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PHARMACOLOGY · ONCOLOGY · CHEMOTHERAPY

Alkylating *Agents*

Cell-cycle non-specific chemotherapy that cross-links DNA strands to kill rapidly dividing cancer cells — and a tightrope walk between tumor death and host toxicity. High-yield NCLEX 2026 review covering mechanism, drugs, adverse effects, contraindications, nursing priorities, and family education.

SOURCE TRANSPARENCY

This topic was not present in the uploaded personal note set. Content compiled from standard NCLEX references: *Saunders Comprehensive Review for the NCLEX-RN Examination (2026)*, *ATI RN Pharmacology Made Easy*, *Lippincott Illustrated Reviews: Pharmacology*, and FDA prescribing information for cyclophosphamide, ifosfamide, busulfan, carmustine, and platinum analogs. Cross-referenced with Student's existing *Chemotherapeutic Agent Toxicities* notes for continuity.

1

DEFINITION · OVERVIEW

What Are Alkylating Agents?

- **Oldest class of chemotherapy** — derived from WWI-era mustard gas research; still backbone of many regimens.
- **Cell-cycle NON-specific** — they kill cells in any phase of division, making them effective against slow-growing tumors and bulky disease.
- **Used to treat:** Hodgkin & non-Hodgkin lymphomas, leukemias (CLL, CML, AML), multiple myeloma, ovarian/breast/lung/bladder cancers, sarcomas, brain tumors (carmustine, temozolomide).
- **Why they matter on NCLEX:** Narrow therapeutic window — every adverse effect is potentially life-threatening, and the nurse owns the prevention plan.

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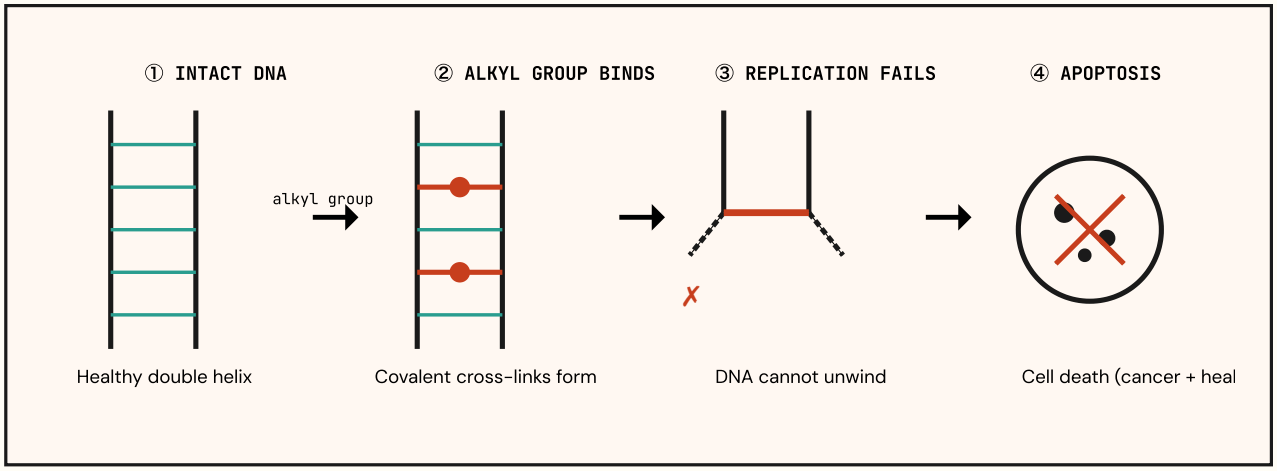
MECHANISM OF ACTION

How They Kill the Cell

- The drug donates an **alkyl group (-CH_2-CH_2-)** that covalently attaches to DNA bases, most commonly the N-7 position of guanine.
- This creates **cross-links** between two strands of DNA (or within one strand) → the helix cannot unwind for replication or transcription.
- Cell attempts to divide → encounters cross-linked DNA → triggers **apoptosis (programmed cell death)**.
- Because all dividing cells are vulnerable, healthy fast-turnover tissues are also damaged: **bone marrow, GI mucosa, hair follicles, gonads, and the bladder epithelium**.



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ADVERSE EFFECTS · SIDE EFFECTS

What You'll See in the Patient

Early / Acute (hours – days)

- **Nausea & vomiting** — HIGHLY emetogenic, especially cisplatin & cyclophosphamide. Premedicate with ondansetron + dexamethasone.
- **Hemorrhagic cystitis** (cyclophosphamide, ifosfamide) — bloody urine, dysuria, suprapubic pain.
- **Acute hypersensitivity / anaphylaxis** — especially platinum analogs.
- **Tumor lysis syndrome** — ↑K+, ↑phosphate, ↑uric acid, ↓Ca^{2+} after first dose in bulky tumors.

Delayed (days – weeks)

- **Myelosuppression** — neutropenia, thrombocytopenia, anemia. NADIR = 7–14 days post-dose.
- **Mucositis & stomatitis** — painful mouth ulcers, GI lining sloughing.
- **Alopecia** — usually 2–3 weeks after first cycle; reversible.
- **Peripheral neuropathy** — paresthesia, foot drop (especially cisplatin, oxaliplatin).

Organ-Specific Toxicity

- **Cardiotoxicity** — high-dose cyclophosphamide → hemorrhagic myocarditis.
- **Pulmonary fibrosis** — busulfan ("busulfan lung"), carmustine.
- **Nephrotoxicity** — cisplatin, ifosfamide.
- **Ototoxicity** — cisplatin (high-frequency hearing loss, tinnitus).
- **SIADH** — cyclophosphamide → hyponatremia.
- **Hepatotoxicity** — busulfan, dacarbazine.

Long-Term / Late

- **Infertility / gonadal toxicity** — often permanent in adults.
- **Secondary malignancies** — acute leukemia (AML) 5–10 years later.
- **Teratogenicity** — Pregnancy Category D; harm to fetus.
- **Premature menopause** in women; **azoospermia** in men.

RED FLAGS — CALL HCP IMMEDIATELY

Temperature ≥ 100.4°F (38°C) in neutropenic patient · Hematuria or pink-tinged urine · ANC < 500/mm^3 · Platelets < 20,000/mm^3 · Sudden dyspnea or dry cough (pulmonary fibrosis) · New tinnitus or hearing changes · Urine output < 100 mL/hr during cyclophosphamide infusion · Signs of TLS (muscle cramps, arrhythmia, oliguria).

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PRIORITY NURSING INTERVENTIONS · ABC FRAMEWORK

What the Nurse Does

A Airway / Breathing

- **Auscultate lungs** every shift — listen for fine crackles (busulfan, carmustine).
- **Monitor SpO_2 & RR**; baseline PFTs before busulfan/carmustine.
- **Stop infusion + epinephrine** for anaphylaxis (platinum agents).

B Circulation / Bleeding

- **Monitor CBC** — especially ANC and platelets before each dose.
- **Bleeding precautions** if platelets < 50,000: soft toothbrush, electric razor, no IM injections.
- **Vital signs** q4h; report SBP drop, tachycardia.

CL Continued Safety

- **Neutropenic precautions** if ANC < 1,000: private room, no fresh flowers/raw fruit, hand hygiene, no live vaccines.
- **Aggressive hydration** — 2–3 L/day PO; IV at 100–150 mL/hr around cyclophosphamide.
- **Administer MESNA** with cyclophosphamide/ifosfamide to bind acrolein and prevent hemorrhagic cystitis.

💧 Hydration & Urinary Monitoring

- Push fluids before, during, and 24–48 hr after cyclophosphamide/ifosfamide.
- Target urine output **> 100 mL/hr** during infusion.
- Empty bladder every 2 hr (including overnight) to flush acrolein.
- Dipstick urine for blood each void; report any hematuria.

🧤 Safe Handling (Nurse Protection)

- Wear **double chemo gloves, gown, eye protection, N95** when handling drug or body fluids.
- Body fluids are considered hazardous for **48 hours** after the last dose — double-flush toilet.
- Use spill kits per facility policy; never recap needles.
- **Pregnant nurses** should not handle alkylating agents.

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DRUG COMPARISON · HIGH-YIELD AGENTS

Know These Drugs Cold

Drug (Brand)	Subclass	Signature Toxicity	Nursing Priority	Used For
Cyclophosphamide (Cytoxan)	Nitrogen mustard	Hemorrhagic cystitis · SIADH · cardiotoxicity (high dose)	Hydrate aggressively; give MESNA; monitor urine for blood	Lymphoma, leukemia, breast, ovarian
Ifosfamide (Ifex)	Nitrogen mustard	Hemorrhagic cystitis · CNS toxicity (encephalopathy)	MESNA is REQUIRED; assess mental status	Testicular, sarcoma
Busulfan (Myleran)	Alkyl sulfonate	**Pulmonary fibrosis** ("busulfan lung") · seizures	Baseline PFTs; seizure precautions; antiepileptic prophylaxis	CML, stem cell transplant prep
Carmustine (BCNU)	Nitrosourea	Delayed myelosuppression (4–6 wk) · pulmonary fibrosis	Crosses BBB; monitor CBC for 6 weeks after dose	Brain tumors, lymphomas
Melphalan (Alkeran)	Nitrogen mustard	Severe myelosuppression · secondary leukemia	Strict neutropenic precautions; monitor for AML long-term	Multiple myeloma, ovarian
Cisplatin (Platinol)	Platinum analog	**Nephrotoxicity · ototoxicity** · peripheral neuropathy · severe N/V	Hydrate; mannitol/amifostine; audiogram; potent antiemetics	Testicular, ovarian, bladder, lung
Carboplatin (Paraplatin)	Platinum analog	Thrombocytopenia (dose-limiting) · less nephro/oto than cisplatin	Monitor platelets closely; bleeding precautions	Ovarian, lung
Temozolomide (Temodar)	Triazene (oral)	Myelosuppression · lymphopenia → PCP pneumonia risk	Take on empty stomach; PCP prophylaxis (Bactrim)	Glioblastoma, brain tumors
Dacarbazine (DTIC)	Triazene	Severe N/V · **flu-like syndrome** · hepatotoxicity	Protect IV bag from light; antiemetics; monitor LFTs	Hodgkin lymphoma, melanoma

MESNA — THE PROTECTIVE PARTNER

MESNA (Mesnex) binds the toxic metabolite **acrolein** in the bladder, neutralizing it before it damages the urothelium. It is given **BEFORE, during, and after** cyclophosphamide/ifosfamide infusion. NCLEX test point: MESNA is not a chemo drug — it is a uroprotectant. If asked "what prevents hemorrhagic cystitis," the answer is **MESNA + hydration**.

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CONTRAINDICATIONS · PRECAUTIONS

When NOT to Give

❌ Absolute Contraindications

- **Pregnancy** — Category D; severe teratogenicity and fetal death.
- **Hypersensitivity** to the agent or component (especially platinum allergy).
- **Severe bone marrow suppression** — ANC < 1,500 or platelets < 100,000 (depends on protocol).
- **Active, uncontrolled infection** — sepsis must be treated first.
- **Severe hemorrhagic cystitis** with cyclophosphamide.
- **Severe hepatic or renal impairment** (specific agents).

⚠️ Use With Caution

- **Older adults** — reduced renal/hepatic clearance.
- **Prior radiation therapy** — increased myelosuppression risk.
- **Live vaccines** — avoid during treatment and up to 3 months after.
- **Concurrent nephrotoxins** (NSAIDs, aminoglycosides) with cisplatin.
- **Breastfeeding** — drug excreted in breast milk; do not nurse.
- **Recent surgery** — impaired wound healing.

HOLD THE DOSE IF…

ANC < 1,500 cells/mm³ · platelets < 100,000/mm³ · creatinine clearance below protocol threshold · active hemorrhagic cystitis · fever of unknown origin · grade 3+ toxicity from prior cycle. The nurse holds the drug and contacts the HCP — never assume "give anyway."

NCLEX TEST TRAPS · WRONG-VS-RIGHT

7 What Trips Students Up

✕ WRONG	✓ RIGHT
"The client on cyclophosphamide should drink fluids when thirsty."	Encourage **2–3 L/day** and void every 2 hours, even overnight. Acrolein damages bladder while urine sits.
"Temperature of 99.8°F in a neutropenic patient — recheck in an hour."	Any fever ≥ **100.4°F (38°C)** in a neutropenic patient is a medical emergency — pan-culture and start broad-spectrum antibiotics within 1 hour.
"Give the flu shot before discharge — it's flu season."	**No LIVE vaccines** (MMR, varicella, nasal flu mist, oral polio) during or 3 months after chemo. **Inactivated** flu shot is allowed and encouraged.
"Cisplatin and carboplatin have the same toxicity profile."	**Cisplatin = kidneys + ears. Carboplatin = platelets.** Different toxicity = different monitoring priority.
"Pink-tinged urine during cyclophosphamide is expected."	ANY hematuria is hemorrhagic cystitis until proven otherwise — **stop infusion, notify HCP, send urine sample**.
"The nurse can administer chemo with standard PPE."	**Double chemo gloves, gown, eye protection, N95**. Body fluids hazardous for 48 hr. Pregnant nurses do not handle alkylating agents.

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PATIENT & FAMILY EDUCATION

What to Teach Before Discharge

💧 Hydration & Bladder Care

- Drink at least **2–3 liters of fluid daily** for 48 hours after each dose.
- Empty the bladder before bed and once during the night.
- Report immediately: pink, red, or brown urine; burning; or pain over the bladder.

🦠 Infection Prevention

- Wash hands often; avoid sick contacts and crowds during nadir (days 7–14).
- Take temperature daily; call for **fever ≥ 100.4°F (38°C)**.
- Avoid raw fruits/vegetables, undercooked meat, sushi, soft cheeses.
- Do not garden, change litter boxes, or handle live plants/flowers.

🩸 Bleeding Precautions

- Use a **soft toothbrush** and electric razor.
- No flossing if platelets are low; no aspirin or NSAIDs.
- Report nosebleeds, bruising, black stools, or pink urine.

🤰 Reproductive & Sexual Health

- Use **two forms of contraception** during and for 6+ months after therapy (both sexes).
- Discuss **sperm/egg banking** before starting therapy — fertility loss may be permanent.
- Do not breastfeed during treatment.
- Body fluids hazardous for 48 hr — use condoms and double-flush toilet.

🍽️ Nutrition & Oral Care

- Small, frequent, bland meals to combat nausea; take antiemetics on schedule.
- Rinse mouth with **salt + baking soda water** (avoid alcohol-based mouthwash) 4× daily.
- Suck on ice chips during infusion to reduce mucositis (cryotherapy).

😊 Daily Life

- Wear a hat/scarf, use sunscreen SPF 30+ on scalp; alopecia is reversible.
- Rest when fatigued; balance activity with naps.
- Keep all lab and infusion appointments — labs are not optional.
- Bring a written medication list to every visit.

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MNEMONICS · PATTERN RECOGNITION

Memory Boosters

"ALKYLATE"

The 8 things that go wrong with alkylating agents.

- **A** **Alopecia** — hair loss in 2-3 weeks
- **L** **Lung fibrosis** — busulfan, carmustine
- **K** **Kidneys** — cisplatin, ifosfamide
- **Y** **Yellow marrow suppression** — nadir 7-14 days
- **L** **Leukemia** — secondary AML years later
- **A** **Acrolein** → hemorrhagic cystitis
- **T** **Teratogenic** — no pregnancy
- **E** **Emesis** — highly emetogenic, premedicate

Drug → Organ Pairings

Quick recall of signature toxicities.

🔥 **Cyclophosphamide** → *Cystitis* (both start with C)

🫁 **Busulfan** → "Busulfan *lung*"

🧠 **Carmustine** → *Crosses* blood-brain barrier (brain tumors)

👂 **Cisplatin** → "Cis-*pl*atin" hits *pl*umbing (kidneys) + ears

🩸 **Carboplatin** → *Coagulation* (platelets ↓)

🤒 **Dacarbazine (DTIC)** → *D*readful flu (flu-like syndrome)

💀 **Melphalan** → *Marrow* wiped out

"MESNA = MEnSurA the cystitis"

MESNA **M**easures and **S**tops **N**asty **A**crolein. Given with cyclophosphamide and ifosfamide to bind acrolein in the bladder before it can ulcerate the urothelium. It is NOT a chemo drug — it's a uroprotectant.

NADIR Rule: "7–14"

Most alkylating agents cause peak myelosuppression **7 to 14 days** after the dose. Schedule CBC checks accordingly. Exception: **nitrosoureas (carmustine, lomustine)** have *delayed* nadir at **4–6 weeks** — keep monitoring long after the dose seems "done."

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NCJMM · 6-STEP CLINICAL JUDGMENT MODEL

Putting It All Together

CLINICAL SCENARIO

A 54-year-old woman with non-Hodgkin lymphoma is on day 10 of her R-CHOP cycle (which includes cyclophosphamide). She calls the oncology nurse line reporting "pink urine since this morning," a temperature of 100.8°F taken at home, mouth sores that hurt with eating, and that she "feels like she might pass out" when standing. She lives alone and last drank fluids "maybe a glass of water yesterday."

1

Recognize Cues

Pink urine (acute) · fever 100.8°F · oral mucositis · orthostatic symptoms · poor PO intake · day 10 post-cyclophosphamide (NADIR window). Patient lives alone — limited safety net.

2

Analyze Cues

Pink urine + recent cyclophosphamide = **hemorrhagic cystitis**. Fever ≥ 100.4°F during nadir = **neutropenic fever** (sepsis risk). Dehydration concentrates acrolein and worsens both. Mucositis impairs intake, perpetuating the cycle.

3

Prioritize Hypotheses

#1 Neutropenic fever / sepsis (life-threatening within hours) · **#2 Hemorrhagic cystitis with hypovolemia** · **#3 Mucositis-related dehydration**. Sepsis trumps everything — fever in a neutropenic patient is a true emergency.

4

Generate Solutions

Direct to ED *now* · STAT CBC with diff, blood cultures × 2, urinalysis, BMP, lactate · IV fluids 0.9% NS bolus · empiric broad-spectrum antibiotics within 1 hour (e.g., piperacillin-tazobactam) · MESNA + continuous bladder irrigation if hematuria worsens · antiemetics and mouth care for mucositis · oncology consult.

5

Take Action

Instruct patient NOT to drive — arrange transport (family or EMS). Notify oncology HCP. Document time of call, vitals reported, and instructions given. Prepare ED report for handoff: drug, cycle day, ANC trend, fluid intake, current symptoms.

6

Evaluate Outcomes

Within 1 hr: antibiotics infusing, IV access established, vital signs stabilizing. Within 6 hr: cultures pending, ANC confirmed, urine clearing with hydration/MESNA. Within 24 hr: afebrile, hemodynamically stable, oral intake resumed, mucositis plan in place. Future cycles: review hydration teaching, consider home health follow-up, reassess premedication and MESNA protocol.

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