MASCC Guidelines for
Antiemetic control: An update
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Linköping University, Sweden

Multinational Association of Supportive Care in Cancer, June 2004
# Antiemetic Guideline Consensus

- **Official Process Subscribed to by 9 International Oncology Groups**

## International:
- **MASCC**

## North America:
- **U.S.**
  - ASCO, ONS, NCCN
- **Canada**
  - CCO

## Europe:
- ESMO, EONS

## Africa:
- SASMO

## Australia:
- COSA

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*Multinational Association of Supportive Care in Cancer, June 2004*
PERUGIA 2004 ANTIEMETIC GUIDELINES
- Committees and their Areas -

I. Emetic classification of antineoplastic agents

II. Acute emesis: Highly emetic chemotherapy

III. Delayed emesis: Highly emetic chemotherapy

IV. Acute emesis: Moderately emetic chemotherapy

V. Delayed emesis: Moderately emetic chemotherapy
PERUGIA 2004 ANTIEMETIC GUIDELINES
- Committees and their Areas -

VI. Emesis induced by minimal or low emetic risk chemotherapy

VII. Additional Issues: Refractory emesis, rescue antiemetic therapy, multiple-day chemotherapy, high-dose chemotherapy

VIII. Anticipatory emesis

IX. Radiotherapy-induced emesis, Antiemetics in children receiving chemotherapy

X. Future Considerations: Research Directions, Study Design, Economic Considerations
2004 ANTIEMETIC GUIDELINES
- The Process -

- Each committee worked on its area of concentration prior to the Perugia Meeting.
- The committee chairs presented the findings and included the suggested rating of the level of evidence / confidence of the guideline (ASCO and MASCC criteria).
- Group discussion and consensus voting then followed each presentation.
- Criteria for consensus: 75% or greater agreement among the panelists
ANTIEMETIC GUIDELINE CONSENSUS
- Official Process Subscribed to by 9 International Oncology Groups -

WWW.MASCC.ORG
### ANTIEMETIC TREATMENT GUIDELINES

**Committee I: The Four Emetic Risk Groups**

<table>
<thead>
<tr>
<th>Risk Group</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>
# ANTIEMETIC TREATMENT GUIDELINES

**Committee I: Emetic Risk Groups – High Risk**

<table>
<thead>
<tr>
<th>Single IV agents</th>
<th>Cisplatin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mechlorethamine</td>
</tr>
<tr>
<td></td>
<td>Streptozotocin</td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide ≥ 1500 mg/m²</td>
</tr>
<tr>
<td></td>
<td>Carmustine</td>
</tr>
<tr>
<td></td>
<td>Dacarbazine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Single oral agents</th>
<th>Hexamethylmelamine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Procarbazine</td>
</tr>
</tbody>
</table>
Guideline for Prevention of Acute Nausea and Vomiting Following Chemotherapy of High Emetic Risk:

To prevent acute vomiting and nausea following chemotherapy of high emetic risk, a three-drug regimen including single doses of a 5-HT₃ antagonist, dexamethasone, and aprepitant given before chemotherapy is recommended.

MASCC Level of Consensus:  High
MASCC Level of Confidence:  High

ASCO Level of Evidence:  I
ASCO Grade of Recommendation:  A
COMMITTEE III

Guideline for Prevention of Delayed Nausea and Vomiting Following Chemotherapy of High Emetic Risk:

In patients receiving cisplatin treated with a combination of aprepitant, a 5-HT$_3$ receptor antagonist and dexamethasone to prevent acute vomiting and nausea, the combination of dexamethasone and aprepitant is suggested to prevent delayed emesis, on the basis of its superiority to dexamethasone alone.

MASCC Level of Consensus: Moderate
MASCC Level of Confidence: High

ASCO Level of Evidence: II
ASCO Grade of Recommendation: A
### ANTIEMETIC TREATMENT GUIDELINES
- Committee I: Emetic Risk Groups – Moderate Risk

#### Single IV agents
- Oxaliplatin
- Cytarabine > 1 g/m2
- Carboplatin
- Ifosfamide
- Cyclophosphamide < 1500 mg/m2
- Doxorubicin
- Daunorubicin
- Epirubicin
- Idarubicin
- Irinotecan

#### Single oral agents
- Cyclophosphamide
- Etoposide
- Temozolomide
- Vinorelbine
- Imatinib
COMMITTEE IV

Guideline for Prevention of Acute Nausea and Vomiting Following Chemotherapy of Moderate Emetic Risk (MEC):

A 5-HT3 receptor antagonist plus dexamethasone is recommended for prophylaxis of acute nausea and vomiting in the first course of MEC.

MASCC level of confidence: High
MASCC level of consensus: High

ASCO level of evidence: I
ASCO grade of recommendation: A
COMMITTEE IV

Guideline for Prevention of Acute Nausea and Vomiting Following Chemotherapy of Moderate Emetic Risk (MEC):

There are no clinically relevant differences in the effectiveness of the 5-HT$_3$ receptor antagonists in the prophylaxis of acute nausea and vomiting when given according to guidelines in the first cycle of MEC*.

MASCC level of confidence: High
MASCC level of consensus: High

ASCO level of evidence: I
ASCO grade of recommendation: A

* Participants felt that the comparative data with palonosetron were interesting, but indicated that studies with this agent which follow guidelines (given with dexamethasone) are needed to change this guideline.
COMMITTEE IV

Guideline for prevention of acute emesis in moderately emetic chemotherapy:

The recommended dose of dexamethasone for prophylaxis of acute nausea and vomiting from MEC is 8 mg intravenously x 1

MASCC level of confidence: Moderate
MASCC level of consensus: High

ASCO level of evidence: II
ASCO grade of recommendation: B
Addressing “AC”* as a Separate Group
Groups II - V

Although not part of the official recommendations for acute emesis in MEC, the panel agreed that it should be recognized that women receiving a combination of anthracycline plus cyclophosphamide represents a situation with a particularly great risk of nausea and vomiting.

Additionally, it appears that the risk of nausea and vomiting increases during multiple cycles.

* AC = Anthracycline + Cyclophosphamide, includes regimens such as: AC, EC, FAC, and FEC. A = doxorubicin, E = epirubicin, C = cyclophosphamide, F = 5-FU.
COMMITTEE V

Guideline for Prevention of Delayed Nausea and Vomiting Following Chemotherapy of Moderate Emetic Risk (MEC):

Patients who receive MEC known to be associated with a significant incidence of delayed nausea and vomiting should receive antiemetic prophylaxis for delayed emesis.

MASCC level of confidence: High
MASCC level of consensus: High

ASCO level of evidence: I
ASCO grade of recommendation: A
COMMITTEE V

Guideline for the Prevention of Delayed Nausea and Vomiting Following Chemotherapy of Moderate Emetic Risk:

Oral dexamethasone is the preferred treatment

MASCC level of confidence: High
MASCC level of consensus: High

ASCO level of evidence: II
ASCO grade of recommendation: A

A 5-HT$_3$ receptor antagonist may be used as an alternative

MASCC level of confidence: Moderate
MASCC level of consensus: Moderate

ASCO level of evidence: II
ASCO grade of recommendation: B
## ANTIEMETIC TREATMENT GUIDELINES
### Committee I: Emetic Risk Groups – Low risk

<table>
<thead>
<tr>
<th>Single IV agents</th>
<th>Paclitaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Docetaxel</td>
</tr>
<tr>
<td></td>
<td>Mitoxantrone</td>
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<tr>
<td></td>
<td>Topotecan</td>
</tr>
<tr>
<td></td>
<td>Etoposide</td>
</tr>
<tr>
<td></td>
<td>Pemetrexed</td>
</tr>
<tr>
<td></td>
<td>Methotrexate</td>
</tr>
<tr>
<td></td>
<td>Mitomycin</td>
</tr>
<tr>
<td></td>
<td>Gemcitabine</td>
</tr>
<tr>
<td></td>
<td>Cytarabine ≤ 100 mg/m2</td>
</tr>
<tr>
<td></td>
<td>5-Fluorouracil</td>
</tr>
<tr>
<td></td>
<td>Bortezomib</td>
</tr>
<tr>
<td></td>
<td>Cetuximab</td>
</tr>
<tr>
<td></td>
<td>Trastuzumab</td>
</tr>
</tbody>
</table>

| Single oral agents | Capecetabine |
Guideline for Prevention of Acute Nausea and Vomiting in Patients Receiving Low Risk Emetic Agents:

A single agent (such as a low dose of a corticosteroid) is suggested for patients receiving agents of low emetic risk.

MASCC: Level of confidence: No confidence possible
MASCC: Level of consensus: Moderate

ASCO level of evidence: III, IV
ASCO grade of recommendation: D
## ANTIEMETIC TREATMENT GUIDELINES
### Committee I: Emetic Risk Groups – Minimal Risk

<table>
<thead>
<tr>
<th>Single IV agents</th>
<th>Bleomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Busulfan</td>
</tr>
<tr>
<td></td>
<td>2-Chlorodeoxyadenosine</td>
</tr>
<tr>
<td></td>
<td>Fludarabine</td>
</tr>
<tr>
<td></td>
<td>Vinblastine</td>
</tr>
<tr>
<td></td>
<td>Vincristine</td>
</tr>
<tr>
<td></td>
<td>Vinorelbine</td>
</tr>
<tr>
<td></td>
<td>Bevacizumab</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Single oral agents</th>
<th>Chlorambucil</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hydroxyurea</td>
</tr>
<tr>
<td></td>
<td>L-Phenylalanine mustard</td>
</tr>
<tr>
<td></td>
<td>6-Thioguanine</td>
</tr>
<tr>
<td></td>
<td>Methotrexate</td>
</tr>
<tr>
<td></td>
<td>Gefitinib</td>
</tr>
</tbody>
</table>

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COMMITTEE VI

**Guideline for prevention of acute nausea and vomiting in patients receiving minimal risk antineoplastic agents***:

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

MASCC level of confidence: No confidence possible
MASCC level of consensus: High

ASCO level of evidence: V and expert consensus
ASCO grade of recommendation: D

*While unusual at this emetic level, if a patient experiences emesis after guideline recommended therapy, it is advised that with subsequent treatment the regimen for the next higher emetic level should be given.*

Multinational Association of Supportive Care in Cancer, June 2004
### Recommended Doses of Serotonin Receptor (5-HT₃) Antagonists for Acute Emesis

<table>
<thead>
<tr>
<th>AGENT</th>
<th>ROUTE</th>
<th>DOSE</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>IV</td>
<td>100 mg or 1.8 mg / Kg</td>
</tr>
<tr>
<td></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>
</tbody>
</table>

* Randomized studies have tested the 8 mg twice daily schedule
** The 1 mg dose preferred by some panelists: small randomized study in MEC, Phase II study in HEC
### Recommended Dexamethasone and Aprepitant Dosing

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Dexamethasone Dose and Schedule</th>
<th>Aprepitant Dose and Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High Risk</strong></td>
<td>- Acute Emesis: 20 mg once</td>
<td>- Acute Emesis: 125 mg orally, once</td>
</tr>
<tr>
<td></td>
<td>- Delayed Emesis: 8 mg bid for 3 - 4 days</td>
<td>- Delayed Emesis: 80 mg orally, once for 2 days</td>
</tr>
<tr>
<td><strong>Moderate Risk</strong></td>
<td>- Acute Emesis: 8 mg once</td>
<td>- Acute Emesis: 125 mg orally, once</td>
</tr>
<tr>
<td></td>
<td>- Delayed Emesis: 8 mg daily for 2 - 3 days (many panelists give the dose as 4 mg bid)</td>
<td>- Delayed Emesis: 80 mg orally, once for 2 days</td>
</tr>
<tr>
<td><strong>Low Risk</strong></td>
<td>- Acute Emesis: 4 - 8 mg once</td>
<td>- Acute Emesis: 125 mg orally, once</td>
</tr>
<tr>
<td></td>
<td>- Delayed Emesis:</td>
<td>- Delayed Emesis: 80 mg orally, once for 2 days</td>
</tr>
</tbody>
</table>

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Guideline for Patients Receiving Multiple-day Cisplatin:

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

MASCC level of confidence: High
MASCC level of consensus: High

ASCO level of evidence: II
ASCO grade of recommendation: A

Note: No guideline was felt to be appropriate for rescue antiemesis or high-dose (i.e. transplant) chemotherapy
The best approach for anticipatory emesis is the best possible control of acute and delayed emesis
COMMITTEE VIII

Guideline for managing anticipatory nausea and vomiting in patients receiving chemotherapy or RT

Anticipatory nausea and vomiting should be managed by psychological techniques.

MASCC level of confidence: High
MASCC level of consensus: High

An alternative to or addition to psychological techniques is the use of benzodiazepines

MASCC level of confidence: Moderate
MASCC level of consensus: High

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<table>
<thead>
<tr>
<th>RISK LEVEL</th>
<th>AREA OF TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH</td>
<td>TBI</td>
</tr>
<tr>
<td>MODERATE</td>
<td>Upper Abdomen</td>
</tr>
<tr>
<td>LOW</td>
<td>Lower thorax region, Pelvis, Cranium (radiosurgery), Craniospinal</td>
</tr>
<tr>
<td>MINIMAL</td>
<td>H &amp; N, Extremities, Cranium, Breast</td>
</tr>
</tbody>
</table>
Guideline for Preventing Nausea and Vomiting in Patients Receiving Highly Emetic RT: TBI

Patients receiving highly emetic RT should receive a 5-HT₃ antagonist plus dexamethasone.

MASCC level of confidence: Moderate
MASCC level of consensus: High

ASCO level of evidence: III
ASCO grade of recommendation: C
Patients receiving moderately emetic RT should receive a 5-HT₃ antagonist.

MASCC level of confidence: High
MASCC level of consensus: High

ASCO level of evidence: II
ASCO grade of recommendation: A
COMMITTEE IX

Guideline for Preventing Nausea and Vomiting in Patients Receiving RT of Low Emetic Risk: Lower thorax region, Pelvis, Cranium (radiosurgery), Craniospinal

Patients receiving RT of low emetic risk should receive rescue with a 5-HT$_3$ antagonist.

MASCC level of confidence: Low
MASCC level of consensus: High

ASCO level of evidence: IV
ASCO grade of recommendation: D

If patients receiving RT of low emetic risk experience emesis, they should then receive prophylaxis with a 5-HT$_3$ antagonist.

MASCC level of confidence: Moderate
MASCC level of consensus: High

ASCO level of evidence: III
ASCO grade of recommendation: B
Guideline for Patients Receiving RT of Minimal Emetic Risk: H & N, Extremities, Cranium, Breast

Patients receiving RT of minimal emetic risk should receive rescue with a dopamine antagonist or a 5HT3 antagonist.

MASCC level of confidence: Low
MASCC level of consensus: High

ASCO level of evidence: IV
ASCO grade of recommendation: D
Committees are permanent
Each chair queries the committee every 6 months regarding whether there is new information which may affect the guideline
A steering committee queries the chairs for these suggestions
If evidence appears compelling, all group members are notified for their opinions
If consensus is achieved, the Web-Guideline document (MASCC) is updated. All participating Societies are notified
The challenge

• …is now to find the best ways to implement these guidelines into clinical practice…….

GOOD LUCK!