CHEMOTHERAPY INDUCED NAUSEA AND VOMITING (CINV)

Antiemetic Guidelines

Background:

Emetogenic potential of chemotherapy depends on many factors, such as:

- Drugs being given (Cisplatin is more emetogenic than paclitaxel)
- Dose of drug (Carboplatin AUC of 6 is more emetogenic than AUC 2)
- Route of administration (IV etoposide is less emetogenic than oral etoposide)
- Combination of medications (doxorubicin and cyclophosphamide are highly emetogenic when given together)

There are different types of CINV:

- Acute onset (mostly serotonin related): occurring within 24 hours of initial administration of chemotherapy
- Delayed onset (in part substance P/NK-1 related): occurring 24 hours to several days after initial treatment
- Anticipatory: often related to an association with a previous experience with chemotherapy. This can be triggered by taste, odor, sight, or thoughts that are often secondary to anxiety
- Breakthrough: occurs despite preventive therapy and is treated as needed
- Refractory: occurs when antiemetic prophylaxis and rescue therapy have failed

Key Points

Antiemetics should be given 30-60 minutes prior to starting chemotherapy

Oral antiemetics are similarly effective, easier to administer, and less expensive

When selecting antiemetic regimens for patients, do not use two agents from the same class of medications (i.e. palanosetron with ondansetron as PRN)

Keep in mind drug interactions with steroids and substance P/NK-1 antagonists (i.e. dexamethasone induces enzyme metabolism and aprepitant/fosaprepitant are strong CYP3A4 inhibitors)

Fosaprepitant is rarely given more than one time per cycle of chemotherapy, even for multi-day regimens. If there is an order for more than one dose of fosaprepitant, please contact the prescriber to clarify. There is rarely a reason to give this drug more than once in a 7 day period.

To determine emetogenic risk category, refer to Table 1 and 2

To determine appropriate premedications based on risk category, refer to Table 3

For help with Breakthrough N/V recommendations, refer to Table 4

For Therapeutic Interchanges, refer to Table 5

Table 1: Emetogenic Potential of INTRAVENOUS Antineoplastic Agents

High emetic risk (>90% frequency of emesis)	• AC combination (defined as any chemotherapy regimen that contains an anthracycline and cyclophosphamide) • Carboplatin AUC ≥ 4 • Carmustine > 250 mg/m^2 • Cisplatin • Cyclophosphamide > 1500 mg/m^2 • Dacarbazine	• Doxorubicin ≥ 60 mg/m^2 • Epirubicin > 90 mg/m^2 • Ifosfamide ≥ 2 gm/m^2 per dose • Mechlorethamine • Streptazocin
Moderate emetic risk (30-90% frequency of emesis)	• Aldesleukin > 12-15 million IU/m^2 • Amifostine > 300 mg/m^2 • Arsenic trioxide • Azacitidine • Bendamustine • Busulfan • Carboplatin AUC < 4 • Carmustine ≤ 250 mg/m^2 • Clofarabine • Cyclophosphamide ≤ 1500 mg/m^2 • Cytarabine > 200 mg/m^2 • Dactinomycin • Daunorubicin	• Dinutuximab • Doxorubicin < 60 mg/m^2 • Epirubicin ≤ 90 mg/m2 • Idarubicin • Ifosfamide < 2 gm/m^2 per dose • Interferon alfa ≥ 10 million IU/m^2 • Irinotecan • Melphalan • Methotrexate ≥ 250 mg/m^2 • Oxaliplatin • Temozolomide • Trabectedin
Low emetic risk (10-30% frequency of emesis)	• Ado-trastuzumab ematansine • Aldesleukin ≤ 12 million IU/m^2 • Amifostine ≤ 300 mg/m^2 • Atezolizumab • Belinostat • Blinatumomab • Brentuximab • Cabazitaxel • Carfilzomib • Cytarabine (low dose) 100-200 mg/m^2 • Docetaxel • Doxorubicin (liposomal) • Eribulin • Etoposide • 5-FU • Floxuridine • Gemcitabine • Interferon alfa >5 - <10 million IU/m^2	• Irinotecan (liposomal) • Ixabepilone • Methotrexate > 50 mg/m^2 - <250 mg/m^2 • Mitomycin • Mitoxantrone • Necitumumab • Omacetaxine • Paclitaxel • Paclitaxel-albumin • Pemetrexed • Pentostatin • Pralatrexate • Romidepsin • Talimogene leherparepvec • Thiotepa • Topotecan • Ziv-aflibercept

Minimal emetic risk (<10% frequency of emesis)	• Almetuzumab • Asparaginase • Bevacizumab • Bleomycin • Bortezomib • Cetuximab • Cladribine • Cytarabine <100 mg/m^2 • Daratumumab • Decitabine • Denileukin diftitox • Dexrazoxane • Elotuzumab • Fludarabine • Interferon alpha ≤ 5 million IU/m^2 • Ipilimumab • Methotrexate ≤ 50 mg/m^2 • Nelarabine	• Nivolumab • Obinutuzumab • Ofatumumab • Panitumumab • Pegasaraginase • Peginterferon • Pembrolizumab • Pertuzumab • Ramicirumab • Rituximab • Siltuximab • Temsirolimus • Traztuzumab • Valrubicin • Vinblastine • Vincristine • Vincristine (liposomal) • Vinorelbine

Table 2: Emetogenic Potential of ORAL Antineoplastic Agents

Moderate to high emetic risk (≥30% frequency of emesis)	• Altretamine • Busulfan (≥ 4 mg/d) • Ceritinib • Crizotinib • Cyclophosphamide (≥ 100 mg/m^2/day) • Estramustine • Etoposide • Lenvatinib	• Lomustine (single day) • Mitotane • Olaparib • Panobinostat • Procarbazine • Rucaparib • Temozolomide (>75 mg/m^2/day) • Trifluridine/tipiracil
Minimal to low emetic risk (<30% frequency of emesis)	• Afatinib • Alectinib • Axitinib • Bexarotene • Bosutinib • Busulfan (4 mg/d) • Cabozantinib • Capecitabine • Chlorambucil • Cobimetinib • Cyclophosphamide (<100 mg/m^2/day) • Dasatinib • Dabrafenib	• Mercaptopurine • Methotrexate • Nilotinib • Osimertinib • Palbociclib • Pazopanib • Pomalidomide • Ponatinib • Regorafenib • Ruxolitinib • Sonidegib • Sorafenib • Sunitinib

	• Erlotinib • Everolimus • Fludarabine • Gefitinib • Hydroxyurea • Ibrutinib • Idelalisib • Imatinib • Ixazomib • Lapatinib • Lenalidomide • Melphalan	• Temozolomide (≤ 75 mg/m^2/day) • Thalidomide • Thioguanine • Topotecan • Trametinib • Tretinoin • Vandetanib • Vemurafenib • Venetoclax • Vismodegib • Vorinostat

Table 3: Appropriate premedications based on risk

Emetic Risk	Recommendation

High emetic risk IV chemotherapy – Acute and delayed emesis prevention	• Prior to chemotherapy:
	  ○ Fosaprepitant 150 mg IV x1 *(Should not be given more than one dose, even on multi-day regimens)*
	  ○ Ondansetron 16 mg IV x1
	  ○ Dexamethasone 10 mg IV x1
	• Days 2, 3, and 4 after chemo:
	  ○ Dexamethasone 8 mg PO daily on days 2, 3, and 4

Moderate emetic risk IV chemotherapy – Acute and delayed emesis prevention	• Prior to chemotherapy:
	  ○ Ondansetron 8-16 mg IV x1
	  ○ Dexamethasone 10 mg IV x1
	• Days 2 and 3:
	  ○ Ondansetron 8 mg PO BID on days 2 and 3 OR
	  ○ Dexamethasone 8 mg PO daily on days 2 and 3

Low emetic risk IV chemotherapy	• Prior to chemotherapy: ○ Ondansetron 8 mg IV/PO x1
Minimal emetic risk IV chemotherapy	• No routine prophylaxis
High to moderate risk ORAL chemotherapy	• Prior to chemotherapy: ○ Ondansetron 8 mg PO x1
Low to minimal emetic risk	• PRN ondansetron 8 mg PO

Table 4 Breakthrough Nausea and Vomiting Recommendations: The general principle of breakthrough treatment is to add one agent from a different drug class to the current regimen

Agent	Additional benefits
Olanzapine 5-10 mg PO daily	Appetite stimulation, anxiety, depression
Lorazepam 0.5-2 mg PO/IV Q6 hours	Anticipatory nausea/vomiting, anxiety
Dronabinol 5-10 mg PO Q12 hours	Appetite stimulation
Haloperidol 0.5-2 mg PO/IV Q6 hours	Often last line
Metoclopramide 10-20 mg PO/IV Q6-12 hours	Gastric emptying
Scopolamine 1.5 mg TD patch Q72 hours	Motion induced nausea/vomiting
Prochlorperazine 10 mg PO/IV Q6 hours	Anxiety
Promethazine 25 mg sup Q6 hours, 12.5-25 mg PO Q6 hours, or 6.25-12.5 mg IV Q6 hours	
Ondansetron 8 mg IV or PO Q8 hours	
Dexamethasone 12 mg IV or PO daily	Appetite stimulation

Table 5: Therapeutic Interchanges

Ordered	Provided
Aprepitant 100mg IV	Fosaprepitant 150mg IV x1
Aprepitant 130mg IV	Fosaprepitant 150mg IV x1
Aprepitant 125 mg, 80 mg x2 PO	Fosaprepitant 150mg IV x1
Netupitant/Palonosetron 300-0.5mg PO	*Inpatient:* Fosaprepitant 150mg IV x1 + Ondansetron 8 mg IV *Outpatient:* Fosaprepitant 150mg IV x1 + Palonosetron 0.25mg IV
Rolapitant 90 mg PO	Fosaprepitant 150 mg IV x1
Rolapitant 166.5mg IV	Fosaprepitant 150mg IV x1
Palonosetron 0.25mg IV (inpatient only)	Ondansetron 8 mg IV Q24 hour x 3 days

** Fosaprepitant is rarely given more than one time per cycle of chemotherapy, even for multi-day regimens. If there is an order for more than one dose of fosaprepitant, please contact the prescriber to clarify. There is rarely a reason to give this drug more than once in a 7 day period.