💥 Alkylating Agents

🔑 Key Concept

- All are cell cycle NON-specific → Can act on cells in any phase (including resting cells)

💡 Core Mechanism (Big Picture)

Alkylating agents add alkyl groups to DNA → cause cross-linking of DNA strands → prevent replication & transcription → cell death 💀

📊 High-Yield Drug Table

Drug/Class	Mechanism	Clinical Use	Adverse Effects
Busulfan	DNA cross-linking	Bone marrow ablation before transplant	Severe myelosuppression, pulmonary fibrosis
Cyclophosphamide, Ifosfamide	DNA cross-linking (liver activation)	Solid tumors, leukemias, lymphomas, SLE	Hemorrhagic cystitis, SIADH
Carmustine, Lomustine	DNA cross-linking, cross BBB	Brain tumors	CNS toxicity
Procarbazine	Unknown (weak MAO inhibitor)	Hodgkin lymphoma	Disulfiram-like reaction

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🧪 Drug-by-Drug Notes

1️⃣ Busulfan

💡 Mechanism

- Direct DNA cross-linking → inhibits replication

📌 Clinical Use

- Used for bone marrow ablation before transplantation 🧬 → Wipes out existing marrow to prepare for donor cells

❗ Adverse Effects

- Severe myelosuppression (almost universal ⚠️)
- Pulmonary fibrosis 🫁

- Hyperpigmentation ("busulfan tan")

🎯 Exam Pearl

- Think: "Busulfan = Bone marrow BUS wiped out"

2️⃣ Nitrogen Mustards

(Cyclophosphamide, Ifosfamide)

💡 Mechanism

- Cross-link DNA
- Require activation by liver (CYP450)

🔄 Flowchart: Cyclophosphamide Toxicity

Cyclophosphamide → Liver metabolism → Formation of toxic metabolite (acrolein) → Accumulates in bladder → Bladder irritation → Hemorrhagic cystitis 🚨

⚠️ Prevention

Acrolein toxicity → Give Mesna → Binds toxic metabolites → Protects bladder 🛡️

📌 Clinical Uses

- Solid tumors
- Leukemias, lymphomas
- Autoimmune diseases (SLE, granulomatosis with polyangiitis)

❗ Adverse Effects

- Myelosuppression
- Hemorrhagic cystitis & bladder cancer 🚨
- SIADH
- Ifosfamide only: Fanconi syndrome (renal tubular damage)

🎯 Exam Pearls

- Mesna = bladder protector 🛡️
- Cyclophosphamide = hemorrhagic cystitis classic question

3️⃣ Nitrosoureas

(Carmustine, Lomustine)

💡 Mechanism

- DNA cross-linking
- Require liver activation
- Highly lipid-soluble → cross BBB easily

🔄 Flowchart: Why Nitrosoureas Are Used for Brain Tumors

Nitrosoureas → Lipophilic structure → Cross blood-brain barrier → Reach CNS tumors → DNA cross-linking → Tumor cell death

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📌 Clinical Use

- Brain tumors (VERY high-yield 🎯) → Especially glioblastoma multiforme

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❗ Adverse Effects

- CNS toxicity:
  - Convulsions
  - Dizziness
  - Ataxia

🧠 Mnemonic

"Put nitro in your Mustang and travel the globe"

-> Nitro = nitrosoureas

-> Mustang = brain (fast access to brain 🚗)

-> Globe: glioblastoma multiforme

4️⃣ Procarbazine

💡 Mechanism

- Mechanism not fully understood
- Acts as a weak MAO inhibitor

📌 Clinical Uses

- Hodgkin lymphoma (part of MOPP regimen)
- Brain tumors

❗ Adverse Effects

- Myelosuppression

- Pulmonary toxicity
- Secondary leukemia
- Disulfiram-like reaction 🍺🚫

🔄 Flowchart: Disulfiram-like Reaction

Procarbazine → Inhibits aldehyde dehydrogenase → Alcohol intake → Acetaldehyde accumulation → Flushing, nausea, vomiting → Patient discomfort

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🎯 Exam Pearls

- Avoid alcohol + tyramine-rich foods (MAO inhibition effect)
- Classic question: patient drinks alcohol → gets sick

🔥 High-Yield Comparison Table

Feature	Nitrogen Mustards	Nitrosoureas	Busulfan	Procarbazine
BBB penetration	❌	✅	❌	✅
Special toxicity	Hemorrhagic cystitis	CNS toxicity	Pulmonary fibrosis	Disulfiram reaction
Unique feature	Mesna protection	Brain tumors	Bone marrow ablation	MAO inhibition

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🔑 Must-Know Points

- All alkylating agents → cell cycle NON-specific
- Cyclophosphamide → hemorrhagic cystitis → prevent with Mesna
- Nitrosoureas → cross BBB → brain tumors

- Busulfan → bone marrow ablation
- Procarbazine → MAO inhibitor → disulfiram-like reaction

-> The End <-