

Alkylating Agents

Alkylating agents are cell-cycle nonspecific drugs that exert effects in all phases of the cell cycle. These agents break the DNA helix strand, which interferes with the DNA replication process and results in cell death. These medications are given intermittently, allowing the patient time to recover from toxicities prior to administering the medication again.

Types of alkylating agents include:

- Nitrogen mustards (e.g., melphalan, ifosfamide, cyclophosphamide, bendamustine)
- Nitrosoureas (cross the blood–brain barrier) (e.g., lomustine, carmustine, streptozocin)
- Platinums (e.g., cisplatin, oxaliplatin, carboplatin)
- Triazines and hydrazines (e.g., dacarbazine, procarbazine, temozolomide)
- Alkyl sulfonates (e.g., busulfan)

Toxicities and Side Effects

Dose-Limiting Toxicities

- Bone marrow suppression, which may include low platelets (thrombocytopenia or risk for bleeding), low hemoglobin (anemia), and low white blood cells (neutropenia or risk for infection).
- Organ-specific toxicities dependent on medication and dose (e.g., renal, and hepatic toxicities, pulmonary and cardiac toxicities, urotoxicity).
- Hemorrhagic cystitis.
- Peripheral neuropathy.

Side Effects

- Gastrointestinal tract (e.g., nausea, vomiting, anorexia, diarrhea, mucositis, stomatitis).
- Neurological (e.g., peripheral neuropathy).
- Tumor lysis syndrome (an oncologic emergency that occurs when many cancer cells are killed within a short period of time, releasing intracellular contents into the blood).
- Risk of developing a new malignancy.
- Other rapidly dividing cells are affected, often causing alopecia, rashes, or infertility.

Pre- and Post-administration Considerations

- Monitor blood counts closely and reference treatment parameters.
 - Chemotherapy plans may include a colony-stimulating factor (e.g., pegfilgrastim), or clinical care teams may add one later as needed.
 - Blood transfusion replacement may be needed.
 - Doses may be held or reduced based on blood counts.
 - Urinalysis may be needed based on medication.
 - Negative pregnancy test is required before treatments.
- Conduct baseline and symptom assessments to closely monitor for side effects, and report or intervene early on.

- Aggressive or extensive hydration is required for some alkylating agents because of the risk of hemorrhagic cystitis and nephrotoxicity.
- Consider an antiemetic premedication 30–60 minutes prior to administration.
- The IV site should be assessed prior to chemotherapy administration with additional attention to vesicant and irritant precautions.
- Reference boxed warnings and drug reference sheets for individual medications. Not all alkylating agents have the same risk for organ toxicity, side effects, or risk for the development of new malignancies and drug interactions (e.g., disulfiram-like reaction, tyramine-induced hypertensive crisis).
- Discuss fertility preservation.

Patient and Caregiver Education Considerations

Providers should have a conversation with patients and caregivers relaying medication information, what to expect during treatment, side effects, home medications for side effect management, discharge instructions, when to notify the healthcare team of adverse effects, and emergency contact information for providers.

References

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