drugs used in breast cancer

🔷 1. ***Cyclophosphamide***

Drug Class:
- Alkylating agent (Nitrogen mustard derivative)

Mechanism of Action:
- Prodrug activated by liver microsomal enzymes into:
- 4-hydroxycyclophosphamide and Aldophosphamide
- Aldophosphamide → nonenzymatically converted into:
- Phosphoramide mustard (cytotoxic: crosslinks DNA) and Acrolein
- Acrolein (toxic metabolite → bladder toxicity)

Therapeutic Uses:
- Breast cancer. •Ovarian cancer • Wilms' tumor •Others (e.g., lymphomas)

Adverse Effects:
(All are dose-related, especially in rapidly dividing tissues)
1. Nausea and vomiting
2. Vesicant effects → local tissue damage at injection site
3. Hemorrhagic cystitis
   - Due to acrolein
   - Prevented by hydration
4. Carcinogenic potential → risk of secondary AML (acute myelogenous leukemia)
5. Bone marrow suppression
   - Leukopenia
   - Thrombocytopenia
   - Bleeding
6. Alopecia

🔷 2. ***Methotrexate (MTX)***

Drug Class:
- Antimetabolite, Folic acid analog

Mechanism of Action:
- Inhibits dihydrofolate reductase (DHFR) → ↓ tetrahydrofolate (THF) → ↓ synthesis of:
- Thymidylate (dTMP)
- Purine nucleotides
- Amino acids (serine, methionine)
- Disrupts DNA, RNA, and protein synthesis

Polyglutamate Activation:
- Converted intracellularly into MTX polyglutamates by folylpolyglutamate synthase.
- Polyglutamates are selectively retained in tumor cells for enhanced effect.

Resistance Mechanisms:
1. ↓ MTX transport via folate carriers/receptors
2. ↓ MTX polyglutamate formation
3. ↑ DHFR enzyme levels (gene amplification)
4. Altered DHFR with reduced MTX affinity
5. Efflux via P170-glycoprotein (MDR transporter)

Routes of Administration:
- Oral, IV, Intrathecal

Cont..

Elimination:
- Renal (active transport)
- Dose adjustment needed in renal dysfunction
- Renal clearance is decreased by:
- Aspirin
- NSAIDs
- Penicillins
- Cephalosporins

Leucovorin Rescue:
- Leucovorin (5-formyltetrahydrofolate) reverses toxic effects
- Used in:
- High-dose MTX therapy
- Accidental overdose

Therapeutic Uses:
- Breast cancer
- Bladder cancer
- Choriocarcinoma
- Others (e.g., leukemia, lymphoma)

Toxicity:
1. Mucositis, diarrhea
2. Hepatotoxicity
3. Myelosuppression (neutropenia, thrombocytopenia)
4. Neurotoxicity: cognitive changes
5. Immunoallergic pneumonitis → can lead to pulmonary fibrosis
6. Chemical pneumonitis
7. Renal dysfunction

🔷***1. Doxorubicin (Anthracycline Anticancer Antibiotic)***

🧬 Mechanism of Action
1. Inhibits topoisomerase II
2. Intercalates into DNA → blocks replication and transcription.
3. Generates free radicals (semiquinone & oxygen species, iron-dependent) → cardiotoxicity.
4. Binds cellular membranes → alters fluidity and ion transport.

💉 Pharmacokinetics
- Route: IV only.
- Metabolism: Liver (extensive).
- Excretion: ~50% in bile.
- Dose adjustment required in: Hepatic dysfunction.

🎯 Therapeutic Uses
1. Breast cancer
2. Endometrial cancer
3. Ovarian cancer
4. Testicular cancer
5. Bladder cancer
6. Others (e.g., lymphomas, sarcomas)

⚠️ Key Toxicity
- Cardiotoxicity:
- Dose-dependent.
- Related to free radical formation.
- Risk of cardiotoxicty
- Cumulative dose limits should be observed.

🔷 ***2. Paclitaxel (Taxane Group)***

Source:
- Alkaloid from Pacific and European yew trees (صنوبريات)

Mechanism of Action:
- Mitotic spindle poison → inhibits mitosis and cell division

Pharmacokinetics:
- Metabolized by CYP enzymes
- ~80% excreted in feces
- Dose reduction in hepatic impairment

Therapeutic Uses:
- Ovarian cancer
- Advanced breast cancer
- Prostate cancer
- Bladder cancer
- Others

Adverse Effects:
1. Dose-limiting:
- Nausea, vomiting
- Myelosuppression
- Peripheral sensory neuropathy
- Hypotension and arrhythmias
2. Hypersensitivity reactions (~5%) → Requires premedication with:
- Dexamethasone
- Diphenhydramine (H1 blocker)
- H2 blocker
3. Albumin-bound formulation (for breast cancer):
- Less hypersensitivity risk
- No premedication required
- Milder myelosuppression
- Reversible neurotoxicity

🔷 ***3. Ixabepilone***

Class:
- Microtubule inhibitor, NOT a taxane

Indication:
- Metastatic breast cancer

Adverse Effects:
- Hypersensitivity reactions
- Myelosuppression
- Neurotoxicity (especially peripheral neuropathy)

🔷 ***4. Bevacizumab***

Class:
- Anti-angiogenesis agent
- Humanized monoclonal antibody targeting VEGF-A

Mechanism of Action:
- Binds VEGF-A → prevents interaction with VEGF receptor → inhibits new blood vessel formation (angiogenesis)

Use:
- Adjunct in tumors that require high vascular supply (e.g., metastatic cancers including breast cancer)

Toxicity:
- Hypertension
- Arterial thromboembolism (TIA, MI, stroke, angina)
- Impaired wound healing
- GI perforation
- Proteinuria

🔷 ***5. Trastuzumab (Herceptin)***

Class:
- Recobinant Humanized monoclonal antibody against HER-2/neu receptor

Mechanism of Action:
- Binds HER-2 receptor → blocks ligand binding to the receptor
- Downregulates receptor expression

Use:
- Metastatic breast cancer in HER-2 positive patients (Used in HER-2 overexpressing tumors)

Adverse Effect:
- Cardiotoxicity → ↓ Left ventricular ejection fraction (LVEF)

🧬 ***Drugs for Ovarian Cancer***

Mainly Used Agents:
- Platinum analogs: Cisplatin, Carboplatin
- Alkylating agents: Cyclophosphamide, Altretamine
- Taxanes: Paclitaxel
- Topoisomerase inhibitors: Topotecan
- Anthracyclines: Doxorubicin

🧪 ***Platinum Analogs (Cisplatin & Carboplatin)***

🔬 Mechanism of Action
- Act like alkylating agents.
- Form DNA intra- and inter-strand cross-links → inhibit DNA synthesis and function.
- Cell cycle non-specific (kill in all phases).

✅ Therapeutic Uses of cisplatin :
- Ovarian cancer
- Breast, testicular, bladder cancers, and others

⚠️ Toxicity:

Cisplatin	Carboplatin
Severe nausea/vomiting	Milder nausea/vomiting
Nephrotoxicity	**Less nephrotoxic**
Ototoxicity	Less ototoxic
Peripheral neuropathy	Less neurotoxicity
	Dose-limiting toxicity = myelosuppression

💡 Note:
- Dose reduction needed in renal dysfunction bcz it is elemenating in kidny

🌿 ***Camptothecins (e.g. Topotecan)***

derived from a tree grown in China.

🔬 Mechanism of Action
- Inhibits topoisomerase I → prevents re-ligation of single-strand DNA breaks → DNA damage → cell death.

🎯 Use
- Second-line therapy for advanced ovarian cancer after platinum-based chemo.

⚠️ Toxicities
1. Nausea and vomiting
2. Myelosuppression
3. Dose reduction needed in renal impairment

💊 ***Altretamine***

🔬 Mechanism of Action
- Alkylating agent
- Forms DNA cross-links → inhibits DNA synthesis and function.

⚠️ Toxicities
1. Nausea and vomiting
2. Myelosuppression
3. Peripheral neuropathy
4. Flu-like syndrome

Prostate Cancer Treatment

✅ Primary Goal:
- Reduce or eliminate testosterone (which stimulates prostate cancer growth)

Main Approaches:
1. Surgical castration (orchiectomy)
2. Hormonal therapy (chemical castration):
- GnRH analogs (e.g., leuprolide)
- Antiandrogens (e.g., flutamide, bicalutamide)
- 5α-reductase inhibitors (e.g., finasteride, dutasteride)

(discussed in previous sections)

🔷 ***Mitoxantrone***

Class:
- Anthracenedione (related to anthracyclines)
- Chemotherapeutic antibiotic

Mechanism of Action:
1. Intercalates into DNA → causes single- and double-stranded breaks
2. Inhibits topoisomerase II → suppresses DNA repair and replication

Used for :
- Advanced, hormone-refractory (castration-resistant) prostate cancer

Toxicity Profile:
1. Myelosuppression (especially leukopenia) → Dose-limiting toxicity
2. Thrombocytopenia
3. Nausea and vomiting
4. Alopecia
5. Mucositis
6. Bluish discoloration of:
- Fingernails
- Sclera
- Urine

(typically 1–2 days post-administration)

🧬 Drugs for Testicular Cancer

📋 Main Drugs
1. Cisplatin. 2. Etoposide. 3.Bleomycin 4.Ifosfamide (similar to cyclophosphamide)

🔬 1. ***Etoposide***

🌱 Source:
- Semisynthetic derivative of podophyllotoxin (from mayapple root).

🧪 Mechanism of Action:
- Inhibits topoisomerase II.
- Forms a ternary complex (drug + DNA + enzyme) → DNA strand breaks → apoptosis.

💊 Formulation:
- IV and oral available.
- Dose adjustment in renal dysfunction.

⚠️ Toxicities:
1. Nausea & vomiting
2. Hypotension
3. Myelosuppression
4. Alopecia

Cont..

🧪 2. ***Bleomycin***

🔬 Mechanism of Action:
- Antitumor antibiotic.
- Binds DNA → generates free radicals (via iron-binding) → causes single & double strand breaks → inhibits DNA synthesis.

⏱️ Cell-cycle specific:
- G2 phase arrest.

💉 Clinical Use:
- Testicular cancer
- Squamous cell carcinoma of cervix & vulva

⚠️ Renal dysfunction requires dose adjustment

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☣️ Dose-Limiting Toxicity: Pulmonary toxicity
- Pneumonitis, dry crackles, dyspnea, infiltrates.
- ↑ Risk in:
- Age > 70
- Dose > 400 units
- Underlying lung disease
- Prior chest radiation

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🧨 Other Toxicities:
1. Allergic reactions
2. Fever
3. Hypotension
4. Dermatotoxicity
5. Alopecia
6. Mucositis

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🧪 3. ***Cisplatin***

راجع معلوماته ضمن أدوية سرطان المبيض، لأن الاستخدام والمضاعفات متشابهة.
• Cell cycle–nonspecific
• Binds DNA, forming cross-links
• Renal excretion → dose adjust in renal dysfunction

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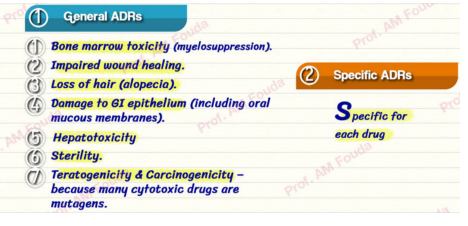
🧪 4. ***Ifosfamide***

- Mechanism: **Like cyclophosphamide.** -so...
  – alkylates DNA → cross-links → cell death.
- Used in germ cell tumors, including testicular cancer.
- Requires co-administration of Mesna to prevent hemorrhagic cystitis.
- Toxicities: Hemorrhagic cystitis, neurotoxicity, nephrotoxicity, myelosuppression.



Done by :shahed jumah