

CANCER DRUG PHARMACOLOGY TABLE

Cytotoxic Chemotherapy

Drugs are classified according to the BC Cancer Drug Manual Monographs, unless otherwise specified (see asterisks). Subclassifications are in brackets where applicable.

Alkylating Agents have reactive groups (usually alkyl) that attach to DNA or RNA, leading to interruption in synthesis of DNA, RNA, or proteins.

- bendamustine (nitrogen mustard)
- busulfan (alkyl sulfonate)
- carboplatin (platinum)
- carmustine (nitrosurea)
- chlorambucil (nitrogen mustard)
- cisplatin (platinum)
- cyclophosphamide (nitrogen mustard)
- dacarbazine (triazine)
- estramustine (nitrogen mustard with 17-beta-estradiol)
- hydroxyurea
- ifosfamide (nitrogen mustard)
- lomustine (nitrosurea)
- mechlorethamine (nitrogen mustard)
- melphalan (nitrogen mustard)
- oxaliplatin (platinum)
- procarbazine (triazine)
- streptozocin (nitrosurea)
- temozolomide (triazine)
- thiotepa (aziridine)
- treosulfan

Antimetabolites are structural analogues of naturally occurring molecules required for DNA and RNA synthesis. When substituted for the natural body substances, they disrupt DNA and RNA synthesis.

- azacitidine (pyrimidine analogue)
- capecitabine (pyrimidine analogue)
- cladribine (adenosine analogue)
- cytarabine (pyrimidine analogue)
- fludarabine (purine analogue)
- fluorouracil (pyrimidine analogue)
- gemcitabine (pyrimidine analogue)
- mercaptopurine (purine analogue)
- methotrexate (folate analogue)
- pralatrexate (folate analogue)
- pemetrexed (folate analogue)
- pentostatin (purine analogue)
- raltitrexed (folate analogue)
- thioguanine (purine analogue)
- trifluridine-tipiracil (pyrimidine analogue/thymidine phosphorylase inhibitor)

Antimicrotubule Agents (Mitotic Inhibitors) inhibit cell mitosis by interfering with microtubule formation or function.

- cabazitaxel (taxane)
- docetaxel (taxane)
- eribulin
- ixabepilone
- paclitaxel (regular and nanoparticle, albumin-bound) (taxane)
- vinblastine (vinca alkaloid)
- vincristine (vinca alkaloid)
- vinorelbine (vinca alkaloid)

Miscellaneous Antineoplastics - Refer to [BC Cancer monographs for pharmacology](#).

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|--------------------|-----------------|--------------|
| • arsenic trioxide | • dactinomycin | • mitotane |
| • asparaginase | • iniparib | • porfimer |
| • bleomycin | • lurbinectedin | • romidepsin |
| • belinostat | • mitomycin | • vorinostat |

Topoisomerase Inhibitors (I and II) cause DNA strand breaks by disrupting the function of topoisomerase enzymes, which are responsible for regulating the 3-D structure of DNA.

Topoisomerase I

- irinotecan
- topotecan

Topoisomerase II

- amsacrine
- anthracyclines
 - daunorubicin
 - doxorubicin (regular and pegylated liposomal)
 - epirubicin
 - idarubicin
- etoposide
- mitoxantrone
- teniposide

Hormonal Therapies

Antiestrogens oppose the effects of estrogen.

- tamoxifen – partial estrogen antagonist (antagonist on breast tissue, agonist on endometrium, bone and lipids)
- fulvestrant – full estrogen antagonist (no agonist activity)

Antiandrogens opposes the effects of androgens.

- apalutamide

Aromatase Inhibitors (AIs) prevent the final step in the conversion of androgens to estrogens in peripheral tissues.

- anastrozole
- exemestane
- letrozole

Luteinizing Hormone Releasing Hormone (LHRH) Agonists (also known as gonadotropin releasing hormone analogues) initially stimulate the release of luteinizing hormone, which leads to an increase in sex hormones

- bicalutamide
- darolutamide
- enzalutamide – more affinity for androgen receptors and Plus inhibits more steps in the androgen inhibition than other agents in this class
- flutamide
- nilutamide

Androgen Biosynthesis Inhibitors

- abiraterone - selectively inhibits the enzyme (CYP17) that converts pregnenolone and progesterone into testosterone precursors.

Androgens

- testosterone - The exact mode of action for androgen therapy in breast cancer is unclear.

Corticosteroids are thought to act via apoptosis induction.

- dexamethasone
- prednisone

Somatostatin Analogues inhibit exocrine and endocrine secretion of hormones, which is useful for hormone-secreting tumours (e.g., neuroendocrine). Additional mechanisms include modulation of biliary/GI motility and apoptosis inductions.

- lanreotide
- octreotide

Thyrotropin Stimulating Hormone Agonist is a recombinant thyrotropin used for serum thyroglobulin testing in thyroid cancer.

(testosterone, estradiol). Chronic use leads to down-regulation of the LHRH receptors, leading to decreased testosterone in men and estrogen in women.

- buserelin
- goserelin
- leuprolide

Luteinizing Hormone Releasing Hormone (LHRH) Antagonist (also known as gonadotropin releasing hormone antagonist) reduce the release of luteinizing hormone, follicle-stimulating hormone, and consequently testosterone by the testes.

- degarelix

Progestins suppress the release of luteinizing hormone from the pituitary gland and subsequently decrease estrogen levels. Additional mechanisms include binding to progesterone, glucocorticoid, and androgen receptors, resulting in decreased number of estrogen receptors and decreased estrogen and progesterone levels peripherally in target tissues.

- medroxyprogesterone
- megestrol

Prolactin Lowering Agents are dopamine antagonists that decrease hormone production and the size of prolactin-dependent pituitary adenomas by inhibiting the release and synthesis of prolactin from the anterior pituitary.

- bromocriptine
- cabergoline
- quinagolide

- thyrotropin alpha

Immunotherapies

Cytokines are proteins that are involved in the cell signaling that leads to immune responses at sites of inflammation, infection, and trauma. They induce various cellular responses, such as suppression of cell proliferation and augmentation of the cytotoxicity of lymphocytes.

- aldesleukin
- interferon
- peginterferon

Vaccine Therapy

- bacillus calmette-guerin (BCG)
 - a live, attenuated bacteria (*Mycobacterium bovis*) that exerts a variety of antitumour actions, including induction of a local granulomatous reaction, activation of histiocytes, and other direct and indirect stimulation of immune responses. The result is a local inflammatory response that destroys tumour cells.

Immunomodulatory Drugs (IMiDs) have multiple mechanisms of action, including inhibition of proliferation of certain hematopoietic tumour cells, enhancing numbers and activity of T, NK, and NK T cells, and inhibition of angiogenesis.

- lenalidomide
- pomalidomide
- thalidomide

Differentiating Agents are vitamin A derivatives. Their proposed mechanism of action is to overcome impaired cellular differentiation.

- acitretin
- bexarotene
- tretinoin

Other Immunotherapies

- imiquimod – TLR7 agonist
- Monoclonal antibodies could also be considered immunotherapies, particularly those that inhibit CTLA-4, PD-1 or PD-L1 (Checkpoint Inhibitors), or IL-6. They are covered on the pages that follow.

Targeted Therapies

Targeted therapies target receptors, ligands, or intracellular molecules involved in the signal transduction of cancer cells. The following table is a listing of targeted therapies with the target(s) listed in brackets. See the following page for more information on targets. Note that the relative affinity to particular targets is not always clear for each agent, and may differ when used in different indications. Some of the available literature refer to drugs by their target, such as EGFR-inhibitors or multikinase inhibitors for oral drugs with multiple targets (e.g., pazopanib, sorafenib, sunitinib).

| | | |
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| <p>abemaciclib (CDK 4/6) acalabrutinib (BTK) afatinib (EGFR, HER2, HER4) AGS-16C3F (MMAF) (antibody conjugated with cytotoxic) alectinib (ALK) alemtuzumab (CD52) amivantamab (low-fucose IgG1 bispecific antibody binding to EGFR and MET) atezolizumab (PD-L1) avelumab (PD-L1) axitinib (VEGFR 1, 2, & 3) bevacizumab (VEGF) belantamab mafodotin (IgG1) (antibody conjugated with cytotoxic) blinatumomab (CD3 & CD19) bortezomib (26S proteasome) brentuximab vedotin (CD30) (antibody conjugated with cytotoxic) cabozantinib (MET, VEGF, FLT3) carfilzomib (26S proteasome) carotuximab (aka TRC105) (CD105) cemiplimab (PD-1) ceritinib (ALK) cetuximab (EGFR) cobimetinib (MEK) crizotinib (ALK, HGFR, C-Met, ROS1) dabrafenib (BRAF) dacomitinib (EGFR)</p> | <p>dasatinib (BCR-ABL, LYN, HCK, c-kit, EPH, PDGFβ) denosumab (RANKL) dinutuximab (GD2) durvalumab (PD-L1) enfortumab vedotin (Nectin-4)(antibody drug conjugate) erlotinib (EGFR) entrectinib (ROS1 and NTRK) everolimus (MTOR) gefitinib (EGFR) gemtuzumab ozogamicin (CD33) (antibody conjugated with cytotoxic) gilteritinib (FLT-3) ibrutinib (BTK) idelalisib (PI3Kδ) imatinib (BCR-ABL, PDGF, c-KIT) inotuzumab ozogamicin (CD22) (antibody conjugated with cytotoxic) ipilimumab (CTLA-4) Isatuximab (IgG1 antibody) (CD38) lapatinib (EGFR, HER2) lenvatinib (VEGFR, FGFR, PDGFRα, KIT, RET) midostaurin (FLT-3, KIT, PDGFR) mogamulizumab (IgG1.k antibody) nilotinib (BCR-ABL, c-KIT, PDGFR) niraparib (PARP-1, PARP-2) nivolumab (PD-1) obinutuzumab (CD20)</p> | <p>palbociclib (CDK 4/6) pazopanib (VEGFR 1, 2, 3, c-KIT, PDGFR-α,β, c-KIT,FGFR-1 and -3, IL-2, and c-Fms) pembrolizumab (PD-1) pertuzumab (HER2) polatuzumab vedotin (CD79b) (antibody conjugated with cytotoxic) ramucirumab (VEGFR2 and VEGF A, C, and D) regorafenib (VEGFR-1, -2, & -3, TIE2, KIT, RET, RAF-1, BRAF, BRAV600E, PDGFR, FGFR) ribociclib (CDK 4/6) rituximab (CD20) ruxolitinib (JAK 1 & 2) sacituzumab govitecan (IgG1.k antibody conjugated with cytotoxic) siltuximab (IL-6) Sonidegib (Hh) sorafenib (c-Raf,b-Raf, V600E,b-Raf,KIT,FLT-3, VEGFR -2, -3 & -beta) sunitinib (VEGFR 1, 2, & 3, PDGFR α & β), KIT, FLT-3, CSF-1R, RET) temsirelimus (MTOR) tislelizumab (IgG4) (PD-1) tocilizumab (IL-6) trametinib (MEK 1 & 2) trastuzumab (HER2) trastuzumab emtansine (HER2) (antibody conjugated with cytotoxic) vandetanib (VEGFR-2, EGFR, RET)</p> |
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|---|--|---|
| daratumumab (CD38) dasatinib (BCR-ABL, LYN, HCK, c-kit, EPH, | ofatumumab (CD20) olaparib (PARP-1, PARP-2, PARP-3) olaratumab (PDGFR α) osimertinib (EGFR) panitumumab (EGFR) | vemurafenib (BRAF) venetoclax (BCL-2) vismodegib (Hh) |
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The last letters in the drug names in the table provide information about the classification of the drug:

- mab = monoclonal antibody
- zomib = proteasome inhibitor
- nib = kinase inhibitors
- olimus = MTOR inhibitor

Target Listing

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| ALK | Anaplastic Lymphoma Kinase | Translocations in this gene lead to oncogenic fusion proteins that play a role in many cancers, including non-small-cell lung cancer. |
| BCL-2 | B-cell chronic lymphoma 2 | BCL-2 is an anti-apoptotic protein |
| BCR-ABL | Breakpoint Cluster Region – Abelson | This is the fusion protein created by the abnormal Philadelphia chromosome, which characterizes chronic myeloid leukemia. |
| BRAF | BRAF Serine-Threonine Kinase | BRAF plays a role in cell growth, differentiation, and survival. |
| BTK | Bruton’s Tyrosine Kinase | BTK is involved in tumour proliferation, migration, and survival. |
| CD | Cluster Of Differentiation Antigens | CDs are a group of antigens present on the surface of all cells in different combinations, which makes them useful for classifying cells. <ul style="list-style-type: none"> • CD3 is found on T cells • CD19 is found on B cells • CD20 is found on B cells • CD30 is expressed on Hodgkin’s Lymphoma and anaplastic large cell lymphoma cells (16) • CD38 is highly expressed on myeloma cells, but is expressed at low levels on normal lymphoid and myeloid cells |

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| | | <ul style="list-style-type: none"> • CD52 is found on the surface of B and T lymphocytes, most monocytes, macrophages and NK cells, and certain granulocytes • CD105 (endoglin) expression is required for vascular endothelial cell proliferation. Targeting CD105 is a novel approach to inhibiting angiogenesis in cancer cells. |
| CDK 4/6 | Cyclin-dependent kinases | CDK4/6 form complexes with cyclin D to promote phosphorylation of retinoblastoma (Rb) protein, which allows cell cycle progression. |
| C-Kit | Stem Cell Factor Receptor | C-Kit is involved in oncogenesis. 95% of GIST cells have c-Kit mutations. |
| CTLA-4 | Cytotoxic T Lymphocyte-Associated Antigen 4 | CTLA-4 acts as an immune response checkpoint by switching off T-cells. Agents that target CTLA-4 are referred to as Checkpoint Inhibitors. |
| EGFR | Epidermal Growth Factor Receptor (also referred to as HER1) | EGFR is involved in cancer cell proliferation, blocking apoptosis, mobilizing cells to promote metastasis, and angiogenesis. |
| EPH | Ephrin Receptor | EPH may be involved in the development of resistance to imatinib. |
| FGFR | Fibroblast Growth Factor Receptor | FGFR contributes to the maintenance of the tumour microenvironment. |
| FLT3 | FMS-Like Tyrosine Kinase 3 | Like other tyrosine kinase inhibitors, FLT3 competes for the ATP binding site in the active domain of the kinase, which inhibits the ability of the protein to be phosphorylated, and subsequently decreases activity of the protein. |
| GD2 | Disialoganglioside | GD2 is a surface antigen found on the surface of neuroblastoma cells. |
| HER | Human Epidermal Growth Factor (also known as EGFR) | HER2 is overexpressed in about 20% of breast cancers, which leads to increased cell proliferation, cancer spread, and apoptosis inhibition. |
| Hh | Hedgehog Pathway | This pathway is normally dormant in adult tissues, but basal cell carcinomas have gene mutations that activate the Hh pathway, which promotes tumour survival and cancer spread. |
| IgG1 | Immunoglobulin G1 | IgG (1-4) provides the majority of antibody-based immunity and is the main type of antibody in blood and extracellular fluid. |
| JAK | Janus Associated kinase | JAK mediates the signaling pathway of cytokines and growth factors for hematopoiesis and immune function. |
| LYN | Lck/Yes novel tyrosine kinase | LYN is involved in BCR-ABL signaling |
| MEK | Mitogen-Activated Extracellular Signal-Regulated Kinase | MEK1 and MEK2 are involved in cell growth, differentiation, inflammation, and apoptosis. |

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| MTOR | Mammalian Target of Rapamycin | Inhibit cell proliferation and angiogenesis. |
| Nectin-4 | Adhesion protein on surface of cells | (Nectin Cell Adhesion Molecule 4) is a Protein Coding gene. In the antibody–drug conjugate (ADC), human anti-nectin-4 antibody is linked to the cytotoxic microtubule-disrupting agent monomethyl auristatin E |
| NTRK | Neurotrophic tyrosine kinase inhibitor | NTRK (NTRK1, NTRK2, NTRK3) gene fusions are oncogenic drivers of various tumour types. TRK proteins are receptor kinases that help regulate cell signaling and function in healthy tissues. |
| PARP | poly (ADP-ribose) polymerase | Binding to PARP inhibits single stranded DNA base excision repair and creates PARP-DNA complexes that lead to double-stranded DNA breaks, ultimately causing cell death. |
| PD-1 PD-L1 | Programmed Death Receptor 1 and Programmed Death Receptor Ligand 1 | PD-1 receptors are located on T-cells. When ligands bind to PD-1 receptors, they switch off T-cells, which fight cancer. Agents that target PD-1 are referred to Checkpoint Inhibitors. |
| PDGF | Platelet-Derived Growth Factor | PDGF contributes to maintenance of tumour microenvironments. |
| PI3K δ | Phosphoinositide 3-kinase | Active in the signalling pathways of B-cell malignancies |
| Proteasome | Proteasome | Proteasomes degrade cellular proteins targeted for destruction. Inhibition of the proteasome results in cell cycle arrest and apoptosis. |
| RANKL | Receptor Activator Of Nuclear Factor Kappa-B Ligand | RANKL activates osteoclasts, leading to bone resorption. |
| RET | Neurotrophic Factor Receptor | RET is involved in oncogenesis. |
| TLR7 | Toll-like receptor 7 | TLR7 stimulates innate and cell-mediated immunity to induce antitumour effects, including the increased production of inflammatory cytokines, such as tumour necrosis factor- α (TNF α), interferon- α , and interleukin-12. |
| VEGF VEGFR | Vascular Endothelial Growth Factor and Vascular Endothelial Growth Factor Receptor | VEGF and VEGFR are involved in the development of a tumour blood supply (angiogenesis). |

References

1. BC Cancer Agency. Cancer Drug Manual Drug Index [Internet]. Vancouver, British Columbia [updated continuously]. Available from: <http://www.bccancer.bc.ca/health-professionals/professional-resources/cancer-drug-manual/drug-index>.
2. Oncology Practice Essentials: Oncology Basics [Internet]. Canadian Association of Pharmacy in Oncology (CAPHO) [updated 2016 January]. Available from: <http://www.capho.org/oncology-practise-essentials-oncology-basics-new>.
3. OnTarget Resource Guide: Common Side Effects of Targeted Therapy [Internet]. Quebec: Groupe d'étude en oncologie du Québec (GEOQ) [updated 2015]. Available from: <http://www.capho.org/ontarget-resource-guide>.
4. BC Cancer Agency. Chemotherapy Protocols [Internet]. Vancouver, British Columbia [updated continuously]. Available from: <http://www.bccancer.bc.ca/health-professionals/professional-resources/chemotherapy-protocols>.
5. Mandal, A. What are Cytokines? [Internet]. News-Medical.net [updated 2013 Dec 2]. Available from: <http://www.news-medical.net/health/What-are-Cytokines.aspx>.
6. Callens C, Coulon S, Naudin J, Radford-Weiss I, Boissel N, Raffoux E, et al. Targeting iron homeostasis induces cellular differentiation and synergizes with differentiating agents in acute myeloid leukemia. *J Exp Med*. 2010 Apr 12;207(4):731-50.
7. Wikipedia contributors. Cluster of differentiation [Internet]. Wikipedia, The Free Encyclopedia [updated 2016 Nov 7; cited 2016 Dec 8]. Available from: https://en.wikipedia.org/w/index.php?title=Cluster_of_differentiation&oldid=748390638.
8. BC Cancer Agency Systemic Therapy Update: Available from: <http://www.bccancer.bc.ca/health-professionals/clinical-resources/systemic-therapy/systemic-therapy-update>.
9. Wikipedia contributors. Philadelphia Chromosome [Internet]. Wikipedia, The Free Encyclopedia [updated 2016 July 6; cited 2016 Dec 8]. Available from: July 6, 2016, 17:46 UTC. Available at: https://en.wikipedia.org/w/index.php?title=Philadelphia_chromosome&oldid=728644023.