

SUPPORTIVE CARE

ACUTE EMESIS PROPHYLAXIS¹⁻⁴

Minimally Emetogenic Regimes (< 10%)

- Prophylactic antiemetic therapy generally is not required.
- If the patient experiences nausea or vomiting, use prophylactic therapy prior to subsequent treatments.
 - One of the following regimens is recommended:
 - ◆ Dexamethasone 8 to 20 mg PO, given 30 minutes before chemotherapy
 - ◆ Prochlorperazine 10 mg PO ± diphenhydramine 25 to 50 mg PO if needed, given 30 minutes before chemotherapy
 - ◆ Metoclopramide 0.5 to 2 mg/kg PO ± diphenhydramine 25 to 50 mg PO if needed, given 30 minutes before chemotherapy
 - ◆ Promethazine 25 to 50 mg PO ± diphenhydramine 25 to 50 mg PO if needed, given 30 minutes before chemotherapy
- If patient still experiences significant nausea or vomiting, add an agent from a different pharmacologic category to the previous prophylactic antiemetic regimen.
 - The following regimens are recommended:
 - ◆ Patients who received a corticosteroid only: Add a dopamine antagonist.
 - ◆ Patients who received a dopamine antagonist only: Add a corticosteroid.
 - ◆ Patients who received a corticosteroid and dopamine antagonist: Substitute a serotonin antagonist for the dopamine antagonist.
 - If a corticosteroid and dopamine antagonist combination is not effective, a serotonin antagonist and corticosteroid combination may be required.
 - ◆ The following regimens are recommended:
 - Ondansetron 8 to 16 mg and dexamethasone 20 mg given PO 30 minutes before chemotherapy
 - Granisetron 1 to 2 mg and dexamethasone 20 mg given PO 30 minutes before chemotherapy

- Dolasetron 100 mg and dexamethasone 20 mg given PO 30 minutes before chemotherapy
- Palonosetron 0.25 mg IV (day 1 only) and dexamethasone 20 mg PO given 30 minutes before chemotherapy

- Patients who do not respond to a 2-drug combination may benefit from the following:
 - A corticosteroid, dopamine antagonist, and serotonin antagonist regimen or
 - Addition of a neurokinin antagonist to their previous regimen.

Mildly Emetogenic Regimens (10% to 30%)

- For most patients, prophylactic antiemetic therapy, particularly with a serotonin antagonist, generally is not required.
- If needed, one of the following regimens may be given 30 minutes prior to therapy:
 - Dexamethasone 8 to 20 mg PO, given 30 minutes before chemotherapy
 - Prochlorperazine 10 mg orally ± diphenhydramine 25 to 50 mg PO if needed, given 30 minutes before chemotherapy
 - Metoclopramide 0.5 to 2 mg/kg PO ± diphenhydramine 25 to 50 mg PO if needed, given 30 minutes before chemotherapy
 - Promethazine 25 to 50 mg PO ± diphenhydramine 25 to 50 mg PO if needed, given 30 minutes before chemotherapy
- If patient still experiences significant nausea or vomiting, add an agent from a different pharmacologic category to the previous prophylactic antiemetic regimen.
 - The following regimens are recommended:
 - ◆ Patients who received a corticosteroid only: Add a dopamine.
 - ◆ Patients who received a dopamine antagonist only: Add a corticosteroid.
 - ◆ Patients who received a corticosteroid and dopamine antagonist: Substitute a serotonin antagonist for the dopamine antagonist.

- If a corticosteroid and dopamine antagonist combination is not effective, a serotonin antagonist and corticosteroid combination may be required.
 - ◆ The following regimens are recommended:
 - Ondansetron 8 to 16 mg and dexamethasone 20 mg given PO 30 minutes before chemotherapy
 - Granisetron 1 to 2 mg and dexamethasone 20 mg given PO 30 minutes before chemotherapy
 - Dolasetron 100 mg and dexamethasone 20 mg given PO 30 minutes before chemotherapy
 - Palonosetron 0.25 mg IV (day 1 only) and dexamethasone 20 mg PO given 30 minutes before chemotherapy
 - Patients who do not respond to a 2-drug combination may benefit from the following:
 - A corticosteroid, dopamine antagonist, and serotonin antagonist regimen or
 - Addition of a neurokinin antagonist to their previous regimen.
- Moderately Emetogenic Regimens (30% to 90%)**
- Prophylactic antiemetic therapy with a serotonin antagonist is recommended but may not be required in all patients.
 - One of the following regimens may be given 30 minutes prior to therapy:
 - Ondansetron 8 to 24 mg PO and dexamethasone 20 mg PO, given 30 minutes before chemotherapy
 - Granisetron 1 to 2 mg PO and dexamethasone 20 mg PO, given 30 minutes before chemotherapy
 - Dolasetron 100 mg PO and dexamethasone 20 mg PO, given 30 minutes before chemotherapy
 - Palonosetron 0.25 mg IV and dexamethasone 20 mg PO, given 30 minutes before chemotherapy on day 1 only
 - Use of a neurokinin (NK₁) antagonist is recommended for regimens that include both doxorubicin and cyclophosphamide.^{2,3,5}
 - ◆ The following regimens are suggested:
 - Ondansetron 8 to 24 mg, dexamethasone 12 mg, and aprepitant 125 mg given PO 30 minutes before chemotherapy
 - Granisetron 1 to 2 mg, dexamethasone 12 mg, and aprepitant 125 mg given PO 30 minutes before chemotherapy
 - Dolasetron 100 mg, dexamethasone 12 mg PO, and aprepitant 125 mg given PO 30 minutes before chemotherapy
 - Palonosetron 0.25 mg IV (day 1 only), dexamethasone 12 mg, and aprepitant 125 mg given PO 30 minutes before chemotherapy
 - Antiemetic therapy should continue for at least 3 days.
 - Prolonged (more than 24 hours) use of serotonin antagonists is **NOT** recommended.⁶
 - A corticosteroid or corticosteroid and dopamine antagonist combination is recommended for follow-up therapy.⁶
 - One of the following regimens is suggested:
 - ◆ Dexamethasone 4 mg PO twice a day for 3 days ± metoclopramide 0.5 to 2 mg/kg PO every 4 to 6 hours ± diphenhydramine 25 to 50 mg PO every 6 hours if needed, starting on day 2 of chemotherapy
 - ◆ Dexamethasone 4 mg PO twice a day for 3 days ± prochlorperazine 10 mg PO every 4 to 6 hours ± diphenhydramine 25 to 50 mg PO every 6 hours if needed, starting on day 2 of chemotherapy
 - ◆ Dexamethasone 4 mg PO twice a day for 3 days ± promethazine 25 to 50 mg PO every 4 to 6 hours ± diphenhydramine 25 to 50 mg PO every 6 hours if needed, starting on day 2 of chemotherapy
 - If a neurokinin antagonist is used, one of the following regimens are suggested:
 - ◆ Ondansetron 16 to 24 mg, dexamethasone 12 mg, and aprepitant 125 mg given PO 30 minutes before chemotherapy
 - ◆ Granisetron 1 to 2 mg, dexamethasone 12 mg, and aprepitant 125 mg given PO 30 minutes before chemotherapy
 - ◆ Dolasetron 100 mg, dexamethasone 12 mg, and aprepitant 125 mg given PO 30 minutes before chemotherapy
 - ◆ Palonosetron 0.25 mg IV (day 1 only), dexamethasone 12 mg, and aprepitant 125 mg given PO 30 minutes before chemotherapy
 - Patients who experience significant nausea or vomiting with one of these regimens should receive an agent from a different pharmacologic category.
 - Substituting granisetron for ondansetron in subsequent treatment cycles has not been shown to be effective and is **NOT** recommended.⁷⁻¹¹

Highly Emetogenic Regimes (>90%)

- Day 1 of each cycle
 - serotonin antagonist
 - neurokinin (NK₁) antagonist
 - corticosteroid
- Days 2 and 3 of each cycle
 - neurokinin antagonist
 - corticosteroid
 - ± a dopamine or serotonin antagonist
- Recommended regimens
 - Day 1
 - ◆ Aprepitant 125 mg, dexamethasone 12 mg, and ondansetron 16 to 24 mg PO 30 minutes before chemotherapy
 - ◆ Aprepitant 125 mg, dexamethasone 12 mg, and granisetron 2 mg PO 30 minutes before chemotherapy
 - ◆ Aprepitant 125 mg, dexamethasone 12 mg, and dolasetron 100 to 200 mg PO 30 minutes before chemotherapy
 - ◆ Aprepitant 125 mg, dexamethasone 12 mg, and palonosetron 0.5 mg PO 30 minutes before chemotherapy
 - Days 2 to 3
 - ◆ A neurokinin antagonist and corticosteroid or neurokinin antagonist, corticosteroid, and dopamine antagonist combination is most appropriate for follow-up therapy. One of the following regimens is recommended:
 - Aprepitant 80 mg PO and dexamethasone 8 mg PO ± one of the following:
 - Metoclopramide 0.5 to 2 mg/kg PO every 4 to 6 hours
 - Prochlorperazine 10 mg PO every 4 to 6 hours
 - Promethazine 25 to 50 mg PO every 4 to 6 hours
 - Aprepitant 80 mg PO and dexamethasone 8 mg PO ± diphenhydramine 25 to 50 mg PO every 6 hours if needed
 - Patients with significant nausea or vomiting while receiving one of these regimens should receive an agent from a different pharmacologic category.¹⁻⁴

Breakthrough Nausea and Vomiting¹⁻⁴

- Patients should have an antiemetic for breakthrough nausea.
- Recommended regimens:
 - Metoclopramide 0.5 to 2 mg/kg PO every 4 to 6 hours if needed, ± diphenhydramine 25 to 50 mg PO every 6 hours if needed
 - Prochlorperazine 10 mg PO every 4 to 6 hours

if needed, ± diphenhydramine 25 to 50 mg PO every 6 hours if needed

- Prochlorperazine 25 mg rectally every 4 to 6 hours if needed, ± diphenhydramine 25 to 50 mg PO every 4 to 6 hours if needed
- Promethazine 25 to 50 mg PO every 4 to 6 hours if needed, ± diphenhydramine 25 to 50 mg PO every 4 to 6 hours if needed

SPECIAL CONSIDERATIONS**Serotonin (5HT₃) antagonists**

- Meta-analysis recommends against use of these agents after the first 24 hours.⁶
- There is no benefit to using granisetron in patients who do not respond to ondansetron.⁷⁻¹¹
- High-dose granisetron (3 mg IV or 40 to 240 mcg/kg)⁷⁻¹¹ for breakthrough nausea provides no benefit.⁷⁻¹¹

Carboplatin

- Causes delayed nausea or emesis similar to cisplatin.
 - Mechanism of action and clinical course differ from cisplatin.^{12,13}
 - Urinary 5-hydroxyindole acetic acid (5-HIAA) excretion indicates carboplatin causes
 - ◆ A lower peak level.
 - ◆ Prolonged release of serotonin.
- The clinical course of nausea or vomiting
 - Reflects this pattern of serotonin release.
 - Usually begins 6 to 7 hours after drug administration.
 - May persist for up to 120 hours.
- Some clinicians divide the daily antiemetic dose into 2 doses on days when carboplatin is administered.

Cisplatin

- Doses > 50 mg/m² (single dose or cumulative over consecutive days) causes delayed:
 - Nausea in 78% of patients.
 - Emesis in 61% of patients.
 - ◆ May begin as soon as 16 hours after administration.
 - ◆ Peak severity occurs at 48 to 72 hours after administration.
 - ◆ Usually abates between 96 to 168 hours after administration.¹⁴

Cyclophosphamide

- Emesis is often delayed for up to 12 hours after drug administration and may persist for up to 120 hours.^{12,15}
- Divide the daily antiemetic dose into 2 doses on days when cyclophosphamide is administered.

HYDRATION**Carboplatin**

- If doses are adjusted for renal function (as in AUC dosing), no prophylactic hydration or diuretic use is required.¹⁶

Cisplatin

- Can cause irreversible kidney damage by acute tubular necrosis.
- Maintain a urine output ≥ 75 to 100 mL/h for several hours before and after each dose.
- Numerous hydration and diuretic regimens have been reported.
- Except possibly the first treatment cycle, diuretics have no benefit over vigorous hydration.¹⁶
- One suggested regimen is D5W-NS or NS at 250 mL/h for 2 to 4 hours before and after each dose.
- Oral hydration regimens are also used, but increased chloride from IV solutions may offer better renal protection.¹⁶
- Mechanism of action of diuretics
 - Intuitively supports their use to prevent nephrotoxicity.
 - There is no evidence to recommend diuretics over vigorous hydration.¹⁷

Cyclophosphamide

- Risk of hemorrhagic cystitis increases with¹⁸
 - Higher total doses.
 - Radiation therapy.
- Patients should empty their bladder frequently.
- Hydration reduces the risk of cystitis.
- Encourage liberal fluid consumption (3 to 4 L/day)
 - On treatment day(s).
 - At least 24 hours after the last cyclophosphamide dose.
- Cystitis has been reported following a single IV dose.¹⁸

HYPERSENSITIVITY PRECAUTIONS**Anthracyclines¹⁹**

- Daunorubicin/doxorubicin/epirubicin/idarubicin¹⁹
- Can cause acute hypersensitivity reactions
- Very rare
- No specific precautions
- "Flare reaction"
 - Not a true hypersensitivity reaction
 - Includes:
 - ♦ Erythema
 - ♦ Pruritis
 - ♦ Urticaria
 - Surrounds the injection site
 - Extends along the vein being infused

- Usually:
 - ♦ Self-limiting
 - ♦ Resolves at the end of the infusion
- Additional doses of the drug can be administered without concern.

Bleomycin¹⁹

- Can induce acute hypersensitivity reactions.
 - Fever \pm chills (common)
 - Most common in lymphoma patients
- Pretreat with
 - Acetaminophen
 - Diphenhydramine
 - 30 minutes prior to each dose of bleomycin
- Test doses²⁰
 - Generally not predictive.
 - Not recommended.

Docetaxel^{21,22}

- Less likely to cause hypersensitivity reactions than paclitaxel
- Manufacturer recommends the following:
 - Dexamethasone 8 mg PO twice daily for 3 days
 - Begin the day *before* the docetaxel infusion
- Some clinicians add a histamine H₂ antagonist \pm a histamine H₁ antagonist
 - If used, the following regimen is suggested:
 - ♦ Cimetidine 300 mg or ranitidine 50 mg
 - ♦ Diphenhydramine 50 mg
 - ♦ All given IV over 30 minutes prior to docetaxel

Doxorubicin, Liposome Encapsulated²³⁻²⁶

- Infusion-related reactions, particularly with the first cycle of treatment
 - Recommended prophylactic medications prior to the first dose, and if necessary, prior to subsequent doses:
 - ♦ Hydrocortisone 100 mg IV **or** dexamethasone 20 mg IV
 - ♦ Diphenhydramine 25 mg **or** 50 mg IV
 - ♦ Cimetidine 300 mg **or** famotidine 20 mg IV
 - ♦ Given 30 minutes prior to liposomal doxorubicin

Oxaliplatin²⁷⁻³⁰

- Reactions occur in 5% to 25% of patients.
- Moderate to severe reactions occur in < 1% to 9% of patients.
- Most reactions occur at or after the seventh to ninth treatment.
- Lengthening the infusion time to 6 hours may reduce the incidence of hypersensitivity reactions.
- Symptoms include the following:
 - Common