Adult Antiemetic Management of Chemotherapy-Induced Nausea and Vomiting (CINV)

Note: The information provided here applies to standard doses of chemotherapy/biotherapy not requiring stem cell rescue.

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?

PREVENTION/PROPHYLAXIS OF ANTICIPATORY NAUSEA/VOMITING

Yes →

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) →
- For IV chemotherapy regimens, see Pages 2 and 3
- For PO chemotherapy regimens, see Page 4
- For IV/PO combination chemotherapy, use highest emetogenic agent to determine antiemetics

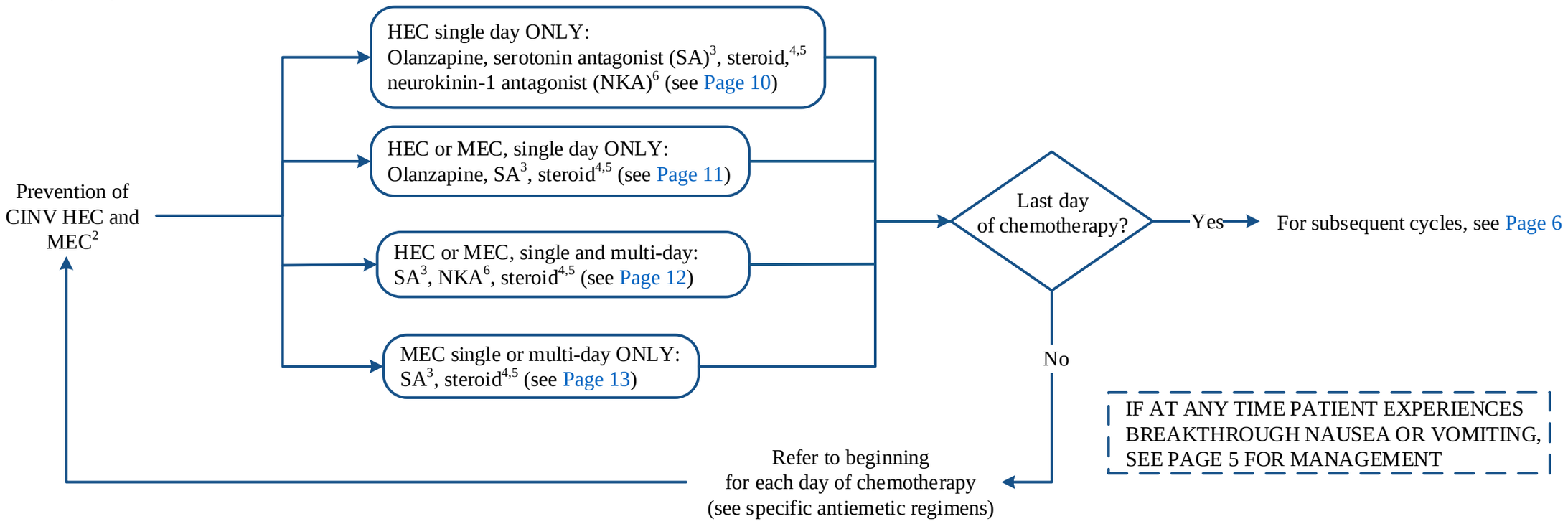
[1] Risk factors for anticipatory nausea/vomiting are not clearly defined in the literature, but could broadly be listed as: nausea/vomiting with prior chemotherapy; history of motion sickness; history of emesis during pregnancy or hyperemesis gravidarum; female gender

Department of Clinical Effectiveness V6
Approved by The Executive Committee of the Medical Staff on 01/29/2019

Adult Antiemetic Management of Chemotherapy-Induced Nausea and Vomiting (CINV)

IV CHEMOTHERAPY HIGH (HEC) AND MODERATE (MEC) RISK[1]

PREVENTION/PROPHYLAXIS



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 immune and/or cellular therapies. See Appendix C for more detail and other safety considerations.

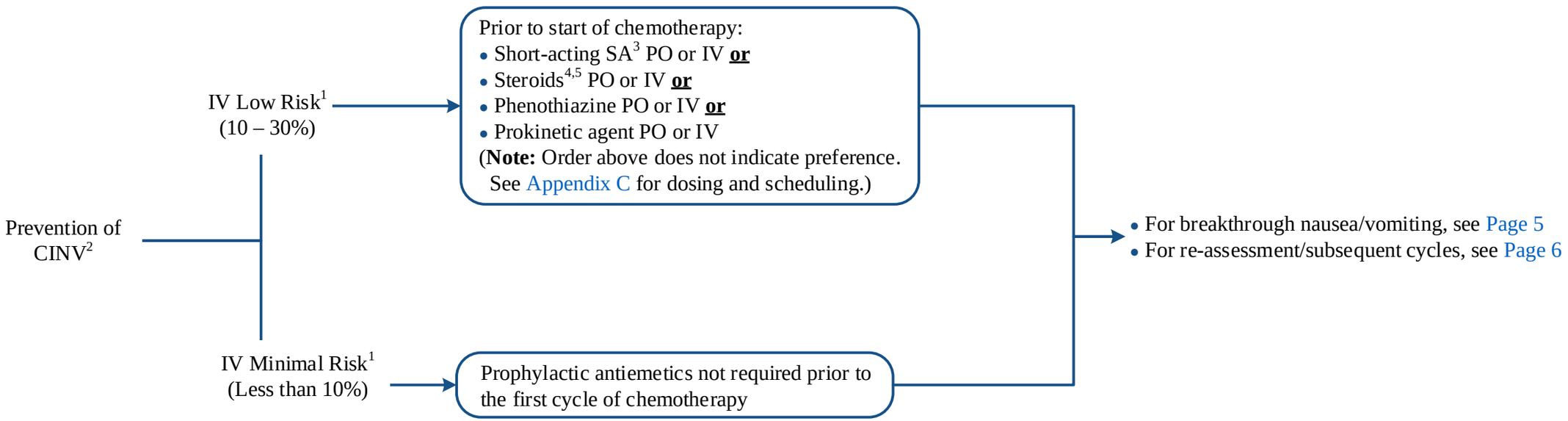
[6] May interact with cytochrome P450 enzyme (CYP enzyme); check for drug interactions – see Appendix C

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 toMD 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 LOW AND MINIMAL EMETOGENIC RISK[1]

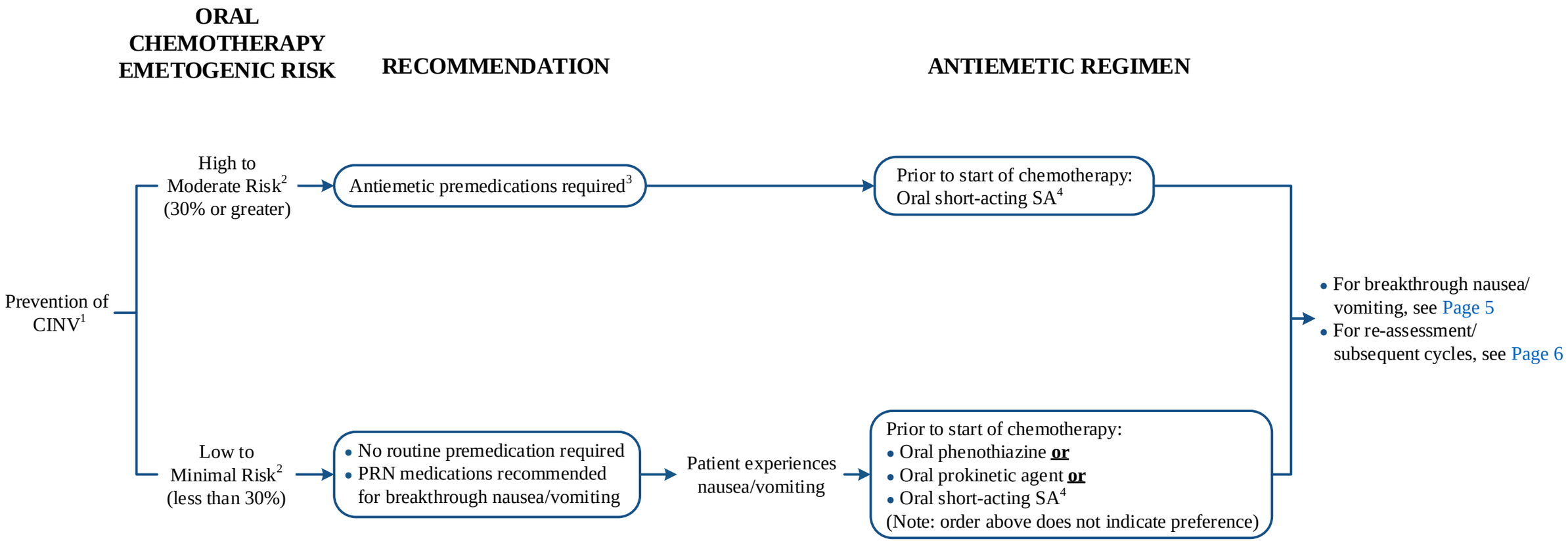
PREVENTION/PROPHYLAXIS



[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 immune and/or cellular therapies. See Appendix C for more detail and other safety considerations.

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 toMD 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.*



[1] Assess need for histamine H_2 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.[1]
[4] All SA are considered therapeutically equivalent when dosed appropriately, see Appendix C (ondansetron preferred)

Adult Antiemetic Management of Chemotherapy-Induced Nausea and Vomiting (CINV)

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 Emergency Center if not improving and/or not able to drink fluids

Patient experiences breakthrough nausea and vomiting

- Patient able to tolerate PO → Choose an oral agent from a class not already given that Day[2,3]:
  a) Phenothiazine **or** prokinetic agent
  b) If persistent nausea, give: short-acting SA, **or** atypical antipsychotic, **or** ABH[4] combination product
  c) Consider adding steroids **and/or** benzodiazepine to other classes for synergy as tolerated
- 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]:
  a) Phenothiazine **or** prokinetic agent (if not already given within 4 hours)
  b) Short-acting SA **or** high-dose prokinetic agent plus diphenhydramine
  c) 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® (lorazepam), Benadryl® (diphenhydramine), Haldol® (haloperidol)

SUBSEQUENT CYCLES OF CHEMOTHERAPY

ASSESSMENT OF PRIOR CHEMOTHERAPY	ANTIEMETIC RESPONSE	SUBSEQUENT CYCLES
For subsequent cycles of the same chemotherapy regimen, re-evaluate effectiveness of antiemetic regimen and side effects of antiemetic premedication	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 • Adding an agent from a different class to the antiemetic regimen (see Appendix C) • 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

Risk Level	Frequency of Emesis (%)	Chemotherapy/Biotherapy Agents	
High	**Greater than 90%**	• AC combination defined as either doxorubicin or epirubicin with cyclophosphamide • Carboplatin[1] (greater than or equal to AUC of 4) • Carmustine (greater than 250 mg/m^2) • Cisplatin[1] • Cyclophosphamide (greater than 1,500 mg/m^2)	• Dacarbazine • Doxorubicin (greater than 50 mg/m^2) • Epirubicin (greater than 90 mg/m^2) • Ifosfamide (high dose: greater than 2 grams/m^2/dose) • Mechlorethamine • Streptozocin
Moderate	**30% to 90%**	• Aldesleukin (greater than or equal to 12 million units/m^2) • Arsenic trioxide • Azacitidine • Bendamustine • Busulfan[1] • Carboplatin[1] (less than AUC of 4) • Carmustine (less than or equal to 250 mg/m^2) • Clofarabine • Cyclophosphamide (less than or equal to 1,500 mg/m^2) • Cytarabine (greater than 200 mg/m^2) • Dactinomycin • Daunorubicin • Dinutuximab	• Doxorubicin (less than or equal to 50 mg/m^2) • Epirubicin (less than or equal to 90 mg/m^2) • Idarubicin • Ifosfamide (less than or equal to 2 grams/m^2/dose) • Interferon alpha (greater than or equal to10 million units/m^2/dose) • Irinotecan • Liposomal irinotecan • Melphalan[1] • Methotrexate (greater than or equal to 250 mg/m^2) • Oxaliplatin[1] • Temozolomide • Trabectedin

[1] Emetogenic risk may vary depending on the dosing, administration and/or concurrently administered chemotherapy

Continued on next page

APPENDIX A Continued: Emetogenic Potential of Parenteral Chemotherapy/Biotherapy – Low and Minimal

Risk Level	Frequency of Emesis (%)	Chemotherapy/Biotherapy Agents
Low	**10% to 30%**	• Ado-trastuzumab emtansine • Aldesleukin (less than 12 million units/m^2/dose) • Altretamine • Belinostat • Brentuximab Vedotin • Cabazitaxel • Carfilzomib • Copanlisib • Cytarabine (low dose:100 – 200 mg/m^2) • Docetaxel • Doxorubicin (liposomal) • Eribulin • Etoposide • Floxuridine • 5-Fluorouracil • Gemcitabine • Interferon Alfa (greater than 5 million but less than 10 million units/m^2/dose) • Ixabepilone • Methotrexate (greater than 50 mg/m^2 but less than 250 mg/m^2) • Mitomycin • Mitoxantrone • Necitumumab* • Omacetaxine • Paclitaxel • Paclitaxel-albumin • Pemetrexed • Pentostatin • Pralatrexate • Romidepsin • Talimogene laherparevec • Thiotepa • Topotecan
Minimal	**Less than 10%**	• Aflibercept (IV agent) • Alemtuzumab • Asparaginase • Atezolizumab[1] • Avelumab*[1] • Axicabtagene ciloleucel (CAR-T)[1] • Bevacizumab • Bleomycin • Blinatumomab • Bortezomib • Cemiplimab-rwlc* • Cetuximab • Cladribine • Cytarabine less than 100 mg/m^2 • Daratumumab • Decitabine • Denileukin diftitox • Durvalumab[1] • Elotuzumab • Fludarabine • Inotuzumab ozogamicin • Interferon Alfa (less than or equal to 5 million units/m^2/dose) • Ipilimumab[1] • Liposomal vincristine • Methotrexate (less than or equal to 50 mg/m^2) • Mogamulizumab-kpkc* • Moxetumomab pasudotox-tdfk* • Nelarabine • Nivolumab[1] • Obinutuzumab • Ofatumumab • Panitumumab • Pegasparaginase • Pembrolizumab[1] • Pertuzumab • Ramucirumab • Rituximab • Siltuximab* • Temsirolimus • Tisagenlecleucel (CAR-T)[1] • Trastuzumab • Valrubicin • Vinblastine • Vincristine • Vinorelbine

*Not on MDACC Pharmacy Formulary as of November, 2018

Continued on next page

[1] Immune therapy – use of steroids not recommended; see Appendix C for more details

APPENDIX A Continued: Emetogenic Potential of ORAL Chemotherapy/Biotherapy

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.

Emetogenic Risk	Chemotherapy/Biotherapy Agents
High to Moderate	• Busulfan (greater than or equal to 4 mg/day) • Cyclophosphamide (greater than or equal to 100 mg/m^2/dose) • Etoposide • Lomustine • Midostaurin* • Olaparib • Niraparib* • Procarbazine • Rucaparib • Temozolomide (greater than 75 mg/m^2/dose)
Low to Minimal	• Abemaciclib* • Acalabrutinib • Afatinib • Alectinib • Altretamine • Apalutamide* • Axitinib • Bexarotene • Binimetinib • Bosutinib* • Brigatinib • Busulfan (less than 4 mg/day) • Cabozantinib* • Capecitabine • Ceritinib • Chlorambucil • Cobimetinib* • Crizotinib • Cyclophosphamide (less than 100 mg/m^2/dose) • Dabrafenib • Dacomitinib* • Dasatinib • Duvelisib* • Enasidenib • Encorafenib • Erlotinib • Estramustine • Everolimus • Fludarabine • Gefitinib • Hydroxyurea • Ibrutinib • Idelalisib* • Imatinib • Ivosidenib* • Ixazomib • Lapatinib • Lenalidomide • Lenvatinib* • Lorlatinib* • Melphalan • Mercaptopurine • Methotrexate • Neratinib maleate* • Nilotinib • Osimertinib • Palbociclib • Panobinostat • Pazopanib • Ponatinib* • Regorafenib • Ribociclib* • Ruxolitinib • Sonidegib* • Sorafenib • Sunitinib • Telazoparib* • Temozolomide (less than or equal to 75 mg/m^2/dose) • Thalidomide • Thioguanine • Topotecan • Trametinib • Trifluridine-tipiracil • Tretinoin • Vandetanib • Vemurafenib • Venetoclax • Vismodegib • Vorinostat

*Not on MDACC Pharmacy Formulary as of November, 2018

APPENDIX B: Antiemetic Regimens for Prevention of Acute and Delayed CINV

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

- Olanzapine[1] 10 mg PO daily on Days 1 – 4

Choose one from **each** category below:

- Serotonin antagonist[2]
  - Granisetron 1 mg IV
  - Ondansetron 8 – 16 mg IV
  - Palonosetron 0.25 mg IV
- Steroids
  - Dexamethasone[3,4] 12 mg IV on Day 1; then 8 mg PO once daily on Days 2 – 3
- Neurokinin-1 antagonist[5]
  - 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)

Continued on next page

[1] Olanzapine 5 mg not as effective, but maybe practical if 10 mg not tolerated
[2] All SAs are considered therapeutically equivalent when dosed appropriately, see Appendix C (ondansetron preferred)
[3] 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.
[4] Use of steroids is not recommended with immune and/or cellular therapies. See Appendix C for other safety considerations.
[5] 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 from previous page

Olanzapine/SA/Steroids - HEC or MEC, single day ONLY

- Olanzapine[1] 10 mg PO daily on Days 1 – 4

Choose one from **each** category below:

- Serotonin antagonist[2]
  - Granisetron 1 mg IV
  - Ondansetron 8 – 16 mg IV
  - Palonosetron 0.25 mg IV
- Steroids
  - Dexamethasone[3,4] 20 mg IV on Day 1; then 8 mg PO twice a day on Days 2 – 3

- 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)

Continued on next page

[1] Olanzapine 5 mg not as effective, but maybe practical if 10 mg not tolerated
[2] All SAs are considered therapeutically equivalent when dosed appropriately, see Appendix C (ondansetron preferred)
[3] 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.
[4] Use of steroids is not recommended with immune and/or cellular therapies. See Appendix C for other safety considerations.

APPENDIX B: Antiemetic Regimens for Prevention of Acute and Delayed CINV – continued from previous page

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

Choose one from **each** category below:

- Serotonin antagonist[1]
  - 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[2,3]
    - If aprepitant/fosaprepitant: dexamethasone 12 mg IV on day 1; then 8 mg PO daily on Days 2 – 3
    - If rolapitant: dexamethasone 20 mg IV on Day 1; then 8 mg PO twice a day on Days 2 – 3
  - For non-cisplatin containing regimens consider steroid sparing options after completion of chemotherapy
- Neurokinin-1 antagonist
  - Aprepitant[4] 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[4]
    - 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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[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 immune and/or cellular therapies. 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 from previous page

SA/Steroids: MEC ONLY, single or multi-day

Choose one from **each** category below:

- Serotonin antagonist[1]
  - 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[2,3] 20 mg IV on Day 1; then 8 mg PO twice a day on Days 2 – 3
  - For some non-cisplatin containing regimens consider steroid sparing options after completion of chemotherapy

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- 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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[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 immune and/or cellular therapies. See Appendix C for other safety considerations.

APPENDIX C: Antiemetic Medication Options

Medication	Adult Dosage	Comments
Anxiolytics		
Alprazolam (Xanax®) Lorazepam (Ativan®)	0.5 – 2 mg PO every 6 hours 0.5 – 2 mg PO, SL or IV every 6 hours	• **Indication:** anticipatory CINV (drug class of choice) • **Class adverse effects[1]:** sedation, dizziness, disorientation, hypotension, amnesia • Lorazepam SL is administered using the oral concentrate formulation • Exert caution when using in the elderly, as they may be more sensitive to the side effects (see Beers Criteria[2] for more information)
Atypical Antipsychotics		
Olanzapine (Zyprexa®)	Prevention: 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) • Olanzapine 5 mg not as effective, but maybe practical if 10 mg not tolerated • **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[2] for more information)

Continued on next page

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

[2] American Geriatrics Society 2015 Beers Criteria Update Expert Panel, Fick, D. M., Semla, T. P., Beizer, J., Brandt, N., Dombrowski, R., . . . Giovannetti, E. (2015). American Geriatrics Society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society, 63*(11), 2227-2246.

[3] For QTc prolongation information, see www.Crediblemeds.org

APPENDIX C: Antiemetic Medication Options – continued from previous page

Medication	Adult Dosage	Comments
Butyrophenones		
Haloperidol (Haldol®)	0.5 – 2 mg IV every 6 hours (see also ABH on Page 19)	• **Indication:** treatment of breakthrough CINV • **Adverse effects[1]:** sedation, tachycardia, hypotension, restlessness, extrapyramidal symptoms (may co-administer with benzodiazepine or antihistamine to avoid this) • **QTc prolongation[2]:** 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[3] for more information)
Cannabinoids		
Dronabinol (Marinol®) Nabilone (Cesamet®)*	2.5 – 10 mg PO either every 3 hours or every 6 hours 1 – 2 mg PO twice a day	• **Indication:** prophylaxis for acute and delayed CINV refractory to other antiemetics • **Adverse effects[1]:** dizziness, somnolence, sleep disturbances, confusion, hallucinations • Avoid abrupt discontinuation of therapy which may precipitate withdrawal

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[1] Adverse effects are not all inclusive, refer to package insert
[2] For QTc prolongation information, see www.Crediblemeds.org
[3] American Geriatrics Society 2015 Beers Criteria Update Expert Panel, Fick, D. M., Semla, T. P., Beizer, J., Brandt, N., Dombrowski, R., . . . Giovannetti, E. (2015). American Geriatrics Society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society, 63*(11), 2227-2246.

APPENDIX C: Antiemetic Medication Options – continued from previous page

Medication	Adult Dosage		Comments
Neurokinin-1 Antagonists	ACUTE (before)	DELAYED	
Aprepitant (Emend®)	125 mg PO	80 mg PO daily for 2 days	• **Indication:** prophylaxis of acute and delayed CINV (with SA plus dexamethasone) • **Class adverse effects**[1]: hiccups, fatigue, dizziness, diarrhea • Decrease dexamethasone dose by 50% with concomitant use (same day) of aprepitant and fosaprepitant • Drug interactions due to CYP3A4 inhibition for aprepitant and fosaprepitant; CYP2D6 with rolapitant • Rolapitant has only been studied with single-day chemotherapy regimens
Fosaprepitant (Emend® IV)	115 mg IV 150 mg IV	Aprepitant 80 mg PO daily for 2 days None recommended (Note: See dosing with dexamethasone)	
Rolapitant (Varubi®)*	180 mg PO	None recommended	
Non-Phenothiazine Antihistamines			
Diphenhydramine (Benadryl®)	12.5 – 50 mg PO or IV every 6 hours (may dose every 4 hours)		• **Indication:** co-administered with other antiemetics to manage toxicity • **Adverse effects**[1]**:** sedation, dry mouth, blurred vision, agitation, paradoxical reactions (excitement) • Exert caution when using in the elderly, as they may be more sensitive to the side effects (see Beers Criteria[2] for more information)

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

[2] American Geriatrics Society 2015 Beers Criteria Update Expert Panel, Fick, D. M., Semla, T. P., Beizer, J., Brandt, N., Dombrowski, R., . . . Giovannetti, E. (2015). American Geriatrics Society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society*, *63*(11), 2227-2246.

APPENDIX C: Antiemetic Medication Options – continued from previous page

Medication	Adult Dosage	Comments
Phenothiazine Antihistamines		
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[1]:** sedation, dry mouth, extrapyramidal symptoms constipation, blurred vision • **QTc prolongation[2]:** 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[3] 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 (MDACC compounded product)	
Prokinetic Agents		
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[1]:** 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[2]:** 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[3] for more information)

[1] Adverse effects are not all inclusive, refer to package insert
[2] For QTc prolongation information, see www.Crediblemeds.org
[3] American Geriatrics Society 2015 Beers Criteria Update Expert Panel, Fick, D. M., Semla, T. P., Beizer, J., Brandt, N., Dombrowski, R., . . . Giovannetti, E. (2015). American Geriatrics Society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society*, *63*(11), 2227-2246.

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Adult Antiemetic Management of Chemotherapy-Induced Nausea and Vomiting (CINV)

APPENDIX C: Antiemetic Medication Options – continued from previous page

Medication	Adult Dosage		Comments
Serotonin Antagonists (SA)	ACUTE (before)	DELAYED	
Dolasetron (Anzemet®)*	100 – 200 mg PO	100 mg PO daily	• **Indication:** prophylaxis of acute and delayed CINV • Dolasetron available as oral tablet only. IV use is not recommended by FDA. • Apply granisetron patch 24 - 48 hours prior to chemotherapy administration • FDA has amended the product information of ondansetron to limit single intravenous doses to 16 mg • Palonosetron: phase III clinical trials did not allow repeat dosing for 7 days. The optimal timing of repeat doses of palonosetron is currently unknown. • **Class adverse effects[1]:** headache, constipation, fatigue • **QTc prolongation[2]:** Increased risk of QTc prolongation has been observed with IV formulations of ondansetron, dolasetron, and granisetron ◦ 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 ◦ 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 • **Short-acting SAs include:** ◦ Dolasetron (all formulations) ◦ Granisetron (IV/PO formulations) ◦ Ondansetron (all formulations)
Granisetron Kytril® – IV/PO	1 – 2 mg PO **or** 1 mg IV	2 mg PO daily **or** 1 mg PO twice a day	
Sancuso® – patch**	3.1 mg/24 hours patch (total dose delivered 34.3 mg/7 days)	Not Applicable	
Ondansetron (Zofran®) (preferred agent) Oral disintegrating tablet, tablet, oral solution, IV	8 – 24 mg PO **or** 8 – 16 mg IV	8 mg PO twice a day **or** 16 mg PO daily **or** 8 mg IV twice a day	
Palonosetron (Aloxi®)	0.25 mg IV	None recommended	

*Not on MDACC Pharmacy Formulary as of November, 2018
** Restricted drug on MDACC Pharmacy Formulary as of November, 2018

[1]Adverse effects are not all inclusive, refer to package insert.
[2] For QTc prolongation information, see www.Crediblemeds.org

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APPENDIX C: Antiemetic Medication Options – continued from previous page

Medication	Adult Dosage		Comments
Steroids	**ACUTE (before)**	**DELAYED**	
Dexamethasone (Decadron®)	Day 1: 10 – 20 mg PO or IV	Days 2 – 4 (or longer): 4 – 8 mg PO or IV twice daily	• **Indication:** prophylaxis of acute and delayed CINV • When administered with aprepitant/fosaprepitant, dexamethasone dose should be decreased to 12 mg instead of 20 mg • Caution in patients with hematologic malignancies[1] • Use of steroids is not recommended with immune and/or cellular therapies[2]. A steroid sparing prophylactic antiemetic regimen is preferred when: ◦ Immune checkpoint inhibitors are administered alone, as these are low emetogenic risk and alternative antiemetics should be considered ◦ Immune checkpoint inhibitors are administered concurrently with moderate-high emetogenic risk chemotherapy due to potential for negative impact on cancer outcomes ◦ 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. • **Class adverse effects[3]:** hyperglycemia, insomnia, hiccups, dyspepsia, agitation, weight gain, hypertension ◦ Increased risk of infection with prolonged use greater than 2 weeks
Dexamethasone with either aprepitant 125 mg PO **or** fosaprepitant 115 mg IV	12 mg PO or IV	8 mg PO daily for 3 days	
Dexamethasone with fosaprepitant 150 mg IV	12 mg PO or IV	Day 2: 8 mg PO daily Days 3 - 4: 8 mg PO twice daily	

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[1] 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

[2] Use of steroids is not recommended with immune and/or cellular therapies

[3] Adverse effects are not all inclusive, refer to package insert

APPENDIX C: Antiemetic Medication Options – continued from previous page

Medication	Adult Dosage	Comments
Combination Products (capsules and suppositories[1] compounded at MDACC Pharmacy)		
ABH capsules: • Lorazepam 0.34 mg • Diphenhydramine 25 mg • Haloperidol 1.5 mg	1 capsule PO every 6 hours	• **Indication:** treatment of breakthrough CINV; prophylaxis of delayed CINV (refractory to other antiemetics) • Adverse effects as per individual agents • Additive amounts are not equal between the routes of administration due to absorption variances • **QTc prolongation[2]:** known risk of TdP - medication causes QT interval prolongation and is clearly associated with a risk of TdP (haloperidol) • Exert caution when using in the elderly, as they may be more sensitive to the side effects (see Beers Criteria[3] for more information)
ABH suppositories[1]: • Lorazepam 1 mg • Diphenhydramine 12.5 mg • Haloperidol 2 mg	1 suppository[1] PR every 6 hours	
ABH IV: • Lorazepam 0.5 mg • Diphenhydramine 12.5 – 25 mg • Haloperidol 0.5 – 1 mg	Given as combination IV every 6 hours (need to order each agent separately)	

[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] For QTc prolongation information, see www.Crediblemeds.org

[3] American Geriatrics Society 2015 Beers Criteria Update Expert Panel, Fick, D. M., Semla, T. P., Beizer, J., Brandt, N., Dombrowski, R., . . . Giovannetti, E. (2015). American Geriatrics Society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society*, *63*(11), 2227-2246.

SUGGESTED READINGS

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