Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. This algorithm should not be used to treat pregnant women.

**RISK ASSESSMENT**

Assess for level of patient risk
- Young age
- Female
- Non-alcohol drinker
- Non-steroid user
- History of motion sickness
- Those previously failing conventional antiemetic therapy

**Note:** These characteristics represent increased risk for CINV; closer monitoring and more frequent reassessment recommended

Determine emetogenicity of chemotherapy/biotherapy (see Appendix A)

Is patient currently nauseated or have risk factors\(^1\) for anticipatory nausea/vomiting?

Yes

**PREVENTION/PROPHYLAXIS OF ANTICIPATORY NAUSEA/VOMITING**

Pharmacologic interventions:
- Alprazolam 0.5 – 2 mg PO prior to chemotherapy or
- Lorazepam 1 – 2 mg IV or PO prior to chemotherapy

Behavioral therapy – consider referral to Integrative Medicine for:
- Relaxation techniques
- Hypnosis
- Systematic desensitization

No

Prevention of chemotherapy-induced nausea and vomiting (CINV)

1 Risk factors for anticipatory nausea/vomiting are not clearly defined in the literature, but could broadly be listed as: nausea/vomiting with prior chemotherapy; history of motion sickness; history of emesis during pregnancy or hyperemesis gravidarum; female gender

\(^1\) For IV chemotherapy regimens, see Pages 2 and 3

\(^2\) For PO chemotherapy regimens, see Page 4

\(^3\) For IV/PO combination chemotherapy, use highest emetogenic agent to determine antiemetics
**Adult Antiemetic Management of Chemotherapy-Induced Nausea and Vomiting (CINV)**

**Disclaimer:** This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. This algorithm should not be used to treat pregnant women.

**IV CHEMOTHERAPY HIGH (HEC) AND MODERATE (MEC) RISK**

- **HEC single day ONLY:**
  - Olanzapine, serotonin antagonist (SA)\(^3\), steroid\(^{4,5}\)
  - neurokinin-1 antagonist (NKA)\(^6\) (see Page 10)

- **HEC or MEC, single day ONLY:**
  - Olanzapine, SA\(^3\), steroid\(^{4,5}\) (see Page 11)

- **HEC or MEC, single and multi-day:**
  - SA\(^3\), NKA\(^6\), steroid\(^{4,5}\) (see Page 12)

- **MEC single or multi-day ONLY:**
  - SA\(^3\), steroid\(^{4,5}\) (see Page 13)

**Prevention/Prophylaxis**

- Last day of chemotherapy?
  - Yes → For subsequent cycles, see Page 6
  - No → Refer to beginning for each day of chemotherapy (see specific antiemetic regimens)

**HEC = Highly Emetogenic Chemotherapy**

**MEC = Moderately Emetogenic Chemotherapy**

\(^{1}\) See Appendix A for Emetogenic Potential of Chemotherapy/Biotherapy Agents

\(^{2}\) Assess need for histamine H2 antagonist or proton pump inhibitor (PPI) for dyspepsia

\(^{3}\) All SAs are considered therapeutically equivalent when dosed appropriately; see Appendix C (ondansetron preferred)

\(^{4}\) The following features of steroids should be considered in patients with hematologic malignancies prior to prescribing them as part of the antiemetic regimen: a) risk of immunosuppression; b) avoid duplicative therapy (may already be part of chemotherapy regimen); c) inherent activity against hematologic malignancies may mask beneficial effects of chemotherapy in clinical trials. See Appendix C for other safety considerations.

\(^{5}\) Use of steroids is not recommended with cellular therapies and when immune checkpoint inhibitors are given alone. See Appendix C for more detail and other safety considerations.

\(^{6}\) May interact with cytochrome P450 enzyme (CYP enzyme); check for drug interactions – see Appendix C

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Department of Clinical Effectiveness V8

Approved by The Executive Committee of the Medical Staff on 06/20/2023
Adult Antiemetic Management of Chemotherapy-Induced Nausea and Vomiting (CINV)

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IV CHEMOTHERAPY LOW AND MINIMAL EMETOGENIC RISK

PREVENTION/PROPHYLAXIS

Prior to start of chemotherapy:
- Short-acting SA\(^1\) PO or IV or
- Steroids\(^2\) PO or IV or
- Phenothiazine PO or IV or
- Prokinetic agent PO or IV

(Note: Order above does not indicate preference. See Appendix C for dosing and scheduling.)

For breakthrough nausea/vomiting, see Page 5
For re-assessment/subsequent cycles, see Page 6

1. See Appendix A for Emetogenic Potential of Chemotherapy/Biotherapy Agents
2. Assess need for histamine H\(_2\) antagonist or proton pump inhibitor (PPI) for dyspepsia
3. All SAs are considered therapeutically equivalent when dosed appropriately, see Appendix C (ondansetron preferred)
4. The following features of steroids should be considered in patients with hematologic malignancies prior to prescribing them as part of the antiemetic regimen: a) risk of immunosuppression; b) avoid duplicative therapy, may already be part of chemotherapy regimen; c) inherent activity against hematologic malignancies may mask beneficial effects of chemotherapy in clinical trials. See Appendix C for other safety considerations.
5. Use of steroids is not recommended with cellular therapies and when immune checkpoint inhibitors are given alone. See Appendix C for more detail and other safety considerations.
**ORAL CHEMOTHERAPY EMETOGENIC RISK**

<table>
<thead>
<tr>
<th>Low to Minimal Risk (less than 30%)</th>
<th>High to Moderate Risk (30% or greater)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevention of CINV¹</td>
<td>Antiemetic premedications required²</td>
</tr>
<tr>
<td></td>
<td>Prior to start of chemotherapy:</td>
</tr>
<tr>
<td></td>
<td>Oral short-acting SA³</td>
</tr>
</tbody>
</table>

**RECOMMENDATION**

- ² No routine premedication required
- ² PRN medications recommended for breakthrough nausea/vomiting

**ANTIEMETIC REGIMEN**

- Prior to start of chemotherapy:
  - Oral short-acting SA³

  **For breakthrough nausea/vomiting, see Page 5**
  **For re-assessment/subsequent cycles, see Page 6**

1. Assess need for histamine H₂ antagonist or proton pump inhibitor (PPI) for dyspepsia
2. See Appendix A for Emetogenic Potential of Chemotherapy/Biotherapy Agents
3. Oral continuous dosing of chemotherapy/biotherapy for prolonged periods of time presents an emetogenic classification challenge as the emetogenic risk is likely overestimated in the product information. Therefore, an individualized approach is recommended and utilizing as needed antiemetics instead of routine premedication is often sufficient.
4. All SA are considered therapeutically equivalent when dosed appropriately, see Appendix C (ondansetron preferred)
BREAKTHROUGH NAUSEA AND VOMITING

General principles:
- SA and NKA generally not effective or approved for treatment of breakthrough nausea/vomiting
- Use antiemetic from another class the patient is not already taking
- Use of suppositories\(^1\) may be helpful if patient cannot take oral medication and IV access is not readily available; however, severity of condition may warrant IV antiemetics
- Instruct the patient to go to Acute Cancer Care Center if not improving and/or not able to drink fluids

Patient able to tolerate PO

- Choose an oral agent from a class not already given that Day\(^{2,3}\):
  - Phenothiazine or prokinetic agent
  - If persistent nausea, give: short-acting SA, or atypical antipsychotic, or ABH\(^4\) capsules combination product
  - Consider adding steroids and/or benzodiazepine to other classes for synergy as tolerated

Patient experiences breakthrough nausea and vomiting

- Patient not able to tolerate PO or has persistent nausea/vomiting with oral antiemetics

- Choose an IV agent from a class not already given that Day\(^{2,3}\):
  - Phenothiazine or prokinetic agent (if not already given within 4 hours)
  - Short-acting SA or high-dose prokinetic agent plus diphenhydramine
  - Consider adding steroids and/or benzodiazepine to other classes for synergy as tolerated

Reassess patient prior to subsequent cycles (see Page 6)

---

\(^1\) Suppositories should not be used in patients with an absolute neutrophil count (ANC) less than 1.0 K/microliter and/or a platelet count less than 50 K/microliter

\(^2\) See Appendix C for medication dosing specifics

\(^3\) If patient responds, consider around-the-clock dosing of the agent to which they responded and re-evaluate appropriateness periodically during period of risk

\(^4\) ABH = Ativan\(^\text{®}\) (lorazepam), Benadryl\(^\text{®}\) (diphenhydramine), Haldol\(^\text{®}\) (haloperidol)
Adult Antiemetic Management of Chemotherapy-Induced Nausea and Vomiting (CINV)

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. This algorithm should not be used to treat pregnant women.

SUBSEQUENT CYCLES OF CHEMOTHERAPY

ASSESSMENT OF PRIOR CHEMOTHERAPY

For subsequent cycles of the same chemotherapy regimen, re-evaluate effectiveness of antiemetic regimen and side effects of antiemetic premedication

ANTIEMETIC RESPONSE

Patient tolerated treatment with minimal nausea and no vomiting

No change in antiemetic regimen

Patient tolerated treatment with minimal nausea and no vomiting, but had side effects due to antiemetics

Consider changes in dosing or other management strategies (i.e., other medications, non-pharmacologic measures)

Patient had one or more episodes of vomiting in a 24 hour period or oral intake significantly decreased due to nausea

Consider any or all of the following:

1. Adding a benzodiazepine to the regimen
2. Adding an agent from a different class to the antiemetic regimen (see Appendix C)
3. Substituting high-dose intravenous metoclopramide (with diphenhydramine) for the SA

---

1 Changing to another SA after failing one has not been shown to be an effective strategy for management of breakthrough nausea and vomiting, although some individual patients have distinct preferences of one SA over another for prophylaxis
## APPENDIX A: Emetogenic Potential of Parenteral Chemotherapy/Biotherapy Agents – High and Moderate

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Frequency of Emesis (%)</th>
<th>Chemotherapy/Biotherapy Agents</th>
</tr>
</thead>
</table>
| High       | Greater than 90%        | • AC combination defined as either doxorubicin or epirubicin with cyclophosphamide  
• Carboplatin¹ (greater than or equal to AUC of 4)  
• Carmustine (greater than 250 mg/m²)  
• Cisplatin¹  
• Cyclophosphamide (greater than 1,500 mg/m²)  
• Dacarbazine  
• Doxorubicin (greater than 50 mg/m²)  
• Epirubicin (greater than 90 mg/m²)  
• Fam-trastuzumab deruxtecan-nxki  
• Ifosfamide (high dose: greater than 2 grams/m²/dose)  
• Methotrexate  
• Melphalan  
• Sacituzumab govitecan-hziy  
• Streptozocin |
| Moderate   | 30% to 90%              | • Aldesleukin (greater than or equal to 12 million units/m³)  
• Arsenic trioxide  
• Azacitidine  
• Bendamustine  
• Busulfan¹  
• Carboplatin¹ (less than AUC of 4)  
• Carmustine (less than or equal to 250 mg/m²)  
• Clofarabine  
• Cyclophosphamide (less than or equal to 1,500 mg/m²)  
• Cytarabine (greater than 200 mg/m²)  
• Dacitoximycin  
• Daunorubicin  
• Daunorubicin + cytarabine combination (Liposomal)  
• Dinutuximab  
• Doxorubicin (less than or equal to 50 mg/m²)  
• Epirubicin (less than or equal to 90 mg/m²)  
• Idarubicin  
• Ifosfamide (less than or equal to 2 grams/m²/dose)  
• Irinotecan  
• Irinotecan (Liposomal)  
• Lubinectedtin  
• Methotrexate (greater than or equal to 250 mg/m²)  
• Oxaliplatin¹  
• Romidepsin  
• Temozolomide  
• Trabectedin |

¹ Emetogenic risk may vary depending on the dosing, administration and/or concurrently administered chemotherapy.
### APPENDIX A: Emetogenic Potential of Parenteral Chemotherapy/Biotherapy – Low and Minimal - Continued

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Frequency of Emesis (%)</th>
<th>Chemotherapy/Biotherapy Agents</th>
</tr>
</thead>
</table>
| Low        | 10% to 30%              | ● Cytarabine (low dose:100 – 200 mg/m²)  
              |                         | ● Docetaxel               
              |                         | ● Doxorubicin (liposomal)  
              |                         | ● Enfortumab vedotin-ejfv  
              |                         | ● Eribulin                
              |                         | ● Etoposide               
              |                         | ● 5-Fluorouracil (5-FU)   
              |                         | ● Gemcitabine             
              |                         | ● Gentuzumab ozogamicin   
              |                         | ● Idecabtagene vicleucel (CAR-T)¹  
              |                         | ● Isatuximab-irfc          
              |                         | ● Ixabepilone             |
|            |                         | ● Lisocabtagene maraleucel (CAR-T)¹  
              |                         | ● Loncastuximab tesirine-lpyl  
              |                         | ● Methotrexate (greater than 50 mg/m² but less than 250 mg/m²)  
              |                         | ● Mirvetuximab soravtansine-gynx  
              |                         | ● Mitomycin               
              |                         | ● Mitomycin pyelocalyceal solution  
              |                         | ● Mitoxantrone            
              |                         | ● Necitumab               
              |                         | ● Omacetaxine             
              |                         | ● Paclitaxel              
              |                         | ● Paclitaxel-albumin       
              |                         | ● Pentostatin              
              |                         | ● Polatuzumab vedotin-piig 
              |                         | ● Pralatrexate            
              |                         | ● Tafasitamab-cxix         
              |                         | ● Tagraxofusp-erzs         
              |                         | ● Tebentafusp-tebn         
              |                         | ● Teclistamab-cqyv         
              |                         | ● Talamogine laherparevec  
              |                         | ● Thiotepa                
              |                         | ● Tisagenlecleucel (CAR-T)¹  
              |                         | ● Tisotumab vedotin-tftv   
              |                         | ● Topotecan               |

¹ Use of steroids is not recommended with cellular therapies and when immune checkpoint inhibitors are given alone; see Appendix C for more details

*Continued on next page*
## APPENDIX A: Emetogenic Potential of Parenteral Chemotherapy/Biotherapy – Low and Minimal - Continued

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Frequency of Emesis (%)</th>
<th>Chemotherapy/Biotherapy Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal</td>
<td>Less than 10%</td>
<td>● Alemtuzumab</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Asparaginase</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Atezolizumab</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Avelumab</td>
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<tr>
<td></td>
<td></td>
<td>● Bevacizumab</td>
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<tr>
<td></td>
<td></td>
<td>● Bleomycin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Blinatumomab</td>
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<tr>
<td></td>
<td></td>
<td>● Bortezomib</td>
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<tr>
<td></td>
<td></td>
<td>● Cemiplimab-rwlc</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Cetuximab</td>
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<tr>
<td></td>
<td></td>
<td>● Cladribine</td>
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<tr>
<td></td>
<td></td>
<td>● Cytarabine (less than 100 mg/m²)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Daratumumab</td>
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<tr>
<td></td>
<td></td>
<td>● Daratumumab + Hyaluronidase-fihj SubQ combination</td>
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<tr>
<td></td>
<td></td>
<td>● Decitabine</td>
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<td></td>
<td></td>
<td>● Denileukin diftitox</td>
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<tr>
<td></td>
<td></td>
<td>● Dostarlimab-gxly</td>
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<td></td>
<td>● Durvalumab</td>
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<td>● Elotuzumab</td>
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<td></td>
<td></td>
<td>● Fludarabine</td>
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<td></td>
<td></td>
<td>● Inotuzumab ozogamicin</td>
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<td></td>
<td></td>
<td>● Ipilimumab</td>
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<tr>
<td></td>
<td></td>
<td>● Luspatercept-aamt</td>
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<tr>
<td></td>
<td></td>
<td>● Methotrexate (less than or equal to 50 mg/m²)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Margetuximab-cmkb</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Mogamulizumab-kpck</td>
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<td></td>
<td></td>
<td>● Moxetumomab pasudotox-tdfk</td>
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<td></td>
<td></td>
<td>● Mosunetuzumab-axgb</td>
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<tr>
<td></td>
<td></td>
<td>● Nivolumab + Relatimab-rmbw¹</td>
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<td></td>
<td></td>
<td>● Obinutuzumab</td>
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<td>● Ofatumumab</td>
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<td></td>
<td></td>
<td>● Panitumumab</td>
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<tr>
<td></td>
<td></td>
<td>● Pegaspargase</td>
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<tr>
<td></td>
<td></td>
<td>● Peginterferon</td>
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<tr>
<td></td>
<td></td>
<td>● Pembrolizumab</td>
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<td>● Pertuzumab</td>
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<td></td>
<td>● Pertuzumab + Trastuzumab + Hyaluronidase-zzxf SubQ combination</td>
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<td>● Ramucirumab</td>
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<tr>
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<td>● Rituximab</td>
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<tr>
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<td>● Siltuximab</td>
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<td></td>
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<td>● Temsirolimus</td>
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<td>● Trastuzumab</td>
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<td></td>
<td></td>
<td>● Trastuzumab + Hyaluronidase- oysk SubQ combination</td>
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<td>● Tremelimumab-actl</td>
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<td></td>
<td>● Valrubicin</td>
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<tr>
<td></td>
<td></td>
<td>● Vinblastine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Vincristine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Vincristine (liposomal)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Vinorelbine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Ziv-aflibercept</td>
</tr>
</tbody>
</table>

¹ Use of steroids is not recommended with cellular therapies and when immune checkpoint inhibitors are given alone; see Appendix C for more details

*Continued on next page*
## APPENDIX A: Emetogenic Potential of ORAL Chemotherapy/Biotherapy - Continued

Note: Oral continuous dosing of chemotherapy/biotherapy for prolonged periods of time presents an emetogenic classification challenge as the emetogenic risk is likely overestimated in the product information. Therefore, an individualized approach is recommended and utilizing as needed antiemetics instead of routine premedication is often sufficient.

<table>
<thead>
<tr>
<th>Emetogenic Risk</th>
<th>Chemotherapy/Biotherapy Agents</th>
</tr>
</thead>
</table>
| High to Moderate | • Avapritinib  
• Azacitidine  
• Busulfan (greater than or equal to 4 mg/day)  
• Cyclophosphamide (greater than or equal to 100 mg/m²/dose)  
• Etoposide  
• Fedratinib  
• Chlorambucil  
• Cobimetinib  
• Crizotinib  
• Cyclophosphamide (less than 100 mg/m²/dose)  
• Dabrafenib  
• Dacomitinib  
• Dasatinib  
• Decitabine + cedazuridine combination  
• Duvelisib  
• Elacestrant  
• Enasidemib  
• Encorafenib  
• Entrectinib  
• Enzalutamide  
• Erdafitinib  
• Erlotinib  
• Estramustine  
• Everolimus  |
| | • Lenvatinib  
• Lomustine  
• Midostaurin  
• Mitotane  
• Niraparib  
• Fludarabine  
• Futibatinib  
• Geftinib Gilteritinib  
• Gladsedge  
• Hydroxyurea  
• Ibrutinib  
• Idelalisib  
• Imatinib  
• Ivosidenib  
• Ixazomib  
• Lapatinib  
• Larotrectinib  
• Lenalidomide  
• Lenvatinib  
• Lorlatinib  
• Melphanal  
• Mercaptopurine  
• Methotrexate  
• Mobocertinib  
• Neratinib maleate  |
| | • Olaparib  
• Procarbazine  
• Rucaparib  
• Selinexor  
• Temozolomide (greater than 75 mg/m²/dose)  |
| Low to Minimal | • Abemaciclib  
• Abiraterone  
• Acalabrutinib  
• Adagrasib  
• Aflatinib  
• Alectinib  
• Alpelisib  
• Amscrinib  
• Altretamine  
• Apalatinib  
• Axitinib  
• Belzutifan  
• Bexarotene  
• Binimetinib  
• Bosutinib  
• Brigatinib  
• Busulfan (less than 4 mg/day)  
• Cabozantinib  
• Capecitabine  
• Capmatinib  
• Ceritinib  |
| | • Chlorambucil  
• Cobimetinib  
• Crizotinib  
• Cyclophosphamide (less than 100 mg/m²/dose)  
• Dabrafenib  
• Dacomitinib  
• Dasatinib  
• Decitabine + cedazuridine combination  
• Duvelisib  
• Elacestrant  
• Enasidemib  
• Encorafenib  
• Entrectinib  
• Enzalutamide  
• Erdafitinib  
• Erlotinib  
• Etsrugustine  
• Everolimus  |
| | • Fludarabine  
• Futibatinib  
• Gefitinib Gilteritinib  
• Gladsedge  
• Hydroxyurea  
• Ibrutinib  
• Idelalisib  
• Imatinib  
• Ivosidenib  
• Ixazomib  
• Lapatinib  
• Larotrectinib  
• Lenalidomide  
• Lenvatinib  
• Lorlatinib  
• Melphanal  
• Mercaptopurine  
• Methotrexate  
• Mobocertinib  
• Neratinib maleate  |
| | • Nilotinib  
• Olutasidenib  
• Osimertinib  
• Palbociclib  
• Panobinostat  
• Pazopanib  
• Pemigatinib  
• Pexidartinib  
• Pirtobrutinib  
• Pomalidomide  
• Ponatinib  
• Pralsetinib  
• Regorafenib  
• Ripretinib  
• Ruxolitinib  
• Selpercatinib  
• Sonidegib  
• Sorafenib  
• Sotorasib  |
| | • Sunitinib  
• Talazapar tosylate  
• Tazemotostat  
• Temozolomide (less than or equal to 75 mg/m²/dose)  
• Tepotinib  
• Thalidomide  
• Thioguanine  
• Tivozanib  
• Topotecan  
• Trametinib  
• Tretinoin  
• Trifluridine-tipiracil  
• Tucatinib  
• Vandetanib  
• Venurafenib  
• Venetoclax  
• Vismodegib  
• Vorinostat  
• Zanubrutinib |
APPENDIX B: Antiemetic Regimens for Prevention of Acute and Delayed CINV

Olanzapine/SA/Steroids/NKA - HEC, single day ONLY

Choose one from each category below:

- Serotonin antagonist
  - Granisetron 1 mg IV
  - Ondansetron 8 – 16 mg IV
  - Palonosetron 0.25 mg IV

- Steroids
  - Dexamethasone 2,3 12 mg IV on Day 1; then 8 mg PO once daily on Days 2 – 3

- Neurokinin-1 antagonist
  - Aprepitant 125 mg PO on Day 1; then 80 mg PO on Days 2 – 3
  - Fosaprepitant 150 mg IV

---

PRN antiemetics at home

- Prochlorperazine 5 – 10 mg PO every 6 hours prn nausea/vomiting
- Ondansetron 8 mg PO every 12 hours prn nausea/vomiting (do not give SA at home if long-acting SA administered on Day 1)

---

1 All SAs are considered therapeutically equivalent when dosed appropriately, see Appendix C (ondansetron preferred)
2 The following features of steroids should be considered in patients with hematologic malignancies prior to prescribing them as part of the antiemetic regimen: a) risk of immunosuppression; b) avoid duplicative therapy, may already be part of chemotherapy regimen; c) inherent activity against hematologic malignancies may mask beneficial effects of chemotherapy in clinical trials. See Appendix C for other safety considerations.
3 Use of steroids is not recommended with cellular therapies and when immune checkpoint inhibitors are given alone. See Appendix C for other safety considerations.
4 May interact with cytochrome P450 enzyme (CYP enzyme); check for drug interactions – see Appendix C
APPENDIX B: Antiemetic Regimens for Prevention of Acute and Delayed CINV - Continued

<table>
<thead>
<tr>
<th>Olanzapine/SA/Steroids - HEC or MEC, single day ONLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Olanzapine 5-10 mg PO daily on Days 1 – 4</td>
</tr>
<tr>
<td>Choose one from each category below:</td>
</tr>
<tr>
<td>● Serotonin antagonist¹</td>
</tr>
<tr>
<td>○ Granisetron 1 mg IV</td>
</tr>
<tr>
<td>○ Ondansetron 8 – 16 mg IV</td>
</tr>
<tr>
<td>○ Palonosetron 0.25 mg IV</td>
</tr>
<tr>
<td>● Steroids</td>
</tr>
<tr>
<td>○ Dexamethasone² 12 mg IV on Day 1</td>
</tr>
<tr>
<td>● PRN antiemetics at home</td>
</tr>
<tr>
<td>○ Prochlorperazine 5 – 10 mg PO every 6 hours prn nausea/vomiting</td>
</tr>
<tr>
<td>○ Ondansetron 8 mg PO every 12 hours prn nausea/vomiting (do not give SA at home if long-acting SA administered on Day 1)</td>
</tr>
</tbody>
</table>

¹ All SAs are considered therapeutically equivalent when dosed appropriately, see Appendix C (ondansetron preferred).
² The following features of steroids should be considered in patients with hematologic malignancies prior to prescribing them as part of the antiemetic regimen: a) risk of immunosuppression; b) avoid duplicative therapy, may already be part of chemotherapy regimen; c) inherent activity against hematologic malignancies may mask beneficial effects of chemotherapy in clinical trials. See Appendix C for other safety considerations.
³ Use of steroids is not recommended with cellular therapies and when immune checkpoint inhibitors are given alone. See Appendix C for other safety considerations.
### APPENDIX B: Antiemetic Regimens for Prevention of Acute and Delayed CINV - Continued

#### SA/Steroids/NKA: HEC or MEC, single or multi-day

<table>
<thead>
<tr>
<th>Category</th>
<th>Option</th>
<th>Dosage Details</th>
</tr>
</thead>
</table>
| ● Serotonin antagonist<sup>1</sup> | Granisetron | - 1 mg IV (multi-day chemotherapy – repeat daily followed by PO at home for 2 - 3 days after chemotherapy completed)  
- 3.1 mcg/24 hour patch* (apply 24 – 48 hours prior to chemotherapy; sustained release over 7 days)  
- Ondansetron 8 – 16 mg IV (multi-day chemotherapy – repeat daily followed by PO at home for 2 – 3 days after chemotherapy completed)  
- Palonosetron 0.25 mg IV (multi-day chemotherapy – data is available to support daily or every other day dosing) |
| ● Steroids | Dexamethasone<sup>2,3</sup> | - If aprepitant/fosaprepitant: dexamethasone 12 mg IV on day 1; then 8 mg PO daily on days 2 – 3  
- If rolapitant: dexamethasone 12 mg IV on day 1; then 8 mg PO daily on days 2-3  
- For non-cisplatin containing regimens consider steroid sparing options after completion of chemotherapy |
| ● Neurokinin-1 antagonist | Aprepitant<sup>4</sup> | 125 mg PO on day 1; then 80 mg PO on Days 2 and 3 (multi-day chemotherapy – may continue 80 mg daily while receiving chemotherapy and 2 days after completion)  
- Fosaprepitant<sup>4</sup> | - 150 mg IV on day 1 only (single day chemotherapy – single dose lasts for 3 days; multi-day chemotherapy - may repeat dosing, but no sooner than 3 days)  
- Rolapitant 180 mg PO on Day 1 only |
| ● PRN antiemetics at home | Prochlorperazine 5 – 10 mg PO every 6 hours prn nausea/vomiting  
Ondansetron 8 mg PO every 12 hours prn nausea/vomiting (do not give SA at home if long-acting SA administered on Day 1)  
Consider scheduled short-acting SA for the first 2 - 3 days after chemotherapy (do not give SA at home if long-acting SA administered on Day 1) |

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<sup>1</sup> All SAs are considered therapeutically equivalent when dosed appropriately, see Appendix C (ondansetron preferred)

<sup>2</sup> The following features of steroids should be considered in patients with hematologic malignancies prior to prescribing them as part of the antiemetic regimen:

- a) risk of immunosuppression; b) avoid duplicative therapy, may already be part of chemotherapy regimen; c) inherent activity against hematologic malignancies may mask beneficial effects of chemotherapy in clinical trials. See Appendix C for other safety considerations.

<sup>3</sup> Use of steroids is not recommended with cellular therapies and when immune checkpoint inhibitors are given alone. See Appendix C for other safety considerations.

<sup>4</sup> May interact with cytochrome P450 enzyme (CYP enzyme); check for drug interactions – see Appendix C
**APPENDIX B: Antiemetic Regimens for Prevention of Acute and Delayed CINV - Continued**

<table>
<thead>
<tr>
<th>SA/Steroids: MEC ONLY, single or multi-day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choose one from each category below:</td>
</tr>
</tbody>
</table>

- **Serotonin antagonist**
  - Granisetron
    - 1 mg IV (multi-day chemotherapy – repeat daily followed by PO at home for 2 – 3 days after chemotherapy completed)
    - 3.1 mcg/24 hour patch* (apply 24 – 48 hours prior to chemotherapy; sustained release over 7 days)
  - Ondansetron 8 – 16 mg IV (multi-day chemotherapy – repeat daily followed by PO at home for 2 – 3 days after chemotherapy completed)
  - Palonosetron 0.25 mg IV (multi-day chemotherapy – data is available to support daily or every other day dosing)

- **Steroids**
  - Dexamethasone1,2,3 12 mg IV on day 1; then 8 mg PO daily on days 2-3
  - For some non-cisplatin containing regimens consider steroid sparing options after completion of chemotherapy

- **PRN antiemetics at home**
  - Prochlorperazine 5 – 10 mg PO every 6 hours prn nausea/vomiting
  - Ondansetron 8 mg PO every 12 hours prn nausea/vomiting (do not give SA at home if long-acting SA administered on Day 1)
  - Consider scheduled short-acting SA for the first 2 – 3 days after chemotherapy (do not give SA at home if long-acting SA administered on Day 1)

* Restricted drug on MDACC Pharmacy Formulary as of May 2023

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1 All SAs are considered therapeutically equivalent when dosed appropriately, see Appendix C (ondansetron preferred)

2 The following features of steroids should be considered in patients with hematologic malignancies prior to prescribing them as part of the antiemetic regimen:
   a) risk of immunosuppression; b) avoid duplicative therapy, may already be part of chemotherapy regimen; c) inherent activity against hematologic malignancies may mask beneficial effects of chemotherapy in clinical trials. See Appendix C for other safety considerations.

3 Use of steroids is not recommended with cellular therapies and when immune checkpoint inhibitors are given alone. See Appendix C for other safety considerations.
# APPENDIX C: Antiemetic Medication Options

<table>
<thead>
<tr>
<th>Medication</th>
<th>Adult Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anxiolytics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alprazolam (Xanax®)</td>
<td>0.5 – 2 mg PO every 6 hours</td>
<td>• <strong>Indication:</strong> anticipatory CINV (drug class of choice)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• <strong>Class adverse effects</strong>: sedation, dizziness, disorientation, hypotension, amnesia</td>
</tr>
<tr>
<td>Lorazepam (Ativan®)</td>
<td>0.5 – 2 mg PO, SL or IV every 6 hours</td>
<td>• Lorazepam SL is administered using the oral concentrate formulation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Exert caution when using in the elderly, as they may be more sensitive to the side effects (see Beers Criteria for more information)</td>
</tr>
<tr>
<td><strong>Atypical Antipsychotics</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Olanzapine (Zyprexa®)    | Prevention: 5-10 mg PO daily on Days 1 – 4  
Breakthrough: 2.5 – 5 mg PO twice a day or 10 mg PO daily times 3 days | • **Indication:** prophylaxis for acute and delayed CINV (with a SA plus dexamethasone with or without an NKA) |
|                         |                                     | • **Adverse effects**¹: drowsiness, dizziness, hyperglycemia, restlessness, extrapyramidal symptoms.                                          |
|                         |                                     | • Avoid concomitant use with metoclopramide and haloperidol due to increased risk of extrapyramidal reactions                                |
|                         |                                     | • **QTc prolongation**³ possible Torsade's de Pointes (TdP) - medication can cause QT prolongation but there is insufficient evidence that when used as directed in official labeling, the medication is associated with a risk of causing TdP |
|                         |                                     | • Exert caution when using in the elderly, as they may be more sensitive to the side effects (see Beers Criteria for more information)     |

¹ Adverse effects are not all inclusive, refer to package insert  
³ For QTc prolongation information, see [www.Crediblemeds.org](http://www.Crediblemeds.org)
This document is part of the Adult Antiemetic Management of Chemotherapy-Induced Nausea and Vomiting (CINV) section, which discusses various antiemetic medication options. The page contains a table listing different medications, their dosages, indications, and comments. The medications include:

- **Butyrophenones**
  - **Haloperidol (Haldol®)**: 0.5 – 2 mg IV every 6 hours (see also ABH on Page 20)
    - **Indication:** treatment of breakthrough CINV
    - **Adverse effects**: sedation, tachycardia, hypotension, restlessness, extrapyramidal symptoms (may co-administer with benzodiazepine or antihistamine to avoid this)
    - **QTc prolongation**: known risk of TdP - medication causes QT interval prolongation and is clearly associated with a risk of TdP
    - Exert caution when using in the elderly, as they may be more sensitive to the side effects (see Beers Criteria for more information)

- **Cannabinoids**
  - **Dronabinol (Marinol®):** 1 – 2 mg PO twice a day
    - **Indication:** prophylaxis for acute and delayed CINV refractory to other antiemetics
  - **Nabilone (Cesamet®)*:** 2.5 – 10 mg PO either every 3 hours or every 6 hours
    - **Indication:** treatment of breakthrough CINV
    - **Adverse effects**: dizziness, somnolence, sleep disturbances, confusion, hallucinations
    - Avoid abrupt discontinuation of therapy which may precipitate withdrawal

*Not on MDACC Pharmacy Formulary as of May 2023

1 Adverse effects are not all inclusive, refer to package insert
2 For QTc prolongation information, see www.Crediblemeds.org
### APPENDIX C: Antiemetic Medication Options – Continued

<table>
<thead>
<tr>
<th>Medication</th>
<th>Adult Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurokinin-1 Antagonists</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aprepitant (Emend®)</td>
<td>125 mg PO</td>
<td>80 mg PO daily for 2 days</td>
</tr>
<tr>
<td>Fosaprepitant (Emend® IV)</td>
<td>115 mg IV</td>
<td>Aprepitant 80 mg PO daily for 2 days</td>
</tr>
<tr>
<td></td>
<td>150 mg IV</td>
<td>None recommended (Note: See dosing with dexamethasone)</td>
</tr>
<tr>
<td>Rolapitant (Varubi®)</td>
<td>180 mg PO</td>
<td>None recommended</td>
</tr>
<tr>
<td><strong>Non-Phenothiazine Antihistamines/Anticholinergics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diphenhydramine (Benadryl®)</td>
<td>12.5 – 50 mg PO or IV every 6 hours (may dose every 4 hours)</td>
<td></td>
</tr>
<tr>
<td>Scopolamine transdermal patch (Transderm Scop®)</td>
<td>1 patch (1.5 mg) every 72 hours</td>
<td></td>
</tr>
</tbody>
</table>

1. **Indication:** prophylaxis of acute and delayed CINV (with SA plus dexamethasone)
2. **Class adverse effects:** hiccups, fatigue, dizziness, diarrhea
3. Decrease dexamethasone dose by 50% with concomitant use (same day) of aprepitant and fosaprepitant
4. Drug interactions due to CYP3A4 inhibition for aprepitant and fosaprepitant; CYP2D6 with rolapitant
5. Rolapitant has only been studied with single-day chemotherapy regimens

1. Adverse effects are not all inclusive, refer to package insert

Continued on next page
## APPENDIX C: Antiemetic Medication Options – continued

<table>
<thead>
<tr>
<th>Medication</th>
<th>Adult Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phenothiazine Antihistamines</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Prochlorperazine (Compazine®️) | • 5 – 10 mg PO or IV every 6 hours (may dose every 4 hours)  
• 25 mg PR every 12 hours | • **Indication:** treatment of breakthrough CINV; prophylaxis for acute and delayed CINV (with low-risk agents)  
• **Class adverse effects**: sedation, dry mouth, extrapyramidal symptoms constipation, blurred vision  
• **QTc prolongation**: possible risk of TdP - medication can cause QT prolongation BUT there is insufficient evidence that when used as directed in official labeling, the medication is associated with a risk of causing TdP (promethazine)  
• Exert caution when using in the elderly, as they may be more sensitive to the side effects (see Beers Criteria for more information) |
| Promethazine (Phenergan®️) | • 12.5 – 25 mg PO or IV every 6 hours (may dose every 4 hours)  
• 25 mg PR every 6 hours  
• 6.25 mg/0.1 mL in PLO gel* topically every 4 hours |                                                                          |

**Prokinetic Agents**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Adult Dosage</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Metoclopramide (Reglan®️)   | • Standard dose 10 – 40 mg PO or IV every 6 hours (may dose every 4 hours)  
• High dose 0.5 – 2 mg/kg IV with diphenhydramine 25 mg IV every 4 hours | • **Indication:** breakthrough CINV, prophylaxis of acute (high-dose only) and delayed (with steroids) CINV  
• **Adverse effects**: sedation, diarrhea, extrapyramidal symptoms (especially with high dose, may co-administer with benzodiazepine or antihistamine to avoid this), tremors, akathisia  
• Contraindication in patients with GI obstruction  
• **QTc prolongation**: Conditional risk of TdP - these drugs are associated with a risk of TdP BUT only under certain conditions (e.g. excessive dose, hypokalemia, congenital long QT or by causing a drug-drug interaction that results in excessive QT interval prolongation)  
• Exert caution when using in the elderly, as they may be more sensitive to the side effects (see Beers Criteria for more information) |

*Not on MDACC Pharmacy Formulary as of May 2023

1. Adverse effects are not all inclusive, refer to package insert
2. For QTc prolongation information, see www.Crediblemeds.org
## APPENDIX C: Antiemetic Medication Options – Continued

<table>
<thead>
<tr>
<th>Medication</th>
<th>Adult Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serotonin Antagonists (SA)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dolasetron (Anzemet®)*</td>
<td>100 – 200 mg PO</td>
<td>● <strong>Indication:</strong> prophylaxis of acute and delayed CINV</td>
</tr>
<tr>
<td></td>
<td>100 mg PO daily</td>
<td>● Dolasetron available as oral tablet only. IV use is not recommended by FDA.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● Apply granisetron patch 24 - 48 hours prior to chemotherapy administration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>● FDA has amended the product information of ondansetron to limit single intravenous doses to 16 mg</td>
</tr>
<tr>
<td></td>
<td>2 mg PO daily</td>
<td>● Palonosetron: phase III clinical trials did not allow repeat dosing for 7 days. The optimal timing of repeat doses of palonosetron is currently unknown.</td>
</tr>
<tr>
<td></td>
<td>1 mg PO twice a day</td>
<td></td>
</tr>
<tr>
<td>Granisetron</td>
<td>1 – 2 mg PO or 1 mg IV</td>
<td>● Class adverse effects¹: headache, constipation, fatigue</td>
</tr>
<tr>
<td>Kytril® – IV/PO</td>
<td>2 mg PO daily or 1 mg PO twice a day</td>
<td>● QTc prolongation²: increased risk of QTc prolongation has been observed with IV formulations of ondansetron, dolasetron, and granisetron</td>
</tr>
<tr>
<td>Sancuso® – patch**</td>
<td>3.1 mg/24 hours patch (total dose delivered 34.3 mg/7 days)</td>
<td>○ Dolasetron and granisetron: possible risk of TdP – these medications can cause QT prolongation BUT there is insufficient evidence that when used as directed in official labeling, the medications are associated with a risk of causing TdP</td>
</tr>
<tr>
<td></td>
<td>Not Applicable</td>
<td>○ Ondansetron: known risk of TdP - medication causes QT interval prolongation and is clearly associated with a risk of TdP, consider EKG monitoring especially with doses greater than 16 mg per day</td>
</tr>
<tr>
<td>Ondansetron (Zofran®) (preferred agent) Oral disintegrating tablet, tablet, oral solution, IV</td>
<td>8 – 24 mg PO or 8 – 16 mg IV</td>
<td>● Short-acting SAs include:</td>
</tr>
<tr>
<td></td>
<td>8 mg PO twice a day or 8 mg PO every 8 hours or 16 mg PO daily or 8 mg IV twice a day or 8 mg IV every 8 hours</td>
<td>○ Dolasetron (all formulations)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>○ Granisetron (IV/PO formulations)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>○ Ondansetron (all formulations)</td>
</tr>
<tr>
<td>Palonosetron (Aloxi®)</td>
<td>0.25 mg IV</td>
<td>None recommended</td>
</tr>
</tbody>
</table>

*Not on MDACC Pharmacy Formulary as of May 2023
** Restricted drug on MDACC Pharmacy Formulary as of May 2023
¹Adverse effects are not all inclusive, refer to package insert.
² For QTc prolongation information, see www.Crediblemeds.org

### Notes
- Adult Antiemetic Management of Chemotherapy-Induced Nausea and Vomiting (CINV)
- **Disclaimer:** This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.
<table>
<thead>
<tr>
<th>Medication</th>
<th>Adult Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Steroids</strong> (Decadron®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 1: 10 – 12 mg PO or IV</td>
<td><strong>Indication</strong>: prophylaxis of acute and delayed CINV</td>
</tr>
<tr>
<td></td>
<td>Days 2 – 4 (or longer): 4 – 8 mg PO or IV twice daily</td>
<td>• Caution in patients with hematologic malignancies²</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Use of steroids is not recommended with immune and/or cellular therapies³</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• A steroid sparing prophylactic antiemetic regimen is preferred when:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ Immune checkpoint inhibitors are administered alone, as these are low emetogenic risk and alternative antiemetics should be considered. When immune and/or cellular therapies are combined with moderate and high emetogenic risk chemotherapy, the panel recommends steroids to be avoided but may be used at the discretion of the disease site service.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>◦ Cellular therapies, including lymphodepleting chemotherapy preparative regimens, as the risk of inactivating the immune response is very high with even small doses of steroids. Avoiding the use of steroids for 3 - 5 days prior to and 90 days after cell administration is optimal.</td>
</tr>
<tr>
<td><strong>Dexamethasone with either aplepitant 125 mg PO or fosaprepitant 115 mg IV</strong></td>
<td>10 – 12 mg PO or IV</td>
<td>• <strong>Class adverse effects</strong>: hyperglycemia, insomnia, hicups, dyspepsia, agitation, weight gain, hypertension</td>
</tr>
<tr>
<td></td>
<td>8 mg PO daily for 3 days</td>
<td>◦ Increased risk of infection with prolonged use greater than 2 weeks</td>
</tr>
<tr>
<td><strong>Dexamethasone with fosaprepitant 150 mg IV</strong></td>
<td>10 – 12 mg PO or IV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 2: 8 mg PO daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Days 3 – 4: 8 mg PO twice daily</td>
<td></td>
</tr>
</tbody>
</table>

¹ Higher doses may be considered in certain circumstances
² The following features of steroids should be considered in patient with hematologic malignancies prior to prescribing them as part of the antiemetic regimen: a) risk of immunosuppression; b) avoid duplicative therapy, may already be part of chemotherapy regimen; c) inherent activity against hematologic malignancies may mask beneficial effects of chemotherapy in clinical trials
³ Use of steroids is not recommended with cellular therapies and when immune checkpoint inhibitors are given alone
⁴ Adverse effects are not all inclusive, refer to package insert
### Appendix C: Antiemetic Medication Options – Continued

<table>
<thead>
<tr>
<th>Medication</th>
<th>Adult Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Combination Products (capsules and suppositories compounded at MDACC Pharmacy)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABH capsules:</td>
<td>1 capsule PO every 6 hours</td>
<td><strong>Indication:</strong> treatment of breakthrough CINV; prophylaxis of delayed CINV (refractory to other antiemetics)</td>
</tr>
<tr>
<td>- Lorazepam 0.34 mg</td>
<td></td>
<td>Adverse effects as per individual agents</td>
</tr>
<tr>
<td>- Diphenhydramine 25 mg</td>
<td></td>
<td>Additive amounts are not equal between the routes of administration due to absorption variances</td>
</tr>
<tr>
<td>- Haloperidol 1.5 mg</td>
<td></td>
<td>QTc prolongation¹: known risk of TdP - medication causes QT interval prolongation and is clearly associated with a risk of TdP (haloperidol)</td>
</tr>
<tr>
<td>ABH IV:</td>
<td>Given as combination IV every 6 hours (need to order each agent separately)</td>
<td>Exert caution when using in the elderly, as they may be more sensitive to the side effects (see Beers Criteria² for more information)</td>
</tr>
<tr>
<td>- Lorazepam 0.5 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Diphenhydramine 12.5 – 25 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Haloperidol 0.5 – 1 mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹For QTc prolongation information, see [www.Crediblemeds.org](http://www.Crediblemeds.org)

SUGGESTED READINGS


DEVELOPMENT CREDITS

This practice consensus statement is based on majority opinion of the Nausea and Vomiting workgroup at the University of Texas MD Anderson Cancer Center for the patient population. These experts included:

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*Clinical Effectiveness Development Team