higher emetic level be given.
COMMITTEE IV (3/3):

Prevention of Delayed Nausea and Vomiting in Patients Receiving Low or Minimally Emetogenic Chemotherapy*

No antiemetic should be administered for prevention of delayed nausea and vomiting induced by low or minimally emetogenic chemotherapy.

MASCC Level of Confidence: No Confidence Possible
MASCC Level of Consensus: High
ESMO Level of Evidence: IV
ESMO Grade of Recommendation: D

* While unusual at this emetic level, if a patient experiences nausea or vomiting, it is advised that, with subsequent chemotherapy treatments, the regimen for the next higher emetic level be given.
COMMITTEE V (1/3):

Prevention of Nausea and Vomiting in Patients Receiving Multiple-Day Cisplatin

Patients receiving multiple-day cisplatin should receive a 5-HT₃ receptor antagonist plus dexamethasone plus aprepitant for acute nausea and vomiting and dexamethasone for delayed nausea and vomiting.

MASCC Level of Confidence:  Moderate
MASCC Level of Consensus:  Moderate
ESMO Level of Evidence:  II
ESMO Grade of Recommendation:  B

NOTE: The 5-HT₃ receptor antagonists should be dosed at day 1-5, except for palonosetron, which should be dosed on days 1, 3, and 5 only.
Prevention of Nausea and Vomiting in Patients Receiving High-Dose Chemotherapy

For patients receiving high-dose chemotherapy for stem cell transplant, a combination of a 5-HT₃ receptor antagonist with dexamethasone and aprepitant (125 mg orally on day 1 and 80 mg orally on days 2 to 4) is recommended before chemotherapy.

MASCC Level of Confidence: High
MASCC Level of Consensus: High
ESMO Level of Evidence: I
ESMO Grade of Recommendation: A
Guideline for Breakthrough Nausea and Vomiting

The available evidence for breakthrough nausea and vomiting suggests the use of 10 mg oral olanzapine, daily for 3 days.

(The mild to moderate sedation in this patient population, especially elderly patients, is a potential problem with olanzapine.)

MASCC Level of Confidence: Moderate
MASCC Level of Consensus: Moderate
ESMO Level of Evidence: II
ESMO Grade of Recommendation: B

NOTE: No guideline was felt to be appropriate for refractory nausea and vomiting.
COMMITTEE VI (1/2):

Prevention of Anticipatory Nausea and Vomiting

The best approach for the prevention of anticipatory nausea and vomiting is the best possible control of acute and delayed nausea and vomiting.

MASCC Level of Confidence: High
MASCC Level of Consensus: High
ESMO Level of Evidence: III
ESMO Grade of Recommendation: A
COMMITTEE VI (2/2):

Prevention of Anticipatory Nausea and Vomiting

Behavioral therapies (progressive muscle relaxation training, in particular), systematic desensitization, and hypnosis may be used to treat anticipatory nausea and vomiting.

MASCC Level of Confidence: Moderate  
MASCC Level of Consensus: Moderate  
ESMO Level of Evidence: II  
ESMO Grade of Recommendation: B

Benzodiazepines can reduce the occurrence of anticipatory nausea and vomiting.

MASCC Level of Confidence: Moderate  
MASCC Level of Consensus: Moderate  
ESMO Level of Evidence: II  
ESMO Grade of Recommendation: A
## Committee VII (1/5): Levels of Emetic Risk with Radiation Therapy

<table>
<thead>
<tr>
<th>RISK LEVEL*</th>
<th>AREA OF TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH</td>
<td>Total body irradiation</td>
</tr>
<tr>
<td>MODERATE</td>
<td>Upper abdomen, craniospinal</td>
</tr>
<tr>
<td>LOW</td>
<td>Cranium, head &amp; neck, thorax region, pelvis</td>
</tr>
<tr>
<td>MINIMAL</td>
<td>Extremities, breast</td>
</tr>
</tbody>
</table>

* in concomitant radiochemotherapy, the antiemetic prophylaxis is according to the chemotherapy-related antiemetic guidelines of the corresponding risk category, unless the risk of nausea and vomiting is higher with radiotherapy than with chemotherapy.
COMMITTEE VII (2/5):

Prevention of Nausea and Vomiting in Patients Receiving Highly Emetic Radiation Therapy: Total Body Irradiation

Patients receiving highly emetic radiation therapy should receive a 5-HT₃ receptor antagonist plus dexamethasone.

MASCC Level of Confidence: High
(For the addition of dexamethasone: Moderate)

MASCC Level of Consensus: High

ESMO Level of Evidence: II
(For the addition of dexamethasone: III)

ESMO Grade of Recommendation: B
(For the addition of dexamethasone: C)
COMMITTEE VII (3/5):

Prevention of Nausea and Vomiting in Patients Receiving Moderately Emetic Radiation Therapy: Upper Abdomen, Craniospinal

Patients receiving moderately emetic radiation therapy should receive a 5-HT₃ receptor antagonist and optional short-course dexamethasone.

MASCC Level of Confidence: High
(For the addition of dexamethasone: Moderate)

MASCC Level of Consensus: High

ESMO Level of Evidence: II

ESMO Grade of Recommendation: A
(For the addition of dexamethasone: B)
COMMITTEE VII (4/5):

Prevention of Nausea and Vomiting in Patients Receiving Low Emetic Radiation Therapy: Cranium, Head & Neck, Thorax Region, Pelvis

Patients receiving low emetic radiation therapy should receive prophylaxis or rescue with a 5-HT\textsubscript{3} receptor antagonist.

**MASCC Level of Confidence:** Moderate  
*For rescue: Low*

**MASCC Level of Consensus:** High

**ESMO Level of Evidence:** III  
*For Rescue: IV*

**ESMO grade of recommendation:** B  
*For Rescue: C*
Patients receiving minimally emetic radiation therapy should receive rescue with a dopamine receptor-antagonist or a 5-HT₃ receptor antagonist.

MASCC Level of Confidence: Low
MASCC Level of Consensus: High
ESMO Level of Evidence: IV
ESMO Grade of Recommendation: D
COMMITTEE VIII (1a/4): Antiemetics in Children

Prevention of Nausea and Vomiting Following Chemotherapy of High Emetic Risk in Children

Children receiving chemotherapy of high emetic risk should receive antiemetic prophylaxis with a 5-HT$_3$ receptor antagonist plus dexamethasone plus aprepitant.

MASCC Level of Consensus: High
MASCC Level of Confidence: High
ESMO Level of Evidence: II
ESMO Grade of Recommendation: B
COMMITTEE VIII (1b/4): Antiemetics in Children

Prevention of Nausea and Vomiting Following Chemotherapy of High Emetic Risk in Children

Children who cannot receive dexamethasone should receive a 5-HT\textsubscript{3} receptor antagonist plus aprepitant.

MASCC Level of Consensus:  High
MASCC Level of Confidence:  Moderate
ESMO Level of Evidence:  II
ESMO Grade of Recommendation:  B

Children who cannot receive aprepitant should receive a 5-HT\textsubscript{3} receptor antagonist plus dexamethasone.

MASCC Level of Consensus:  High
MASCC Level of Confidence:  Moderate
ESMO Level of Evidence:  II
ESMO Grade of Recommendation:  B
Children receiving moderately emetogenic chemotherapy should receive antiemetic prophylaxis with a 5-HT$_3$ receptor antagonist plus dexamethasone.

**MASCC Level of Consensus:** High  
**MASCC Level of Confidence:** Moderate  
**ESMO Level of Evidence:** II  
**ESMO Grade of Recommendation:** B

Children who cannot receive dexamethasone should receive a 5-HT$_3$ receptor antagonist and aprepitant.

**MASCC Level of Consensus:** High  
**MASCC Level of Confidence:** Moderate  
**ESMO Level of Evidence:** II  
**ESMO Grade of Recommendation:** B
Children receiving chemotherapy of low emetogenicity should receive antiemetic prophylaxis with a 5-HT\textsubscript{3} receptor antagonist.

**MASCC Level of Consensus:** Moderate  
**MASCC Level of Confidence:** Moderate  
**ESMO Level of Evidence:** II  
**ESMO Grade of Recommendation:** B
Prevention of Nausea and Vomiting Following Chemotherapy of Minimal Emetic Risk in Children

Children receiving chemotherapy of minimal emetogenicity should receive no antiemetic prophylaxis.

MASCC Level of Consensus: High
MASCC Level of Confidence: Moderate
ESMO Level of Evidence: V
ESMO Grade of Recommendation: D
ANTIEMETIC GUIDELINES: MASCC/ESMO

COMMITTEE IX (1a/3): Advanced Cancer

Treatment of Nausea and Vomiting in Advanced Cancer: Drugs of Choice

The antiemetic drug of choice in advanced cancer is metoclopramide (titrated to effect).

MASCC Level of Consensus: High
MASCC Level of Confidence: Moderate
ESMO Level of Evidence: III
ESMO Grade of Recommendation: C
COMMITTEE IX (1b/3): Advanced Cancer

Treatment of Nausea and Vomiting in Advanced Cancer: Drugs of Choice

Alternative options include haloperidol, levomepromazine, or olanzapine.

MASCC Level of Consensus: High
MASCC Level of Confidence: Low
ESMO Level of Evidence: V
ESMO Grade of Recommendation: D

The use of cyclizine or 5-HT<sub>3</sub> receptor antagonists is poorly defined to date and may be used when dopamine antagonists are contraindicated or ineffective.

MASCC Level of Consensus: Low
MASCC Level of Confidence: Low
ESMO Level of Evidence: V
ESMO Grade of Recommendation: D

**NOTE**: The evidence to support combinations of drugs with antiemetic effect and different mechanisms of action is minimal (except in bowel obstruction)
COMMITTEE IX (2a/3): Advanced Cancer

Treatment of Nausea and Vomiting in Advanced Cancer: Bowel Obstruction

The drug recommended in bowel obstruction is octreotide, dosed around the clock, and given alongside a conventional antiemetic (with the committee recommending haloperidol).

MASCC Level of Consensus: High
MASCC Level of Confidence: High
ESMO Level of Evidence: II
ESMO Grade of Recommendation: A

If octreotide plus antiemetic is suboptimal, the use of anticholinergic anti-secretory agents (e.g. scopolamine butylbromide, glycopyrronium bromide) and/or corticosteroids is recommended as either adjunct / alternative interventions.

MASCC Level of Consensus: High (Moderate for corticosteroids)
MASCC Level of Confidence: Moderate (Low for corticosteroids)
ESMO Level of Evidence: IV
ESMO Grade of Recommendation: D
COMMITTEE IX (2b/3): Advanced Cancer

Treatment of Nausea and Vomiting in Advanced Cancer: Bowel Obstruction

The use of cyclizine* or 5HT₃ receptor antagonists is poorly defined in this setting**. Metoclopramide should be used with caution in partial bowel obstruction and should not be used in complete bowel obstruction.

MASCC Level of Consensus: Low
MASCC Level of Confidence: Low
ESMO Level of Evidence: V
ESMO Grade of Recommendation: D

* Unavailable in some countries.
** Caution should be exercised because of the risk of drug interactions.
No recommendation can be made about specific antiemetics, although various antiemetics may help. Opioid rotation and route switching may be effective approaches. There is no data to support prophylactic antiemetics in this situation.

MASCC Level of Consensus: High
MASCC Level of Confidence: Low
ESMO Level of Evidence: V
ESMO Grade of Recommendation: D