🚀 Platinum Compounds / Topoisomerase Inhibitors / Tamoxifen

💎 Platinum Compounds

(Cisplatin, Carboplatin (less toxic), Oxaliplatin)

🔑 Key Concept

- Cell cycle NON-specific ❗
- Functionally similar to alkylating agents

💡 Mechanism

- Form DNA cross-links (especially at guanine bases) → Prevent DNA replication & transcription → Cell death 💀

🔄 Flowchart: Platinum Drug Action

Platinum compound → Binds DNA (guanine residues) → DNA cross-linking → DNA distortion → Inhibition of replication → Cell death

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📌 Clinical Uses

- Testicular cancer 🎯 (very high-yield for cisplatin)
- Ovarian cancer
- Bladder cancer
- Lung cancer
- GI cancers

- Lymphomas

❗ Adverse Effects

🔄 Toxicity Pattern

Platinum drugs → Accumulate in tissues → Cause organ toxicity:

- Nephrotoxicity → Can cause Fanconi syndrome → Prevention: Amifostine 🛡️
- Ototoxicity 👂 (hearing loss)
- Peripheral neuropathy 🧠

🎯 Exam Mnemonic

"Platinum = Precious but KEN – TOXIC" → Kidneys, Ears, Nerves

🔬 Topoisomerase Inhibitors

🔑 Key Concept

- Cause DNA strand breaks → degradation
- Active in S and G2 phases 📍

💡 Core Mechanism

Topoisomerases normally:

- Relieve DNA supercoiling during replication

Inhibitors:

- Block this process → DNA damage accumulates 💥

🔄 Flowchart: Topoisomerase Inhibition

Topoisomerase inhibited → DNA cannot unwind properly → DNA strand breaks accumulate → Replication stress → Cell cycle arrest (S/G2) → Cell death

📊 Drug Table

Class	Drugs	Mechanism	Clinical Use	Adverse Effects
Topo I inhibitors	Irinotecan, Topotecan	Inhibit topoisomerase I	Colon, ovarian, SCLC	Myelosuppression, diarrhea

Topo II inhibitors	Etoposide, Teniposide	Inhibit topoisomerase II	Testicular, lung cancer	Myelosuppression, alopecia

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🧪 Drug-by-Drug Notes

1️⃣ Topoisomerase I Inhibitors

(Irinotecan, Topotecan)

💡 Mechanism

- Inhibit topoisomerase I → Prevent single-strand DNA repair → DNA damage accumulates

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📌 Clinical Uses (COS)

- Colon cancer 🎯 (irinotecan classic)
- Ovarian cancer
- Small cell lung cancer

❗ Adverse Effects

- Severe diarrhea 🚨 (VERY high-yield)
- Myelosuppression

🎯 Mnemonic

"I ran to the can"

-tecan = Topo I

2️⃣ Topoisomerase II Inhibitors

(Etoposide, Teniposide)

💡 Mechanism

- Inhibit topoisomerase II → Prevent double-strand DNA repair

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📌 Clinical Uses

- Testicular cancer 🎯
- Small cell lung cancer
- Leukemia, lymphoma

❗ Adverse Effects

- Myelosuppression 💉
- Alopecia 💇‍♂️

🎯 Mnemonic

"-poside = both sides (double-strand breaks)"

💊 Tamoxifen

💡 Mechanism

- Selective Estrogen Receptor Modulator (SERM) → Tissue-specific effects:

🔄 Flowchart: Tamoxifen Action

Tamoxifen→ Binds estrogen receptor:

- In breast tissue → Antagonist → ↓ tumor growth

- In endometrium & bone → Partial agonist → Estrogen-like effects

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📌 Clinical Uses

- Treatment & prevention of breast cancer 🎯
- Prevention of gynecomastia in prostate cancer therapy

❗ Adverse Effects (VERY important ⚠️)

🔄 Toxicity Pattern

Tamoxifen → Estrogenic effects in some tissues → Leads to:

- Hot flashes 🌡️
- ↑ Thromboembolism risk (DVT, PE) 🩸
- ↑ Endometrial cancer risk 🚨

🎯 Exam Pearls

- Breast = antagonist (good)
- Endometrium = agonist (bad → cancer risk)
- Common vignette → Woman on tamoxifen → abnormal uterine bleeding

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🔥 Summary

- Platinum drugs → DNA cross-linking + nephrotoxicity
- Amifostine protects kidneys
- Topo I → diarrhea (irinotecan)

- Topo II → alopecia + marrow suppression
- Tamoxifen → SERM
    - Breast: antagonist
    - Endometrium: agonist → cancer risk

-> The End <-