

Adult Guidelines for Assessment and Management of Nausea and Vomiting

To Prevent and Manage Nausea and Vomiting
Induced by Anticancer Agents Or
Related to Other Oncologic Etiologies

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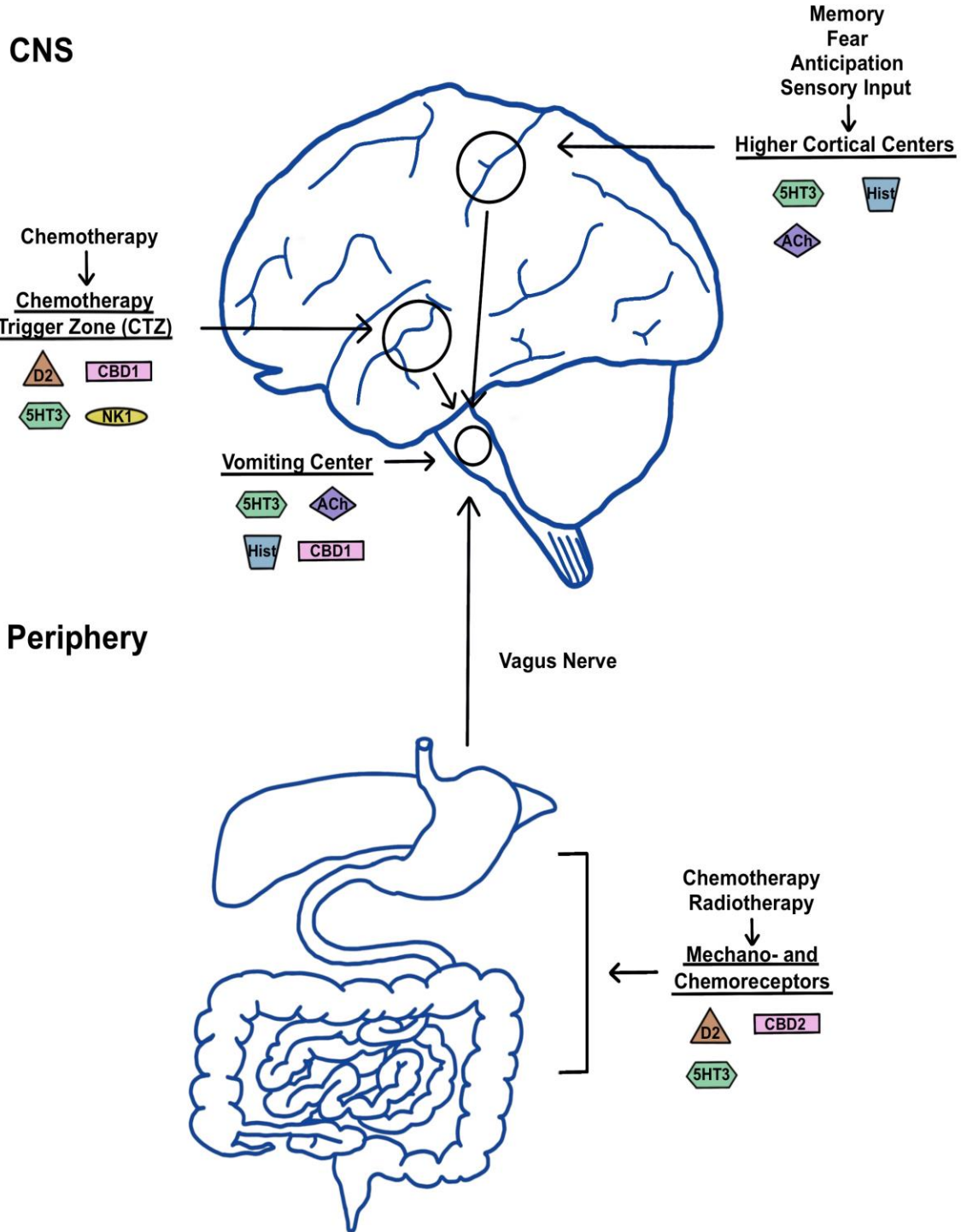
Dana-Farber Cancer Institute/Brigham and Women's Hospital Adult Guidelines for assessment and management of nausea and vomiting (Green Book) provides educational information for healthcare professionals at Dana-Farber and Brigham and Women's Hospital. This information is not medical advice. The Green Book is not continually updated, and new safety information may emerge after the most recent publication date. Health care providers should always exercise their own independent clinical judgment and consult other relevant and up-to-date experts and resources. Official prescribing information should be consulted before any product is used or recommendation made.

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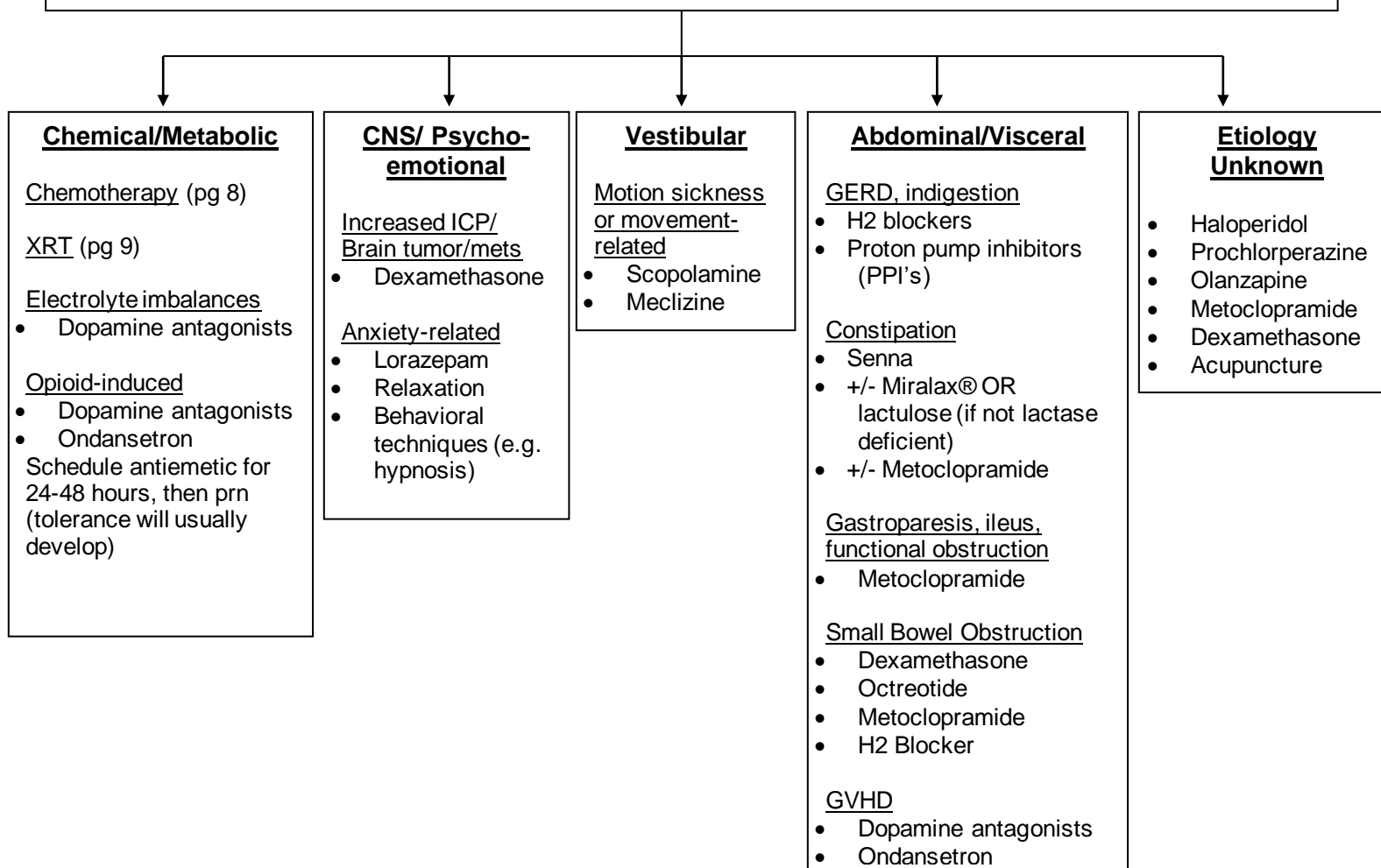
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Pathophysiology of Nausea and Vomiting

5HT3 = serotonin receptor
 D2 = dopamine-2 receptor
 Hist = histamine receptor
ACh = acetylcholine receptor
 NK1 = neurokinin-1 receptor
CBD 1,2 = cannabinoid-1,2



Possible Etiologies and Suggested Treatment for Nausea and Vomiting



Patient Assessment for Nausea and Vomiting

History: past antiemetics use/effects.

Nausea intensity (0-10), duration, description.

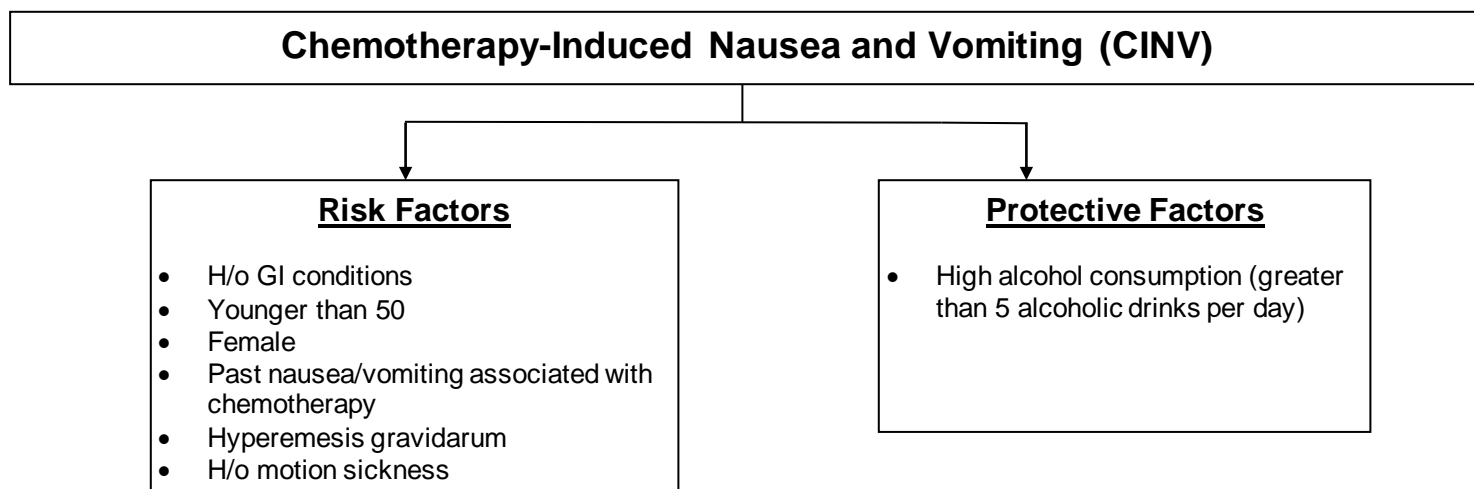
Aggravating or activating factors (thought/smell of food, eating, drinking, not eating, medications, movement, time of day).

Quality of life disturbances resulting from nausea and vomiting.

Symptoms associated with nausea/vomiting: Dizziness, fatigue, anxiety/depression, sweating, pain, constipation/diarrhea.

Emetic episodes per 24 hours.

Alleviating factors: Distraction, lying down, medication, food, vomiting, time.



CINV Related Definitions

Acute chemotherapy induced nausea and vomiting usually begins within minutes to hours after chemotherapy and lasts up to 24 hours.

Delayed nausea and vomiting develops more than 24 hours after chemotherapy and may last several days.

Anticipatory nausea and vomiting begins before chemotherapy, and is often associated with poorly controlled acute and delayed nausea and vomiting.

Breakthrough nausea and vomiting occurs despite preventive therapy and is treated with an as needed regimen.

Refractory nausea and vomiting occurs when antiemetic prophylaxis and/or rescue have failed. See page 14 for therapy considerations.

Classification of anticancer agent emetogenicity

Emetogenicity is based on the percentage of patients who experience emesis in the absence of effective antiemetic prophylaxis.

Chemotherapy/biotherapy

All anticancer agents used to treat cancer, given through oral and parenteral routes or other routes as specified as the standard. Types include targeted agents, cytotoxic agents, immunotherapies, and biologics, when used for the purpose of treating malignancy or similar proliferative diseases, or as conditioning for cellular therapies.

General Concepts in the Management of CINV

Goal: To prevent nausea/vomiting in patients receiving anticancer agents.

Antiemetic selection:

- Selection of an appropriate antiemetic regimen should be based on the emetic risk of anticancer agents, prior experience with antiemetics, and patient-specific risk factors (see page 5).
- The emetic risk for biosimilars is expected to be the same as the parent compound.
- The health literacy of the patient must also be considered, including sociocultural differences, language, and literacy barriers and addressed with effective provider-patient communication. Resources such as printed calendars and interpreter services can help address communication barriers.

Route of administration:

- Oral and intravenous antiemetic formulations have equivalent efficacy when used at appropriate doses.
- Continuous infusion of chemotherapy may make an agent less emetogenic.

Anticipatory, anxiety-related nausea and vomiting: May respond to prophylactic use of anti-anxiety agents (e.g. lorazepam by mouth the night before treatment and the next day 1–2 hours before anticancer therapy begins) and behavioral interventions (eg. meditation, relaxation, hypnosis) along with aggressive control of acute and delayed nausea/vomiting and avoiding smells that may precipitate symptoms.

Delayed nausea: For regimens that are frequently associated with delayed nausea/vomiting, treat patient with **scheduled** oral antiemetics that include dexamethasone. Olanzapine may also be considered. Carboplatin, cisplatin, oxaliplatin, cyclophosphamide, and doxorubicin are frequently associated with delayed nausea and vomiting.

Other etiologies: Other possible etiologies of nausea/vomiting should be addressed and properly managed (e.g. use of H₂ blockers or proton pump inhibitors* for management of dyspepsia which may mimic nausea).

*Caution: potential drug interactions with TKIs

Combination antiemetic treatment: Has been shown to improve the efficacy of the primary antiemetic. However, **do not** use two agents from the same class of antiemetics in combination (e.g. metoclopramide and prochlorperazine); this can significantly increase the side effects and does not increase efficacy (see pages 15&16). Olanzapine should be used with caution in combination with other dopamine antagonists and other CNS depressants.

Emetogenic Potential of Intravenous Anticancer Agents

<p>High emetic risk (> 90% frequency of emesis):</p>	<ul style="list-style-type: none"> ▪ AC combination (any regimen w/ an anthracycline and cyclophosphamide) ▪ Carboplatin AUC ≥ 4 ▪ Carmustine > 250 mg/m² ▪ Cisplatin ▪ Cyclophosphamide > 1,500 mg/m² ▪ Dacarbazine ▪ Doxorubicin ≥ 60 mg/m² 	<ul style="list-style-type: none"> ▪ Epirubicin > 90 mg/m² ▪ Fam-trastuzumab deruxtecan-nxki ▪ Ifosfamide $\geq 2,000$ mg/m² per dose ▪ Mechlorethamine ▪ Melphalan ≥ 140 mg/m² ▪ Sacituzumab govitecan-hziy ▪ Streptozocin
<p>Moderate emetic risk (30-90% frequency of emesis):</p>	<ul style="list-style-type: none"> ▪ Aldesleukin > 12-15 million international units/m² ▪ Amifostine > 300 mg/m² ▪ Bendamustine ▪ Busulfan ▪ Carboplatin AUC < 4 ▪ Carmustine ≤ 250 mg/m² ▪ Clofarabine ▪ Cyclophosphamide $\leq 1,500$ mg/m² ▪ Cytarabine > 200 mg/m² ▪ Dactinomycin ▪ Daunorubicin ▪ Dual-drug liposomal encapsulation of cytarabine and daunorubicin ▪ Dinutuximab ▪ Doxorubicin < 60 mg/m² 	<ul style="list-style-type: none"> ▪ Dual-drug liposomal encapsulation of cytarabine and daunorubicin ▪ Epirubicin ≤ 90 mg/m² ▪ Idarubicin ▪ Ifosfamide < 2,000 mg/m² per dose ▪ Irinotecan ▪ Irinotecan liposomal ▪ Lurbinectedin ▪ Melphalan < 140 mg/m² ▪ Methotrexate ≥ 250 mg/m² ▪ Mirvetuximab soravtansine-gynx⁺ ▪ Naxitamab-gqgk ▪ Oxaliplatin ▪ Romidepsin ▪ Temozolomide ▪ Trabectedin
<p>Low emetic risk (10-30% frequency of emesis):</p>	<ul style="list-style-type: none"> ▪ Ado-trastuzumab emtansine ▪ Aldesleukin ≤ 12 million IU/m² ▪ Amifostine ≤ 300 mg/m² ▪ Amivantamab-vmjw ▪ Arsenic trioxide ▪ Axicabtagene ciloleucel ▪ Azacitidine ▪ Belinostat ▪ Brentuximab vedotin ▪ Brexucabtagene autoleucel ▪ Cabazitaxel ▪ Carfilzomib ▪ Ciltacabtagene autoleucel ▪ Copanlisib ▪ Cytarabine 100-200 mg/m² ▪ Docetaxel ▪ Doxorubicin liposomal ▪ Enfortumab vedotin-ejfv ▪ Eribulin ▪ Etoposide ▪ 5-fluorouracil ▪ Floxuridine ▪ Gemcitabine ▪ Gemtuzumab ozogamicin ▪ Idecabtagene vicleucel ▪ Inotuzumab ozogamicin ▪ Isatuximab-irfc 	<ul style="list-style-type: none"> ▪ Ixabepilone ▪ Lisocabtagene maraleucel ▪ Loncastuximab tesirine-lpyl ▪ Methotrexate > 50 – <250 mg/m² ▪ Mitomycin ▪ Mitomycin pyelocalyceal solution ▪ Mitoxantrone ▪ Mogamulizumab-kpkc ▪ Mosunetuzumab-axgb⁺ ▪ Moxetumomab pasudotox-tdfk ▪ Necitumumab ▪ Omacetaxine ▪ Paclitaxel ▪ Paclitaxel, albumin bound ▪ Pemetrexed ▪ Pentostatin ▪ Polatuzumab vedotin-piig ▪ Pralatrexate ▪ Tafasitamab-cxix ▪ Tagraxofusp-erzs ▪ Talimogene laherparepvec ▪ Tebentafusp-tebn ▪ Thiotepe ▪ Tisagenlecleucel ▪ Tisotumab vedotin-tftv ▪ Topotecan ▪ Ziv-aflibercept

<p>Minimal emetic risk (< 10% frequency of emesis):</p>	<ul style="list-style-type: none"> ▪ Alemtuzumab ▪ Asparaginase* ▪ Atezolizumab ▪ Avelumab ▪ Belantamab mafodotin-blmf ▪ Bevacizumab ▪ Bleomycin ▪ Blinatumomab ▪ Bortezomib ▪ Cemiplimab-rwlc ▪ Cetuximab ▪ Cladribine (2-chlorodeoxyadenosine) ▪ Cytarabine < 100 mg/m² ▪ Daratumumab ▪ Daratumumab and hyaluronidase-fihj ▪ Decitabine ▪ Dexrazoxane ▪ Dostarlimab-gxly ▪ Durvalumab ▪ Elotuzumab ▪ Fludarabine ▪ Ipilimumab ▪ Luspatercept-aamt ▪ Margetuximab-cmkb ▪ Methotrexate ≤ 50 mg/m² ▪ Nelarabine 	<ul style="list-style-type: none"> ▪ Nivolumab ▪ Nivolumab/relatlimab-rmbw ▪ Obinutuzumab ▪ Ofatumumab ▪ Panitumumab ▪ Pembrolizumab ▪ Pertuzumab ▪ Pertuzumab/trastuzumab and hyaluronidase-zzxf ▪ Ramucirumab ▪ Rituximab ▪ Rituximab and hyaluronidase ▪ Siltuximab ▪ Sirolimus-albumin ▪ Teclistamab-cqyv ▪ Temsirolimus ▪ Trastuzumab ▪ Trastuzumab and hyaluronidase-osyk ▪ Tremelimumab-actl ▪ Valrubicin ▪ Vinblastine ▪ Vincristine ▪ Vincristine (liposomal) ▪ Vinorelbine
<p>* Asparaginase includes pegasparaginase, asparaginase erwinia chrysanthemi, and asparaginase erwinia chrysanthemi (recombinant)-rywm. + FDA approved post 2023 NCCN Guideline Update</p>		

Adapted from NCCN Clinical Practice Guidelines in Oncology. V.1.2023. Antiemesis.

Emetogenic Potential of Oral Anticancer Agents

<p>Moderate-high emetic risk (≥30% frequency of emesis): <i>Required prophylaxis on days of oral anticancer agent administration</i></p>	<ul style="list-style-type: none"> ▪ Azacitidine ▪ Busulfan ≥ 4 mg/day ▪ Ceritinib ▪ Cyclophosphamide ≥ 100 mg/m²/day ▪ Fedratinib 	<ul style="list-style-type: none"> ▪ Lomustine (single day) ▪ Midostaurin ▪ Mitotane ▪ Mobocertinib ▪ Selinexor ▪ Temozolomide > 75 mg/m²/day
<p>Moderate-high emetic risk (≥30% frequency of emesis): <i>As needed (PRN) dosing is initially appropriate on days of oral anticancer agent administration</i></p>	<ul style="list-style-type: none"> ▪ Adagrasib⁺ ▪ Avapritinib ▪ Binimetinib ▪ Bosutinib > 400 mg/day ▪ Cabozantinib ▪ Crizotinib ▪ Dabrafenib ▪ Enasidenib ▪ Encorafenib 	<ul style="list-style-type: none"> ▪ Estramustine ▪ Etoposide ▪ Imatinib >400 mg/day ▪ Lenvatinib >12 mg/day ▪ Niraparib ▪ Olaparib ▪ Procarbazine ▪ Rucaparib
<p>Minimal-low emetic risk (<30% frequency of emesis):</p>	<ul style="list-style-type: none"> ▪ Abemaciclib ▪ Acalabrutinib ▪ Afatinib ▪ Alectinib ▪ Alpelisib ▪ Asciminib ▪ Axitinib ▪ Belzutifan ▪ Bexarotene ▪ Bosutinib ≤ 400 mg/day ▪ Brigatinib ▪ Busulfan < 4 mg/day ▪ Capecitabine ▪ Capmatinib ▪ Chlorambucil ▪ Cobimetinib ▪ Cyclophosphamide < 100 mg/m²/day ▪ Dacomitinib ▪ Dasatinib ▪ Dabrafenib ▪ Decitabine and cedazuridine ▪ Duvelisib ▪ Elacestrant⁺ ▪ Entrectinib ▪ Erdafitinib ▪ Erlotinib ▪ Everolimus ▪ Fludarabine ▪ Futibatinib ▪ Gefitinib ▪ Gilteritinib ▪ Glasdegib ▪ Hydroxyurea ▪ Ibrutinib ▪ Idelalisib ▪ Imatinib ≤ 400 mg/day ▪ Ivosidenib ▪ Ixazomib ▪ Lapatinib ▪ Larotrectinib ▪ Lenalidomide ▪ Lenvatinib ≤12 mg/day ▪ Lorlatinib 	<ul style="list-style-type: none"> ▪ Melphalan ▪ Mercaptopurine ▪ Methotrexate ▪ Neratinib ▪ Nilotinib ▪ Olutasidenib⁺ ▪ Osimertinib ▪ Pacritinib ▪ Palbociclib ▪ Pazopanib ▪ Pemigatinib ▪ Pexidartinib ▪ Pomalidomide ▪ Ponatinib ▪ Pirtobrutinib⁺ ▪ Pralsetinib ▪ Regorafenib ▪ Ribociclib ▪ Ripretinib ▪ Ruxolitinib ▪ Selpercatinib ▪ Sonidegib ▪ Sorafenib ▪ Sotorasib ▪ Sunitinib ▪ Talazoparib tosylate ▪ Tazemetostat ▪ Temozolomide ≤ 75 mg/m²/day ▪ Tepotinib ▪ Thalidomide ▪ Thioguanine ▪ Tivozanib ▪ Topotecan ▪ Trametinib ▪ Tretinoin ▪ Trifluridine/tipiracil ▪ Tucatinib ▪ Vandetanib ▪ Vemurafenib ▪ Venetoclax ▪ Vismodegib ▪ Vorinostat ▪ Zanubrutinib

* FDA approved post 2023 NCCN Guideline Update

Adapted from NCCN Clinical Practice Guidelines in Oncology, V.1.2023, Antiemesis.

Combination Chemotherapy Regimens

- Give agents that are effective for the highest emetogenic risk level of any single agent in the regimen (e.g. cisplatin and etoposide: use agents recommended for cisplatin) with the exception of anthracycline and cyclophosphamide combinations which synergistically lead to high emetogenicity.
- Select combination regimens of moderately emetogenic therapy may be classified as highly emetogenic chemotherapy based on clinical experience. Examples include doxorubicin/cyclophosphamide (AC) for breast cancer, and FOLFIRINOX (fluorouracil, irinotecan, oxaliplatin, leucovorin calcium) for pancreatic cancer.

Consecutive-day Chemotherapy Regimens

- Risk of acute and delayed nausea/vomiting is based on the risk of each agent.
- Antiemetic prophylaxis for a given day should be based on the agent with the highest emetogenicity administered on that day.
- Prophylaxis for delayed nausea/vomiting should continue for 2-3 days after the last dose of high- to moderately emetogenic chemotherapy.

Suggested Antiemetics for Highly Emetogenic Chemotherapy (HEC)

Day 1 (30 minutes prior to chemotherapy)	Days 2-4
<ul style="list-style-type: none"> • NK1 receptor antagonist PO* or IV • 5HT3 receptor antagonist PO or IV • Dexamethasone 12 mg PO or IV • +/- Olanzapine 5-10 mg PO once 	<ul style="list-style-type: none"> • Dexamethasone 8 mg PO daily • +/- Olanzapine 5-10 mg PO daily

Clinical Pearls for Highly Emetogenic Chemotherapy

- In HEC treatment regimens where the HEC is only given on day 1 and not days 8 or 15, the NK1 antagonist is only given on day 1 (e.g. cisplatin/gemcitabine or cisplatin/navelbine).
- For HEC regimens given over consecutive days (e.g. 3-5 days of cisplatin), the NK-1 antagonist is given on day 1. For select NK1 receptor antagonists, a repeat dose may be necessary to cover the delayed CINV period (e.g. day 5 administration of fosaprepitant in a 5-day cisplatin regimen).
- Emerging data suggests dexamethasone doses may be individualized by giving higher, lower, or eliminating dexamethasone on subsequent days. Consider other antiemetics if eliminated. According to the ASCO 2017 Antiemetic Guideline Update, dexamethasone may be omitted in the delayed setting for AC containing chemotherapy regimens.
- In-clinic dexamethasone should be held if patient took sufficient corticosteroid pre-medication at home on the day of chemotherapy.
- Olanzapine may be added to cisplatin and other highly emetogenic chemotherapy regimens especially where nausea is a concern, and has been found to be efficacious at 5 mg.
 - Use caution and strongly consider starting at 5 mg in high-risk patients such as:
 - Patients who are older (≥ 65 years)
 - Patients taking other CNS depressants or are over sedated
 - Patients at risk of orthostatic hypotension
 - Recommend taking at bedtime.
 - If used prophylactically as part of the antiemetic regimen, olanzapine may be used once daily (prior to chemotherapy or at bedtime) and continued for 2–3 days after chemotherapy for regimens that are likely to cause significant delayed emesis.
- In selected HEC and MEC regimens, ondansetron may be replaced with palonosetron 0.25 mg IV prior to chemotherapy. This requires the discontinuation of all other 5HT3 antagonists, including those taken at home, for 48 hours after palonosetron is administered.
- Consider H2 blocker or PPI if patient exhibits reflux symptoms.
- *If oral aprepitant is used on day 1, course must be completed with doses on days 2-3.

Suggested Antiemetics for Moderately Emetogenic Chemotherapy (MEC)

Day 1 (30 minutes prior to chemotherapy)	Days 2-3
<ul style="list-style-type: none"> • 5HT3 receptor antagonist PO or IV 	Dexamethasone 8 mg PO daily
<ul style="list-style-type: none"> • Dexamethasone 12 mg PO or IV 	
<ul style="list-style-type: none"> • +/- NK1 receptor antagonist 	

Clinical Pearls for Moderately Emetogenic Chemotherapy

- Dexamethasone may be omitted in the delayed setting for regimens in which delayed CINV is not common.
- In-clinic dexamethasone should be held if patient took sufficient corticosteroid pre-medication at home on the day of chemotherapy.
- NK1 receptor antagonist may be added for prevention of nausea and vomiting from moderately emetogenic chemotherapy regimens in patients with refractory nausea and vomiting from previous regimens/cycles or other risk factors (see page 5).
- In selected MEC and HEC regimens, ondansetron may be replaced with palonosetron 0.25 mg IV prior to chemotherapy. This requires the discontinuation of all other 5HT3 antagonists, including those taken at home, for 48 hours after palonosetron is administered.
- Consider H2 blocker or PPI if patient exhibits reflux symptoms.

Suggested Antiemetics for Low Emetogenic Chemotherapy

Prophylaxis may consist of one dose before treatment of any ONE of the following:

- Dexamethasone 8-12 mg PO or IV
- Ondansetron 8-16 mg PO
- Metoclopramide 10-20 mg PO or IV
- Prochlorperazine 10 mg PO or IV

Suggested Antiemetics for Minimally Emetogenic Chemotherapy

Routine prophylaxis is not necessary for minimally emetogenic chemotherapy.

Suggested Antiemetics for Oral Chemotherapy

- Ondansetron 8 – 16 mg daily is recommended for highly and moderately emetogenic **ORAL** anticancer agents requiring daily CINV prophylaxis. Start prior to anticancer therapy.
- As needed (PRN) use is recommended for low to minimally emetogenic **ORAL** anticancer agents.

Suggested Modifications for Specific Circumstances

- Chimeric antigen receptor (CAR) T-cell therapy: avoid corticosteroid antiemetic premedication for 3–5 days prior to and 90 days after CAR T-cell therapies. *Corticosteroids may be resumed if needed upon progression of disease.*
- Lymphodepleting chemotherapy: employ a corticosteroid-sparing approach to antiemetic prophylaxis

Suggested Antiemetics for Radiation-Induced Emesis

Emetic risk*	Radiation field	Recommended prophylaxis
High (>90%)	Total-body irradiation	Ondansetron 8-24 mg/day +/- corticosteroid prior to each fraction (eg. dexamethasone 4 mg daily)
Moderate (30-90%)	Upper abdomen, craniospinal irradiation	Ondansetron 8-16 mg/day +/- corticosteroid prior to each fraction
Low (10-30%)	Brain, head and neck, thorax, pelvis	No routine prophylaxis recommended
Minimal (<10%)	Extremities, Breast	No routine prophylaxis recommended
*Combination radiation with chemotherapy antiemetic prophylaxis is based upon the modality (radiation or chemotherapy) with the highest emetic risk.		

Refractory Chemotherapy-Induced Nausea and Vomiting

If initial therapy is ineffective:

1. Reevaluate for additional cause(s) (see page 4).
2. Increase dose of selected agent(s) (see pages 15&16).
3. Ensure patient's antiemetic regimen includes both scheduled and as needed agents.
4. Consider adding an additional agent or rotating to a different drug in the same class.
 - Additional agents to consider include (see chart on pages 15&16):
 - Corticosteroid
 - Ondansetron (If the patient has not received palonosetron within the last 48-72 hours)
 - NK1 receptor antagonist (only if patient receiving a corticosteroid and 5HT3 receptor antagonist).
 - NK1 receptor antagonists should not be used to treat ongoing nausea and vomiting rather used in the prophylactic setting on subsequent cycles of chemotherapy. Additional doses post-chemotherapy have not been shown to be efficacious.
 - Olanzapine (use caution in combination with dopamine antagonists due to similar MOA; consider discontinuation of prochlorperazine, metoclopramide or haloperidol)
 - Rotate to a different dopamine antagonist (e.g. haloperidol, metoclopramide)
 - In refractory setting, palonosetron may be substituted for ondansetron.
 - Consider H2 blocker or PPI if patient exhibits reflux symptoms.
 - Cannabinoids – dronabinol (Marinol, Syndros), nabilone (Cesamet).

Note: excessive non-pharmaceutical cannabinoid use can lead to cannabinoid hyperemesis. Please assess patient's medical cannabis use.

Classes of Commonly Used Antiemetics		
	<u>Dose/Routes</u>	<u>Side effects/Management</u>
Serotonin Antagonists		
Ondansetron [‡] (Zofran®)	8-24 mg IV/PO/day MAX single IV dose is 16 mg	Constipation (provide prophylactic bowel management) QT prolongation
Palonosetron [‡] (Aloxi®)	0.25 mg IV x 1 (may repeat in 48-72 hours with multi-day chemo regimens)	
Granisetron [‡] (Kytril®)	10 mcg/kg IV (MAX 1 mg IV) OR 2mg PO once OR 10 mg SQ once OR 3.1 mg/24-h transdermal patch applied 24-48 h prior to first dose of anticancer therapy	
Dolasetron [‡] (Anzemet®)	100 mg PO daily	
Substance P (NK1) Antagonists		
Aprepitant (Emend®)	125 mg PO day 1 80 mg PO days 2-3	Infusion site reactions; IV contains polysorbate 80 = risk of HSR ↑ dexamethasone levels ↓ warfarin levels (monitor INR closely)
Fosaprepitant (Emend IV®)	150 mg IV on day 1	
Aprepitant injectable emulsion (Cinvanti®)	130 mg IV day 1 (highly emetogenic) 110 mg IV day 1 (moderately emetogenic)	Does not contain polysorbate 80 110 mg dose to be followed day aprepitant 80 mg on days 2, 3
Netupitant/palonosetron (Akynzeo®)	300 mg / 0.5 mg PO day 1	Available as fixed combination product only
Fosnetupitant/palonosetron (Akynzeo®)	235 mg / 0.25 mg IV day 1	Available as fixed combination product only
Rolapitant (Varubi®)	180 mg PO day 1 OR 166.5 mg IV day 1	↑ Thioridazine and Pimozide- avoid combo Monitor digoxin and warfarin Monitor AEs of BCRP substrates (methotrexate, topotecan, irinotecan) May increase levels of antidepressants (due to CYP2D6 inhibition)
Dopamine Antagonists		
Prochlorperazine [‡] (Compazine®)	10 mg PO TID-QID (max 40 mg/day) 25 mg PR BID	EPS (see page 17 for definitions and management) QT prolongation
Perphenazine (Trilafon®)	2-8 mg PO q 4-6 hours (max 24 mg/day)	
Metoclopramide [‡] (Reglan®)	10-40 mg PO/IV TID-QID	
Haloperidol [‡] (Haldol®)	0.5-2 mg IV/PO q 4-8 hours	
Droperidol [‡] (Inapsine®)	2.5-5 mg IV q 3-4 hours	EKG (electrocardiogram) monitoring required Not available at BWH
Corticosteroids		
Dexamethasone (Decadron®)	4-20 mg PO/IV daily-bid	Delirium, anxiety, insomnia (reduce dose if possible), hiccups, increased serum glucose (caution in patients with diabetes mellitus), dyspepsia (take with food to minimize), facial erythema
Methylprednisolone (Solu-medrol®)	50-100 mg IV daily	

Classes of Commonly Used Antiemetics (continued)

Atypical Antipsychotics		
¥Olanzapine (Zyprexa®)	2.5-10 mg PO daily	Sedation, orthostatic hypotension, Consider lower dose for older, frail, debilitated patients
Antihistamines		
Dimenhydrinate (Dramamine®)	50-100 mg PO/IV q 4-6 hours	Sedation, confusion (especially in patients ≥ 65 years)
Meclizine (Antivert®)	25-50 mg PO daily	
Promethazine (Phenergan®)	12.5-25 mg PO/PR q 4 hours	Avoid use of promethazine with dopamine antagonists due to similar MOA
Trimethobenzamide (Tigan®)	300 mg PO TID-QID 200mg PR TID-QID	
Anticholinergics		
Scopolamine (Transderm Scop®)	1.5-3 mg TD q 72 h	Dry mouth, blurred vision, delirium
Cannabinoids		
Dronabinol (Marinol®)	2.5-10 mg PO BID-TID	Confusion, ataxia
Nabilone (Cesamet®)	1-2 mg PO BID	
Dronabinol (Syndros®)	2.1 mg/m ² -4.2 mg/m ² 1-3 hours prior to chemo then every 2-4 hours post chemo	Oral Solution 5 mg/ml (2.1 mg = 2.5 mg capsules)
Anxiolytics		
Lorazepam (Ativan®)	0.5-1 mg PO/IV/SL q 6 hours	Confusion, sedation Start with 0.5 mg in older patients, benzodiazepine naïve patients, or concomitant opioid use Use caution in patients at risk for falls or at risk for dependence Use the lowest effective dose and widest dosage interval possible
H2 Blockers/ PPIs		
Famotidine (Pepcid®)	10-20 mg PO BID	May interfere with absorption of other drugs, including oral anticancer agents
Omeprazole (Prilosec®)	20 mg PO daily - BID	

¥ These medications have been known to prolong the QTc interval and lead to Torsades de Pointes. EKG monitoring is recommended when using these medications with other QTc prolonging medications (e.g. methadone) or in patients with a previous prolonged QTc.

Extrapyramidal Symptoms (EPS)/Movement Disorders

Many antiemetics are related to the antipsychotic class of medications and therefore pose a risk of movement disorders including: akathisia, extrapyramidal side effects, Tardive Dyskinesia (TD), and Parkinsonism.

Akathisia

Motor restlessness manifesting as inability to keep still, rocking back and forth, purposeless shaking of foot/leg, or pacing.

- Reduce or stop the agent if possible
- Add beta blocker (propranolol preferred)
- **NOT** effective: anticholinergics (diphenhydramine, benztropine)

Dystonic reactions

Acute onset of muscle spasm, commonly involving neck muscles (torticollis). Can be very painful and poses the highest risk in young males, but can be seen in all age groups and can occur after a single dose.

- Reduce or stop the agent if possible
- Benztropine 1-2 mg PO daily or BID (may give first dose IV) or diphenhydramine 25-50 mg PO/IV Q 4-6 hours PRN
 - If intolerant to anticholinergics, consider amantadine 100 mg PO BID-TID.
- Benzodiazepine (lorazepam, clonazepam)

Parkinsonism

May be reported as a new tremor, sense of being slowed down or stiff movements; manifest as “pill rolling” tremor at rest, cogwheeling, bradykinesia, and even mask-like facies. Patients can seem more depressed, stooped and slowed.

- Reduce or stop the agent if possible
- Benztropine 1-2 mg PO daily or BID (may give first dose IV) or diphenhydramine 25-50 mg PO/IV Q 4-6 hours PRN
- Amantadine 100 mg PO BID-TID

Tardive dyskinesia (TD)

Irregular stereotyped or choreoathetoid movements which are under temporary volitional control and are ameliorated by action and sleep and augmented by distraction and stress. Patients are often not aware or distressed despite visually obvious movements.

- Stop the agent if possible
- **May not resolve if treatment is continued**

Manifestations of TD-

- Orofacial: (most common) lip smacking, chewing, tongue thrusting, lateral jaw movements, grimacing, eye blinking.
- Limb: fidgety movements of hands and feet, or writhing (athetoid) movements.
- Trunk: slow, writhing movements.
- Respiratory: asynchronous breathing, tachypnea, or grunting due to diaphragmatic involvement. May be misinterpreted as anxiety or COPD.
- Speech: impaired phonation and articulation due to tongue, laryngeal, and diaphragmatic involvement. Speech may be unintelligible.

Note: New onset EPS have been reported with all of the antipsychotic agents, although the reported incidence of EPS in association with the newer antipsychotics (atypicals or second-generation) is lower than with conventional agents.

Movement Disorder Screening

For patients on neuroleptics*, metoclopramide+, or prochlorperazine:

Every visit watch for **PUR**

Postural abnormalities

- Pregnancy stance
- Pelvic thrust
- Altered gait

Unintentional movements

- Finger tap
- Mouth and leg movement

Restless

- Hands, arms, and legs

*chlorpromazine, thioridazine, haloperidol, clozapine, risperidone, olanzapine, quetiapine

+the FDA recommends short-term use (<12 weeks) of metoclopramide to decrease risk of tardive dyskinesia

If a patient is believed to be exhibiting signs of a movement disorder, the use of the Abnormal Involuntary Movement Scale (AIMS) is recommended. An example of this scale can be found at: <https://www.ohsu.edu/sites/default/files/2019-10/%28AIMS%29%20Abnormal%20Involuntary%20Movement%20Scale.pdf>

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