

**Name: Mechlorethamine (Mustargan)**

**Class:** Antineoplastic (Cell Cycle-Nonspecific) (Alkylating Agent) (Mustard)

**Mech.:** Alkylates DNA → crosslinkages.

**Absorption:**

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** N/V. DLT = bone marrow suppression, esp. leukocytosis. Max. suppression at 10-12 days, recovery around 42 days.

**Utility:** Hodgkin's disease (in combination therapy—MOPP).

**Special Features:** Fast-acting. Active against a wide variety of cancers. Not widely used due to toxicity.

**Name: Chlorambucil (Leukeran)**

**Class:** Antineoplastic (Cell Cycle-Nonspecific) (Alkylating Agent) (Mustard)

**Mech.:** Alkylates DNA → crosslinkages.

**Absorption:**

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** Seizures DLT = bone marrow suppression, pulmonary fibrosis.

**Utility:** CLL

**Special Features:** Slow-acting. Good activity against some chronic cancers.

**Name: Melphalan (Alkeran)**

**Class:** Antineoplastic (Cell Cycle-Nonspecific) (Alkylating Agent) (Mustard)

**Mech.:** Alkylates DNA → crosslinkages.

**Absorption:**

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** Nausea, hypersensitivity rxns. DLT = bone marrow suppression, esp. platelets.

**Utility:** Multiple myeloma.

**Special Features:** Slow-acting. Good activity against some chronic cancers.

**Name: Cyclophosphamide (Cytoxan)**

**Class:** Antineoplastic (Cell Cycle-Nonspecific) (Alkylating Agent) (Mustard)

**Mech.:** Alkylates DNA → crosslinkages.

**Absorption:** Oral (preferred), IV.

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** N/V. Anaphylaxis rxns. DLT = bone marrow suppression. Max. suppression at 10-12 days, recovery by 21 days. Hemorrhagic cystitis, sterility.

**Utility:** Non-Hodgkin's lymphomas, cancers of breast and ovary, Wilm's tumor, rhabdosarcoma, Burkitt's lymphoma.

**Special Features:** Most useful alkylating agent. Requires metabolic activation. Fast-acting. Active against a wide variety of cancers.

**Name: BCNU (Carmustine)**

**Class:** Antineoplastic (Cell Cycle-Nonspecific) (Alkylating Agent) (Nitrosourea)

**Mech.:** Alkylates DNA → crosslinkages.

**Absorption:**

**Dist.:** Crosses BBB.

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** N/V. DLT = bone marrow suppression. Max. suppression at 28 days, recovery around 42 days. Pulmonary fibrosis, renal toxicity.

**Utility:** Hodgkin's and non-Hodgkin's lymphomas, primary glioblastoma, brain tumors.

**Special Features:** Fast-acting. Active against a wide variety of cancers. Not widely used due to toxicity.

**Name: CCNU (Lomustine)**

**Class:** Antineoplastic (Cell Cycle-Nonspecific) (Alkylating Agent) (Nitrosourea)

**Mech.:** Alkylates DNA → crosslinkages.

**Absorption:** Crosses BBB.

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** N/V. DLT = bone marrow suppression. Max. suppression at 28 days, recovery around 42 days. Pulmonary fibrosis, renal toxicity.

**Utility:** Hodgkin's and non-Hodgkin's lymphomas, primary glioblastoma, brain tumors.

**Special Features:** Fast-acting. Active against a wide variety of cancers. Not widely used due to toxicity.

**Name: Streptozocin (Zanosar)**

**Class:** Antineoplastic (Cell Cycle-Nonspecific) (Alkylating Agent) (Nitrosourea)

**Mech.:** Alkylates DNA

**Absorption:**

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** N/V. DLT = renal damage in 2/3 patients. Hypo/hyperglycemia, liver toxicity.

**Utility:** Malignant pancreatic insulinoma, pancreatic carcinoid.

**Special Features:**

**Name: Busulfan (Myleran)**

**Class:** Antineoplastic (Cell Cycle-Nonspecific) (Alkylating Agent)

**Mech.:** Alkylates DNA.

**Absorption:**

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** N/V. DLT = leukopenia and thrombocytopenia.

**Utility:** CML (chronic phase).

**Special Features:**

**Name: Procarbazine (Mutalane)****Class:** Antineoplastic (Cell Cycle-Nonspecific) (Alkylating Agent)**Mech.:** Alkylates DNA.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** N/V. Leukopenia and thrombocytopenia. Inhib. MAO (danger w/tyramine-containing foods). Disulfiram-type rxn w/alcohol.**Utility:** Hodgkin's disease.**Special Features:****Name: Dacarbazine (DTIC)****Class:** Antineoplastic (Cell Cycle-Nonspecific) (Alkylating Agent)**Mech.:** Alkylates DNA.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** N/V. Leukopenia and thrombocytopenia.**Utility:** Melanoma.**Special Features:****Name: Cisplatin (Platinol)****Class:** Antineoplastic (Cell Cycle-Nonspecific)**Mech.:** Forms coordinate covalent bonds in DNA → inter- and intrastrand crosslinks → inhib. of DNA and RNA synth.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** Major N/V, hearing loss at high end. DLT = kidney toxicity.**Utility:** Curative for testicular tumors. Small cell lung, head, neck tumors.**Special Features:** Prophylaxis w/5HT<sub>3</sub> antagonists (e.g., Ondansetron) may help with N/V. Renal toxicity can be minimized by adequate hydration and production of elevated urine volumes.**Name: Carboplatin (Paraplatin)****Class:** Antineoplastic (Cell Cycle-Nonspecific)**Mech.:** Forms coordinate covalent bonds in DNA → inter- and intrastrand crosslinks → inhib. of DNA and RNA synth.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** Mild N/V. DLT = myelosuppression.**Utility:** Curative for testicular tumors. Small cell lung, head, neck tumors.**Special Features:**

**Name: Doxorubicin (Adriamycin)****Class:** Antineoplastic (Cell Cycle-Nonspecific) (Antibiotic) (Anthracycline)**Mech.:** Intercalation into DNA → stabilization of topoisomerase II-DNA cleavable complexes → DNA breaks. Quinone structure reduced by cyt. P-450 → oxygen radical production → DNA strand breaks.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** Myelosuppression—max. in week 2, recovery in week 4. Radiation recall (hypersensitivity and necrosis in prev. or subseq. irradiated tissue). DLT = cardiomyopathy in 1/3 of pts if total dose exceeds 550 mg/m<sup>2</sup>.**Utility:** One of the most useful cancer drugs. Soft-tissue tumors, osteogenic and other sarcomas, small cell CA of lung, Hodgkin's and non-Hodgkin's lymphomas, acute leukemias, others.**Special Features:****Name: Daunomycin (Daunorubicin)****Class:** Antineoplastic (Cell Cycle-Nonspecific) (Antibiotic) (Anthracycline)**Mech.:** Intercalation into DNA → stabilization of topoisomerase II-DNA cleavable complexes → DNA breaks. Quinone structure reduced by cyt. P-450 → oxygen radical production → DNA strand breaks.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** Myelosuppression—max. in week 2, recovery in week 4. Radiation recall. DLT = cardiomyopathy in 1/3 of pts if total dose exceeds 550 mg/m<sup>2</sup>.**Utility:** AML (+ cytarabine).**Special Features:****Name: Mitoxantrone (Novantrone)****Class:** Antineoplastic (Cell Cycle-Nonspecific) (Antibiotic) (Anthracycline)**Mech.:** Intercalation into DNA → interference w/topoisomerase II-catalyzed breakage-reunion reaction of DNA strands to cause unreparable breaks. Quinone structure reduced by cyt. P-450 → oxygen radical production → DNA strand breaks.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** Myelosuppression—max. in week 2, recovery in week 4. Radiation recall. DLT = cardiomyopathy.**Utility:** One of the most useful cancer drugs. Soft-tissue, osteogenic and other sarcomas, small cell CA of lung, Hodgkin's and non-Hodgkin's lymphomas, acute leukemias, others.**Special Features:** Synthetic doxorubicin with reduced cardiotoxicity.**Name: Dactinomycin (Actinomycin D, Cosmegen)****Class:** Antineoplastic (Cell Cycle-Nonspecific) (Antibiotic)**Mech.:** Intercalation into DNA (small groove between G-C pairs) → stable dactinomycin-DNA complex → interference w/DNA-dependent RNA polymerase.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** N/V. Radiation recall. DLT = bone marrow suppression. Immunosuppression.**Utility:** Choriocarcinoma, Wilm's tumor, others.**Special Features:**

**Name: Mitomycin C (Mutamycin)**

**Class:** Antineoplastic (Cell Cycle-Nonspecific) (Antibiotic) (Quinone)

**Mech.:** DNA alkylation/adduction, formation of oxygen radicals.

**Absorption:**

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** N/V. DLT = bone marrow suppression (cumulative). Very toxic.

**Utility:** Bladder cancer, some GI cancers.

**Special Features:**

**Name: Bleomycin (Blenoxane)**

**Class:** Antineoplastic (Cell Cycle-Specific) (Antibiotic)

**Mech.:** Binds DNA and copper or iron. The metals generate reactive oxygen species → double strand breaks in DNA.

**Absorption:**

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** N/V, skin toxicity. DLT = pulmonary fibrosis at total dose of 400 units (can be fatal).

**Utility:** Testicular tumors (curative), head and neck tumors, cervical tumors, squamous cell CA, lymphomas.

**Special Features:** Myelosuppression is rare.

**Name: 5-FU/5-Fluorouracil (Adrucil)**

**Class:** Antineoplastic (Cell Cycle-Specific) (Antimetabolite) (Pyrimidine Analog)

**Mech.:** Inhibits thymidine synthesis → ↓ DNA synthesis.

**Absorption:**

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** N/V, GI toxicity. DLT = bone marrow suppression.

**Utility:** Solid, slow growing tumors, including breast, colon, ovarian, pancreatic, and gastric carcinomas. Used topically for premalignant skin lesions, basal cell carcinomas.

**Special Features:**

**Name: Cytarabine/ara-C (Cytosar-U)**

**Class:** Antineoplastic (Cell Cycle-Specific) (Antimetabolite) (Pyrimidine Analog)

**Mech.:** Inhibits DNA synthesis.

**Absorption:**

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** GI toxicity, N/V. DLT = bone marrow suppression.

**Utility:** AML. + daunomycin for CML, acute phase.

**Special Features:**

**Name: 6-Mercaptopurine/6-MP (Purinethol)****Class:** Antineoplastic (Cell Cycle-Specific) (Antimetabolite) (Guanine Analog)**Mech.:** Inhibits DNA and protein synthesis.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** N/V. DLT = bone marrow suppression.**Utility:** Maintenance of remission of ALL.**Special Features:****Name: Methotrexate (Amethopterin)****Class:** Antineoplastic (Cell Cycle-Specific) (Antimetabolite) (Folic Acid Analog)**Mech.:** Inhib. dihydrofolate reductase and thymidylate synthase → ↓ DNA synth.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** GI toxicity, N/V. DLT = bone marrow suppression. Renal tubular damage w/↑ doses**Utility:** Curative for choriocarcinoma and osteogenic sarcoma. ALL maintenance. Breast cancer.**Special Features:** Follow treatment w/leucovorin admin. to rescue the bone marrow.**Name: Leucovorin****Class:** Adjunct to Methotrexate Anti-Cancer Chemotherapy**Mech.:** Folinic acid. Converted to N<sup>5</sup>N<sup>10</sup>-methylene FH<sub>4</sub> (reduced folate).  
Bypasses inhibited dihydrofolate reductase (courtesy of methotrexate)  
→ renewed DNA synth.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:****Utility:** Used after methotrexate treatment to rescue patient's bone marrow.**Special Features:****Name: Etoposide (VP-16, Vepesid)****Class:** Antineoplastic (Cell Cycle-Specific) (Podophylin)**Mech.:** Binds topoisomerase II-DNA complex → persistence of transient cleavable form → ↑ susceptibility to irreversible double strand breaks.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** N/V. DLT = bone marrow suppression.**Utility:** Testicular CA, oat cell CA of the lung.**Special Features:**

**Name: Vincristine (Oncovin)****Class:** Antineoplastic (Cell Cycle-Specific) (Vinca Alkaloid)**Mech.:** Binds tubulin → prevention of microtubule formation → block of mitosis in metaphase.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** N/V. Bone marrow suppression. DLT = neurotoxicity.**Utility:** Hodgkin's disease and other lymphomas. ALL in kids, Wilm's tumor, Ewing's soft-tissue sarcomas.**Special Features:****Name: Vinblastine (Velban)****Class:** Antineoplastic (Cell Cycle-Specific) (Vinca Alkaloid)**Mech.:** Binds tubulin → prevention of microtubule formation → block of mitosis in metaphase.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** N/V. DLT = Bone marrow suppression.**Utility:** Hodgkin's disease and other lymphomas, testicular tumors + bleomycin and cisplatin.**Special Features:****Name: Taxol (Paclitaxel)****Class:** Antineoplastic (Cell Cycle-Specific)**Mech.:** Binds tubulin → polymerization and stabilization of microtubules → dysfunctional tubules (i.e., cell locked in metaphase) → cell death.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** DLT = Neutropenia. Severe hypersensitivity rxns.**Utility:** Ovarian and breast cancers.**Special Features:** Vomiting and diarrhea are uncommon.**Name: Prednisone****Class:** Antineoplastic (Hormone) (Corticosteroid)**Mech.:** Suppresses mitosis in lymphocytes.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** Cushingoid symptoms.**Utility:** Acute leukemias in kids, CLL, palliative effects in some adult cancers.**Special Features:**

**Name: Tamoxifen (Nolvadex)****Class:** Antineoplastic (Hormone) (Estrogen Analog)**Mech.:** Antiestrogen → depletion of estrogen receptors.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** Rarely severe. N/V, hot flashes.**Utility:** Estrogen receptor positive breast cancer. Has potential to cause endometrial cancer.**Special Features:****Name: Leuprolide (Lupron)****Class:** Antineoplastic (Hormone) (GnRH Analog)**Mech.:** Occupies GnRH receptor in pituitary → desensitization → inhib. of release of FSH and LH.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** Less toxic than DES. N/V, hot flashes, impotence.**Utility:** Prostatic cancer.**Special Features:****Name: Goserelin (Zoladex)****Class:** Antineoplastic (Hormone) (GnRH Analog)**Mech.:** Occupies GnRH receptor in pituitary → desensitization → inhib. of release of FSH and LH.**Absorption:****Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** Less toxic than DES. N/V, hot flashes, impotence.**Utility:** Prostatic cancer.**Special Features:****Name: Flutamide (Eulixen)****Class:** Antineoplastic (Hormone) (Testosterone Receptor Antagonist)**Mech.:** Binds androgen receptors → block of inhibitory effect of testosterone on gonadotropin secretion → ↑ serum LH and testosterone. Blocks actions of testosterone on prostate gland.**Absorption:** Oral.**Dist.:****Metab.:****Excretion, t<sub>1/2</sub>:****Toxicity/S.E.s:** Gynecomastia, GI distress.**Utility:** Prostatic cancer.**Special Features:** Always administered with leuprolide or goserelin.



**Name:** Interferon  $\alpha$

**Class:** Immunostimulant

**Mech.:** Binds to cell-surface receptors  $\rightarrow$  inhib. of viral replication, inhib. of cell proliferation.

**Absorption:**

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** Fever w/chills; dose-related leukopenia, thrombocytopenia; fatigue, malaise, anorexia, weight loss, alopecia, transient elevation of liver enzymes. High doses may  $\rightarrow$  transient & reversible nephrotoxicity.

**Utility:** IFN  $\alpha$ 2A is approved for mgt. of hairy cell leukemia. Also useful for chronic hepatitis B, virally induced tumors, recurrent varicella zoster, HSV keratitis, Kaposi's sarcoma, cutaneous T cell lymphoma.

**Special Features:** Produced by mononuclear leukocytes. Interferon production is induced by dsRNA (poly I:C), ampligen (mismatched nucleotides), LPS.

**Name:** Bacillus Calumet-Guerin (BCG)

**Class:** Immunostimulant

**Mech.:** Viable strain of Mycobacterium bovis. Enhances M $\phi$  activity, promotes M $\phi$  tumoricidal activity.

**Absorption:**

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:**

**Utility:** Treat bladder carcinoma and melanomas.

**Special Features:**

**Name:** Levamisole (Ergamisol)

**Class:** Slow-Acting Antirheumatic Agent (Veterinary Anti-Helminthic Agent)

**Mech.:** Enhances cell-mediated immune responses ( $\uparrow$  chemotaxis & phagocytosis of PMNs and M $\phi$ s,  $\uparrow$  T cell fxn). How these effects ameliorate RA is unknown.

**Absorption:**

**Dist.:**

**Metab.:**

**Excretion, t<sub>1/2</sub>:**

**Toxicity/S.E.s:** Rash (most common), leukopenia, agranulocytosis, thrombocytopenia, influenza-like illnesses, mouth ulcers, n/v.

**Utility:** Treat rheumatoid arthritis (off-label use). + 5-Fluorouracil for colonic cancer.

**Special Features:**

There is an ancient story that King Midas hunted in the forest a long time for the wise Silenus, the companion of Dionysus, without capturing him. When Silenus at last fell into his hands, the king asked what was the best and most desirable of all things for man. Fixed and immovable, the demigod said not a word, till at last, urged by the king, he gave a shrill laugh and broke out into these words: "Oh, wretched ephemeral race, children of chance and misery, why do you compel me to tell you what it would be most expedient for you not to hear? What is best of all is utterly beyond your reach: not to be born, not to *be*, to be *nothing*. But the second best for you is - to die soon."

- Nietzsche