

CARE GUIDE: *Antiemesis* (*Cancer Chemotherapy-Induced Nausea and Vomiting*)

General Principles of Breakthrough Treatment for Chemotherapy Induced Nausea and Vomiting

TREATMENT OF BREAKTHROUGH EMESIS

ANY NAUSEA/VOMITING	<p>Give an additional agent from a different drug class</p> <ul style="list-style-type: none"> • Antipsychotic: • Benzodiazepine • Cannabinoid • Dopamine receptor antagonist • Phenothiazine • Serotonin 5 – HT3 antagonist • Steroid <p>❖ PO route not likely feasible due to ongoing vomiting. Rectal or IV therapy is often required.</p> <p>❖ Ensure adequate hydration or fluid repletion</p>	<div style="display: flex; justify-content: space-between;"> <div style="border: 1px solid black; padding: 5px; width: 45%;">Nausea/vomiting controlled</div> <div style="border: 1px solid black; padding: 5px; width: 45%;">Continue breakthrough medications on a schedule, not prn</div> </div> <div style="display: flex; justify-content: space-between; margin-top: 20px;"> <div style="border: 1px solid black; padding: 5px; width: 25%;">Nausea and/or vomiting uncontrolled</div> <div style="border: 1px solid black; padding: 5px; width: 30%;">Re-evaluate and consider dose adjustments and/or switching to a different therapy</div> <div style="border: 1px solid black; padding: 5px; width: 40%;">Consider changing antiemetic therapy to higher level primary treatment for next cycle</div> </div>
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Chemotherapy Induced Nausea/Vomiting

EMETIC RISK	Day 1	Day 2 – 4
HIGH	<p>Start before chemotherapy</p> <ul style="list-style-type: none"> • Serotonin (5-HT3) antagonist <p>AND</p> <ul style="list-style-type: none"> • IV or PO Steroid <p>AND</p> <ul style="list-style-type: none"> • Neurokinin 1 antagonist • ± Lorazepam 0.5 – 2 mg PO or IV or sublingual either every 4 hours or 6 hours • ± H2 blocker or proton pump inhibitor 	<ul style="list-style-type: none"> • PO steroid <p>AND</p> <ul style="list-style-type: none"> • Neurokinin 1 antagonist days 2 – 3 <p>± Lorazepam 0.5 – 2 mg PO or IV or sublingual either every 4 hours or every 6 hours days 2 - 4</p>
MODERATE	<p>Start before chemotherapy</p> <ul style="list-style-type: none"> • <u>Serotonin (5-HT3) antagonist</u> <p>AND</p> <ul style="list-style-type: none"> • <u>IV or PO Steroid</u> <p>With/Without</p> <ul style="list-style-type: none"> • <u>Neurokinin 1 antagonist</u> • ± Lorazepam 0.5 – 2 mg PO or IV or sublingual either every 4 hours or 6 hours prn • + H2 blocker or proton pump inhibitor 	<p>DAYS 2 and 3</p> <ul style="list-style-type: none"> • <u>Serotonin (5-HT3) antagonist monotherapy</u> <p>OR</p> <ul style="list-style-type: none"> • <u>IV or PO Steroid monotherapy</u> <p>OR</p> <ul style="list-style-type: none"> • Neurokinin 1 antagonist ± steroid (if neurokinin – 1 antagonist used on day 1) • ± Lorazepam 0.5 – 2 mg PO or IV or sublingual either every 4 hours or 6 hours prn • ± H2 blocker or proton pump inhibitor
LOW	<p>Start before chemotherapy</p> <p>Repeat daily for fractionated doses of chemotherapy</p> <p>Dexamethasone 12 mg PO or IV daily</p> <p>OR</p> <p>Prochlorperazine 10 mg PO or IV then q 4-6 h prn</p> <p>OR</p> <p>Metoclopramide 10-40 mg PO or IV then q 4-6 h prn</p> <ul style="list-style-type: none"> • ± Lorazepam 0.5 – 2 mg PO or IV or sublingual either every 4 hours or 6 hours prn • ± H2 blocker or proton pump inhibitor 	<ul style="list-style-type: none"> • See breakthrough treatment for CIN V
MINIMAL	<ul style="list-style-type: none"> • No routine prophylaxis 	<p>See breakthrough treatment for CIN V</p>

ANTICIPATORY NAUSEA & VOMITING	<p>Prevention Use optimal antiemetic therapy during every cycle of treatment Behavioral Therapy:</p> <ul style="list-style-type: none"> • Relaxation/Systemic desensitization • Hypnosis/guided imagery • Music therapy <p>Acupuncture/acupressure Alprazolam 0.5-2 mg PO tid on the night before treatment Lorazepam 0.5-2 mg PO on the night before and morning of treatment</p>	
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Principles of Emesis Control in the Cancer Patient

- Prevention of nausea/vomiting is the goal.
- Risk of nausea/vomiting for patients receiving chemotherapy of high and moderate emetic risk lasts for at least 3 days. Patients need to be protected throughout the full period of emetic risk of the chemotherapy agent(s) being administered, and possibly afterwards.
- Oral and IV antiemetic formulations have equivalent effectiveness.
- Use the lowest fully efficacious dose of the antiemetic(s) prior to chemotherapy.
- Consider the toxicity of the specific antiemetic(s).
- Choice of antiemetic(s) used should be based on the emetic risk of the therapy as well as patient factors.
- Other potential causes of emesis in cancer patients may include:
 - Partial or complete bowel obstruction
 - Vestibular dysfunction
 - Brain metastases
 - Electrolyte imbalance: hypercalcemia, hyperglycemia, hyponatremia
 - Uremia
 - Concomitant drug treatments including opiates
 - Gastroparesis, tumor or chemotherapy (vincristine, etc.) induced
 - Psychophysiologic:
 - Anxiety
 - Anticipatory nausea and vomiting

Emetogenic Potential of Antineoplastic Agents

Level	Agent
High emetic risk (> 90% frequency of emesis)*	AC combination defined as either doxorubicin or epirubicin with cyclophosphamide; Carmustine > 250 mg/m ² ; Cisplatin ≥ 50 mg/m ² ; Cyclophosphamide > 1,500 mg/m ² ; Dacarbazine; Mechlorethamine; Streptozocin
Moderate emetic risk (30-90% frequency of emesis)*	Aldesleukin > 12 – 15 million IU/ m ² ; Altretamin; Amifostine > 300 mg/ m ² ; Arsenic trioxide; Azacitidine; Bendamustine; Busulfan; Carboplatin; Carmustine ≤ 250 mg/ m ² ; Cisplatin < 50 mg/ m ² ; Clofarabine; Cyclophosphamide ≤ 1,500 mg/ m ² ; Cytarabine > 200 mg/ m ² ; Dactinomycin; Doxorubicin; Epirubicin; Idarubicin; Ifosfamide; Interferon alfa ≥ 10 million IU/ m ² ; Irinotecan; Melphalan; Methotrexate 250 - > 1,000 mg/ m ² ; Oxaliplatin; Temozolomide
Low emetic risk (10-30% frequency of emesis)*	Amifostine ≤ 300 mg; Aldesleukin ≤ 12 million IU/ m ² ; Cytarabine (low dose) 100 – 200 mg/ m ² ; Docetaxel; Doxorubicin (liposomal); Etoposide; 5-Fluorouracil; Floxuridine; Gemcitabine; Interferon alfa > 5 < 10 million IU/ m ² ; Ixabepilone; Methotrexate > 50 mg/ m ² < 250 mg/ m ² ; Mitomycin; Mitoxantrone; Paclitaxel; Paclitaxel – albumin; Pemetrexed; Pentostatin; Romidepsin; Topotecan
Minimal emetic risk (< 10% frequency of emesis)*	Alemtuzumab; Asparaginase; Bevacizumab; Bleomycin; Bortezomib; Cetuximab; Cladribine (2 – chlorodeoxyadenosine); Cytarabine < 100 mg/ m ² ; Decitabine; Denileukin diftitox; Dexrazoxane; Fludarabine; Gemtuzumab oxogamicin; Interferon alpha ≤ 5 million IU/ m ² ; Methotrexate ≤ 50 mg/ m ² ; Nelarabine; Panitumumab; Pegaspargase; Rituximab; Temozolomide; Trastuzumab; Valrubicin; Vinblastine; Vincristine; Vinorelbine
Prophylaxis recommended	Altretamine; Busulfan (≥ 4 mg/d); Cyclophosphamide (≥ 100 mg/ m ² /d); Estramustine; Etoposide; Lomustine (single day); Procarbazine; Temozolomide (. 75 mg/ m ² /d)
PRN recommended	Bexarotene; Busulfan (< 4 mg/day); Capecitabine; Chlorambucil; Cyclophosphamide (< 100 mg/ m ² /d); Dasatinib; Erlotinib; Everolimus; Fludarabine; Gefitinib; Hydroxyurea; Imatinib; Lapatinib; Lanalidomide; Melphalan; Mercaptopurine ; Methotrexate; Nilotinib; Pazopanib; Sorafenib; Sunitinib; Temozolomide (≤ 75 mg/ m ² /day); Thalidomide; Thioguanine; Topotecan; Tretinoin; Vorinostat

*Proportion of patients who experience emesis in the absence of effective antiemetic prophylaxis.

In individual cases, if feasible, consider erring on the side of treatment vs. not, since nausea and vomiting have a large impact on quality of life.

Key Points: Chemotherapy Induced Nausea & Vomiting (CINV)

1. CINV can lead to poor compliance with further chemotherapy treatment, metabolic imbalance, diminished QOL, nutrient depletion and decline of mental status.
2. Assess emetic risk and prevent CINV. Classify level of emetic risk as high, moderate, low or minimal based on patient treatment regimen. Regrettably, complete prevention of CINV is not achievable for up to 15-20% of patients receiving chemotherapy.
3. Assess diabetic patients for increased blood sugar when high dose dexamethasone is administered.
4. Antiemetic therapy should start before the administration of chemotherapy and cover the 24 hours of the acute phase. Antiemetic therapy should be continued for the duration of the chemotherapy administration and/or a period of time after the administration depending on the emetic risk of the chemotherapeutic agent.
5. For breakthrough emesis, a different pharmacologic class should be added. Before administering the next cycle of chemotherapy, reassess the patient for non-chemotherapy related reasons for breakthrough emesis. Routine around-the-clock administration of antiemetics should be strongly considered to prevent emesis, rather than PRN treatment.
6. Prevent anticipatory CINV by using optimal antiemetic therapy during every cycle of treatment. Consider adding anti-anxiety medication to the antiemetic regimen and/or behavioral modification therapy.
7. Screen for depression and QOL using validated tools (e.g. PHQ – 2, CARES, QOL – CA, FACT)
8. Prevent a Common Toxicity Terminology Criteria for Adverse Events (CTCAE) CINV score of 3 or 4 to avoid ER visits or hospitalization.

Types of Emesis (CINV)

1. Acute-onset CINV usually occurs within a few minutes to several hours after drug administration and commonly resolves within the first 24 hours.
2. Delayed-onset CINV develops in patients more than 24 hours after chemotherapy administration.
3. Anticipatory CINV is the occurrence of nausea and/or vomiting before patients receive their next chemotherapy treatment. It is a conditioned response to a negative past experience with chemotherapy.
4. Breakthrough emesis refers to vomiting that occurs despite prophylactic treatment and/or requires “rescue.”
5. Refractory emesis refers to emesis that occurs during subsequent treatment cycles when antiemetic prophylaxis and/or rescue have failed in earlier cycles.

References

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