

Table 18.2 Chemotherapy Medications

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
Antimetabolites: Inhibit DNA action or replication.				
Cytarabine (Cytosine, Cytosine arabinoside, Ara-C)	Acute myelogenous leukemia, acute lymphocytic leukemia, chronic myelogenous leukemia, leptomeningeal carcinomatosis, non-Hodgkin's lymphoma	Dosing varies with protocol. Reduce dose with renal and hepatic dysfunction. Metabolized by deamination in liver, plasma, and peripheral tissues; half-life is 2-6 h.	Cog: +++ S: + A: + Motor: +++ D: +++ Com: +++ F: +++	DLT: Myelosuppression. Mild nausea with lower-dose regimens, alopecia (common). With high doses >1 g/m ² : Severe nausea, neurotoxicity, dysarthria, nystagmus, ataxia, encephalopathy, seizures, chemical conjunctivitis; CNS, ocular, hepatic, dermatologic, and pulmonary toxicity. Other: Use steroid eye drops and saline eye drops to prevent ocular toxicity. Drug interactions: Antagonizes activity of gentamicin and 5-FU; decreases levels and activity of digoxin. Enhances cytotoxicity of alkylating agents. Pretreatment with methotrexate, fludarabine, and hydroxyurea enhances activity. Granulocyte- and monocyte-stimulating factors and interleukin-3 potentiate cytotoxic effects. Increased risk of pancreatitis when L-asparaginase is given before cytarabine.
Gemcitabine (Gemzar)	Pancreatic cancer, non-small-cell lung cancer, breast cancer, ovarian cancer, bladder cancer, soft-tissue sarcoma	Dosing varies with protocol. Hold medication with elevated bilirubin.	Cog: ++ S: ++ A: 0 Motor: 0 D: + Com: + F: ++	DLT: Myelosuppression, with WBCs affected to a greater extent than platelets. Nadir on days 10-14; recovery by day 21. Others: Infusion reactions are related to infusion rate and include flushing, facial swelling, headache, dyspnea, hypotension, elevated LFTs, proteinuria, mild hematuria (50%). Flu-like syndrome 6-12 h after dose (20%), rash 2-3 days after administration (25%), mild to moderate nausea and vomiting (70%), diarrhea or mucositis (15%-20%), pulmonary toxicity, dyspnea, pneumonitis, maculopapular skin rash (trunk and extremities with pruritus). Potent radiosensitizer. Drug interactions: Enhances cytotoxicity of cisplatin. Etoposide may enhance cytotoxicity.

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
6-Mercaptopurine	Acute lymphoblastic leukemia	Dosing varies with protocol. Reduce dose with renal or hepatic dysfunction.	Cog: + S: + A: 0 Motor: 0 D: ++ Com: + F: +	Mild bone marrow suppression with WBC nadir days 10-14; recovery by day 21; mucositis or diarrhea with higher doses; elevated serum bilirubin, liver enzymes, jaundice (onset occurs 2-3 mo after therapy). Other: Elevated serum bilirubin and liver enzymes; mild nausea and vomiting (dose related). Drug interactions: Reduce dose by 50% when combined with allopurinol. Inhibits anticoagulant effects of warfarin (Coumadin). Bactrim DS may enhance myelosuppressive effects.
6-Thioguanine (6-TG)	Acute and chronic myelogenous leukemia, acute lymphoblastic leukemia	Dosing varies with protocol. No dosage reduction required with renal or liver dysfunction. Metabolized in the liver; metabolites eliminated in feces and urine. Half-life is 80-90 min.	Cog: ++ S: ++ A: 0 Motor: 0 D: +++ Com: + F: ++	DLT: Myelosuppression where leukopenia precedes thrombocytopenia; nadir is 10-14 days; recovery by day 21. Severe mucositis and diarrhea. Other: Elevated serum bilirubin and liver enzymes; mild nausea and vomiting (dose-related). Drug interactions: None known.
5-Fluorouracil (5-FU) (Efudex)	Cell cycle specific, active in S phase. Used in colorectal, breast, GI, head and neck, liver, ovarian, skin cancers	Dosage varies with protocol.	Cog: +++ S: +++ A: +++ Motor: +++ D: +++ Com: ++ F: +++	DLT: Myelosuppression, mucositis, diarrhea, neurotoxicity (head-foot syndrome, ataxia, seizures). Use pyridoxine 50 mg bid prophylaxis to reduce neurotoxic effects. Others: Ischemia in patients with cardiac disease, conjunctivitis, blepharitis, skin discoloration, metallic taste. Drug interactions: Leucovorin enhances activity, toxicity. Methotrexate pretreatment increases 5-FU metabolite formation and effects. Thymidine or vistonuridine rescue patient from toxic effects of 5-FU.
Fludarabine monophosphate (F-ara-A, Fludara)	Chronic lymphocytic leukemia, non-Hodgkin's lymphoma	Dosing varies with protocol. Prophylaxis with Bactrim is required.	Cog: +++ S: +++ A: +++ Motor: +++ D: +++ Com: ++ F: +++	DLT: Myelosuppression with WBC nadir is 10-13 days; recovery by days 14-21. Immunosuppression common with decreased CD4+ and CD8+ T-cells. Recovery of CD4+ count is slow and may take more than 1 yr to return to normal. With high dose: Weakness, agitation, confusion, progressive encephalopathy, cortical blindness, seizures, coma.

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
				<p>Other: Tumor lysis syndrome (1%-2%), hypersensitivity reaction (maculopapular skin rash, erythema, pruritus), reversible interstitial pneumonitis after several courses of therapy, neurotoxicity (somnolence, mild peripheral neuropathy, paresthesias, visual disturbances), autoimmune hemolytic anemia (rare), drug-induced aplastic anemia (rare). Fever, fatigue, malaise, myalgias, arthralgias, and chills (20%-30%) 5-7 days after dose due to release of pyrogens from tumor cells.</p> <p>Drug interactions: Enhances the antitumor activity of cytarabine, cyclophosphamide, cisplatin, and mitoxantrone. Increases incidence of fatal pulmonary toxicity when used with pentostatin. Use of this combination is absolutely contraindicated.</p>
Cladribine (Leustatin)	Hairy cell leukemia, chronic lymphocytic leukemia, non-Hodgkin's lymphoma	Dosing varies with protocol.	Cog: ++ S: ++ A: + Motor: ++ D: + Com: ++ F: ++	<p>DLT: Myelosuppression with WBC nadir is 7-14 days; recovery in 3-4 wks. Immunosuppression with decrease in CD4+ and CD8+ cells and increased risk of opportunistic infections. Recovery of CD4+ takes up to 40 months.</p> <p>Other: Erythema, pain, pruritus, swelling at injection site, neurotoxicity (headache, insomnia, dizziness). Fever, fatigue, malaise, myalgias, arthralgias, and chills occur in 40%-50% of patients on days 5-7 of therapy.</p> <p>Drug interactions: None known.</p>
Methotrexate (MTX, Trexall, Rheumatrex)	Breast cancer, head and neck cancer, osteogenic sarcoma, acute lymphoblastic leukemia, non-Hodgkin's lymphoma, meningeal leukemia, bladder cancer, colorectal cancer, gestational cancer, trophoblastic cancer	Dosing varies with protocol.	Cog: ++ S: ++ A: + Motor: ++ D: +++ Com: ++ F: ++	<p>DLT: Myelosuppression and mucositis. Mucositis occurs 3-7 days after dose. Mucosal ulceration can be life threatening and can require dose interruption. Renal toxicity is prevented with vigorous hydration and IV administration of bicarbonate and leucovorin rescue to prevent crystallization in the renal tubules. Leucovorin rescues the host toxic effects of methotrexate but may impair antitumor activity.</p> <p>Other: Mild nausea and vomiting, photosensitivity, eye discomfort, allergic reactions; hepatic, renal, neurologic, and pulmonary toxicities (can be fatal). Symptoms of pulmonary toxicity are fever, dry cough, dyspnea, and chest pain. CNS toxicities include chemical arachnoiditis (headache, nuchal rigidity,</p>

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
				<p>vomiting, fever) with initial doses, motor paralysis, cranial nerve palsy, seizures, and coma in wk 2-3.</p> <p>Irreversible chronic demyelinating encephalopathy with dementia, spasticity, and coma can occur months or years after treatment (usually occurs with cranial irradiation).</p> <p>Drug interactions: Cisplatin decreases elimination.</p> <p>Aspirin, penicillins, probenecid, nonsteroidal anti-inflammatory drugs, cephalosporins, and phenytoin inhibit renal excretion, increasing toxicity.</p> <p>Increases anticoagulant effect of warfarin (Coumadin).</p> <p>Enhances antitumor activity of 5-fluorouracil when given 24 h before fluoropyrimidine treatment.</p> <p>Thymidine rescues the host toxic effects of methotrexate, causing impaired antitumor activity.</p> <p>Folic acid supplements may counteract the antitumor effects.</p> <p>Omeprazole increases serum methotrexate levels, leading to enhanced antitumor activity and host toxicity.</p> <p>L-asparaginase antagonizes the antitumor activity of MTX.</p>
<p>Microtubule-targeting alkaloids: Vinca alkaloids are mitotic inhibitors that reduce cell replication and cause apoptosis.</p> <p>Taxane alkaloids, which have antimetabolic effects by microtubule polymerization in the mitotic phase of tumor cell replication, induce angiogenesis and promote cell death.</p>				
Vinca alkaloid: Vincristine (Oncovin)	Acute lymphoblastic leukemia, Hodgkin's and non-Hodgkin's lymphoma, multiple myeloma, rhabdomyosarcoma, neuroblastoma, Ewing's sarcoma, Wilms' tumor, chronic leukemias, thyroid cancer, brain tumors, trophoblastic neoplasm	Dosing varies with protocol. Maximum dose of 2 mg.	<p>Cog: ++</p> <p>S: ++</p> <p>A: +</p> <p>Motor: +++++</p> <p>D: +++++</p> <p>Com: ++</p> <p>F: +++++</p>	<p>DLT: Dose-limiting toxicity is neurotoxicity (distal, symmetric; affects sensation and motor function; earliest symptoms are depressed deep-tendon reflexes, paresthesias of the fingers and toes, and cranial nerve toxicities of hoarseness, facial palsies, and jaw pain).</p> <p>Autonomic neuropathy, constipation, colicky abdominal pain, orthostasis, paralytic ileus, cranial nerve palsies (ataxia, cortical blindness, seizures, coma), and pain in the bone, back, limb, jaw, and parotid gland. Alopecia, skin rash, fever; a prophylactic bowel regimen for neurotoxicity-associated constipation is recommended.</p> <p>Other: SIADH form of hyponatremia.</p> <p>Vesicant; treat with warm compresses if extravasation occurs.</p> <p>Drug interactions: Occur with medications</p>

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
				<p>metabolized by the CYP 3A liver enzymes. Reduces the blood levels of phenytoin and digoxin.</p> <p>Concurrent administration with other neurotoxins (cisplatin, paclitaxel) increases neurotoxicity.</p> <p>Should be administered 12-24 hrs before L-asparaginase when used in combination; L-asparaginase inhibits vincristine clearance and increases its toxicity.</p> <p>Increases the cellular uptake of methotrexate, resulting in enhanced antitumor activity and host toxicity.</p> <p>Concurrent use with filgrastim may result in severe atypical neuropathy.</p>
<p>Vinca alkaloids:</p> <p>Vinblastine (Velban)</p> <p>Vinorelbine (Navelbine)</p>	<p>Hodgkin's and non-Hodgkin's lymphomas, testicular cancer, breast cancer, Kaposi's sarcoma, renal cell carcinoma</p>	<p>Dosage varies with protocol.</p>	<p>Cog: ++</p> <p>S: ++</p> <p>A: +</p> <p>Motor: ++++</p> <p>D: ++++</p> <p>Com: ++</p> <p>F: ++++</p>	<p>DLT: Myelosuppression with WBC nadir at days 4-6.</p> <p>Neurotoxicity presents with the same manifestations as seen with vincristine. Peripheral neuropathy (paresthesias, paralysis, loss of deep-tendon reflexes, constipation) and dysfunction of the autonomic nervous system (orthostatic hypotension, paralytic ileus, urinary retention).</p> <p>Other: Mucositis, stomatitis, nausea, vomiting, anorexia, diarrhea, alopecia (common, mild, and reversible), SIADH, headache, depression, vascular events (stroke, myocardial infarction, Raynaud's syndrome).</p> <p>Less common: Cranial nerve paralysis, ataxia, cortical blindness, seizures, coma.</p> <p>Vesicant; treat with warm compresses if extravasation occurs.</p> <p>Drug interactions: Occur with medications that are metabolized by CYP 3A liver enzymes, such as the calcium channel blockers, cimetidine, cyclosporine, erythromycin, metoclopramide, and ketoconazole.</p> <p>Reduces blood levels of phenytoin through either reduced absorption of phenytoin or an increase in the rate of its metabolism and elimination.</p> <p>Risk of Raynaud's syndrome increases when combined with bleomycin.</p>
<p>Taxane alkaloid:</p> <p>Paclitaxel (Taxol)</p>	<p>Ovarian cancer, breast cancer, non-small-cell and small-cell lung cancer, head and neck</p>	<p>Dosing varies with protocol. Reduce dose in patients with elevated</p>	<p>Cog: ++</p> <p>S: ++</p> <p>A: 0</p> <p>Motor: +++</p> <p>D: +++</p>	<p>DLT: Myelosuppression with WBC nadir at days 8-10; recovery by day 15-21; nadir is decreased with shortened infusion.</p> <p>Cumulative and dose-dependent neurotoxicity (sensory neuropathy with</p>

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
	cancer, esophageal cancer, prostate cancer, bladder cancer, Kaposi's sarcoma related to acquired immune deficiency syndrome	bilirubin or elevated liver enzymes.	Com: ++ F: +++	<p>numbness and paresthesias, motor and autonomic neuropathy); more frequent with longer infusions and at doses >175 mg/m².</p> <p>Other: Bradycardia (30% of patients), alopecia (all patients; total loss of hair), mucositis or diarrhea (30%-40%).</p> <p>Hypersensitivity (skin rash, flushing, erythema, hypotension, dyspnea, bronchospasm) occurs in first 2-10 min of an infusion in 30%-60% of patients due to the Camphor-EL vehicle. Pretreatment reduces hypersensitivity reaction incidence to 2%-4%.</p> <p>Pretreatment regimen: Decadron 20 mg given by mouth or by IV at 12 h and at 6 h prior to the dose hour plus Benadryl 50 mg IV and oral cimetidine 300 mg given 30-60 minutes before the chemo dose.</p> <p>Radiosensitizing agent.</p> <p>Drug interactions: Concomitant use of inhibitors or activators of CYP3A4 liver enzymes may affect metabolism levels and toxicity.</p> <p>Phenytoin and phenobarbital increase metabolism.</p> <p>Myelosuppression increases when a platinum compound or cyclophosphamide is administered before paclitaxel. Must be given first when administered with platinum analog.</p> <p>Decreases clearance of doxorubicin by 30%-35%; administer after doxorubicin to reduce severity of neutropenia.</p>
Taxane alkaloid: Docetaxel (Taxotere)	Breast cancer, locally advanced or metastatic breast cancer, non-small-cell lung cancer, small-cell lung cancer, head and neck cancer, gastric cancer, refractory ovarian cancer, bladder cancer. Antimitotic effects by microtubule polymerization that prevent tumor cell replication and induce angiogenesis promoting cell	Dosing varies with protocol. Reduce dose in patients with elevated bilirubin or elevated liver enzymes.	Cog: +++ S: +++ A: 0 Motor: ++++ D: ++++ Com: ++ F: +++	<p>DLT: Myelosuppression with WBC nadir at days 7-10 and recovery by day 14.</p> <p>Cumulative peripheral neuropathy (sensory, motor neuropathy, autonomic neuropathy, and CNS effects).</p> <p>Others: Hypersensitivity reactions associated with the Camphor-EL vehicle (severe <5%); skin rash, erythema, hypotension, dyspnea, bronchospasm; usually occurs in first 2-10 min of an infusion with first 2 treatments; reduced with weekly dosing regimens. Pretreat with dexamethasone (Decadron) 80 mg by mouth every 12 h starting 24 h before dose and continued every 12 h after dose for 3 more days.</p> <p>Fluid-retention syndrome (50%): Weight gain, peripheral or generalized edema,</p>

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
	death.			<p>pleural effusion, ascites. Incidence increases with total doses >400 mg/m². Pretreat with steroid to prevent edema and allergic reactions.</p> <p>Phlebitis, swelling at the injection site, maculopapular skin rash (50% in first week), alopecia (up to 80% of patients), mucositis or diarrhea (40% of patients), generalized fatigue, arthralgias, myalgias and asthenia (60-70%), reversible elevations in liver enzymes and bilirubin, fever (30%).</p> <p>Vesicant.</p> <p>Radiosensitizing agent.</p> <p>Drug interactions: Medications metabolized by CYP3A4 liver enzymes such as cyclosporine, ketoconazole, and erythromycin alter metabolism, blood levels, and toxicity of the taxanes.</p>
Podophyllin derivatives cause breakage of DNA strands by inhibiting double-stranded DNA repair enzyme topoisomerase II, resulting in tumor cell death.				
Podophyllotoxin derivative: Etoposide (Toposar, Vepesid)	<p>Germ cell tumors, small-cell lung cancer, non-small-cell lung cancer, non-Hodgkin's lymphoma, gastric cancer.</p> <p>Active against tumor cells in DNA synthesis or second gap phases.</p>	<p>Dosing varies with protocol. Most effective given in divided doses over several days. 40-60% eliminated unchanged in urine and metabolized by the liver; dosing adjustments recommended for liver or renal dysfunction.</p>	<p>Cog: + S: + A: 0 Motor: + D: + Com: ++ F: +</p>	<p>DLT: Infusion reactions; propylene glycol vehicle contributes to infusion reaction. Orthostasis can be prevented with slowed infusion over 30-60 min.</p> <p>Others: Metallic taste during infusion, reaction at local injection site, radiation recall skin changes.</p> <p>Drug interactions: Prolongs INR with warfarin (Coumadin) therapy.</p>
Teniposide (Vumon)	<p>Acute lymphoblastic leukemia.</p> <p>Active against tumor cells in DNA synthesis or second gap phases.</p>	<p>Orthostasis prevented with slow infusion over 30-60 min. Most effective given in divided doses over several days. 90% metabolized by liver; no dosing adjustments for liver dysfunction.</p>	<p>Cog: ++ S: ++ A: 0 Motor: 0 D: ++ Com: + F: ++</p>	<p>DLT: Myelosuppression is dose-limiting toxicity. Neutrophil nadir is 7-10 days; recovery by day 21.</p> <p>Severe, life-threatening hypersensitivity reactions (tachycardia, bronchospasm, facial and tongue swelling, hypotension chills, fever, flushing, urticaria) can occur. Camphor-EL vehicle contributes to allergic reactions.</p> <p>Mucositis may be dose limiting with high-dose regimens.</p> <p>Other: Diarrhea; prevent dose-associated diarrhea with atropine. Treat delayed-onset diarrhea with loperamide (Imodium) 4 mg</p>

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
				at symptom onset, then 2 mg every 2 h until no bowel movement for 12 h. Reaction at local injection site, mild nausea and vomiting (30%; pretreat for nausea and vomiting), alopecia (10%-30%). Drug interactions: Incompatible with heparin; precipitates can form.
Camptothecin alkaloids: Cause breakage of DNA strands by inhibiting single-stranded DNA repair enzyme topoisomerase I.				
Irinotecan (Camptosar)	Colorectal cancer, non-small-cell lung cancer, small-cell lung cancer	Dosing varies with protocol. Eliminated by biliary secretion; reduce dose with elevated bilirubin to reduce myelosuppression and gastrointestinal toxicity.	Cog: ++ S: ++ A: 0 Motor: 0 D: ++++ Com: + F: ++	DLT: Myelosuppression with WBC nadir is 7-10 days; recovery by days 21-28. Dose-limiting diarrhea, early and late forms. Early form occurs within 24 h with flushing, diaphoresis, abdominal pain, and diarrhea. Late form occurs 3-10 days after treatment (severe and prolonged with dehydration and electrolyte imbalance in 20%). 80%-90% of patients experience late diarrhea. Other: Mild alopecia, rash, low-grade fevers, malaise, elevated liver enzymes, eosinophilia (20%), severe nausea and vomiting. Drug interactions: None known.
Topotecan (Hycamtin)	Ovarian cancer, small-cell lung cancer, acute myelogenous leukemia	Dosing varies with protocol. 50% renal elimination; reduce dose for renal dysfunction.	Cog: + S: + A: 0 Motor: ++ D: +++ Com: + F: ++	DLT: Myelosuppression is dose limiting with WBC nadir at days 7-10; recovery by days 21-28. Others: Headache, fever, malaise, arthralgias, myalgias, alopecia, mild to moderate nausea and vomiting (60-80%; dose related). Drug interactions: None known.
Anthracycline antibiotics and anthracenediones: Cause breakage of DNA strands by inhibiting double-stranded DNA repair enzyme topoisomerase II; bind with iron to form free radicals that cleave DNA.				
Anthracycline antibiotic: Doxorubicin (Adriamycin)	Breast cancer, Hodgkin's and non-Hodgkin's lymphomas, soft tissue sarcoma, ovarian cancer, non-small-cell and small-cell lung cancers, bladder cancer, thyroid cancer, hepatoma, gastric cancer, Wilms' tumor, neuroblastoma, acute lymphoblastic leukemia	Chronic cardiomyopathy line limits cumulative dose to >550 mg/m ² ; 50% incidence with doses >1000 mg/m ² . Extensive tissue binding; half-life is 20-30 h, detectable months after administration. Metabolized by liver to active alcohol metabolites; excreted in the	Cog: ++ S: ++ A: 0 Motor: 0 D: +++ Com: + F: ++	DLT: Cardiotoxicity; acute, chronic, and late onset. Acute; ST wave changes, tachycardia, and PVC can occur with dose. Chronic cardiomyopathy limits cumulative dose to >550 mg/m ² ; 50% incidence with doses >1000 mg/m ² . Liposomal forms produce less cardiotoxicity. Cardiac monitoring of ejection fraction is recommended. Cardiotoxic effects inhibited by dexrazoxane (Zinecard). Small weekly doses or continuous infusion for 2-4 days markedly decrease cardiotoxicity. Late onset (5-20 yr after treatment); progressive left ventricular dysfunction, arrhythmias, sudden death. Myelosuppression with WBC nadir at days 10-14; recovery by day 21. Mucositis and diarrhea (dose limiting with infusion protocols).

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
		bile (small amount eliminated in the urine). Reduce dose with elevated bilirubin levels.		Others: Red–orange discoloration of urine within 1-2 days after dose, mild nausea and vomiting (50% in first 1-2 h of dose; premedicate for nausea and vomiting), alopecia in all (reverses in 3 mo), dermatologic flare at site during infusion, radiation recall skin reaction, acute myeloid leukemia. Extravasation is associated with significant tissue damage; application of ice is recommended. Drug interactions: Incompatible with dexamethasone, 5-fluorouracil, and heparin; leads to precipitate formation. Increased risk of hemorrhagic cystitis and cardiotoxicity when combined with cyclophosphamide. Levels decreased when used with barbiturates and phenytoin. Increased cardiotoxicity when used with herceptin or mitomycin C. Decreases oral bioavailability of digoxin. Increased risk of hepatotoxicity when used with 6-mercaptopurine.
Anthracycline antibiotic: Daunorubicin (Cerubidine)	Acute myelogenous leukemia (remission induction and relapse), acute lymphoblastic leukemia (remission induction and relapse)	Dosing varies with protocol. Extensive tissue binding; half-life is 20-30 h; detectable months after administration. Metabolized by liver to active alcohol metabolites; excreted in the bile (small amount eliminated in the urine). Reduce dose with elevated bilirubin levels.	Cog: ++ S: ++ A: 0 Motor: 0 D: +++ Com: + F: ++	DLT: Myelosuppression with WBC nadir at 10-14 days; recovery by day 21. Cardiotoxicity; acute, chronic, and delayed. Acute occurs within the first 2-3 days as arrhythmias and electrocardiography changes; transient and asymptomatic. Chronic cardiomyopathy and CHF can limit cumulative dose to >550 mg/m ² ; 50% incidence with doses >1000 mg/m ² . Delayed (5-20 yr after treatment); progressive left ventricular dysfunction, arrhythmias, and sudden death. Mucositis can be dose limiting in infusion protocols. Others: Nausea and vomiting (usually mild; 50% in first 1-2 h of dose; premedicate for nausea and vomiting), photosensitivity, hyperpigmentation of nails, skin rash (rare), urticaria, alopecia (occurs in all; reverses 5-7 wk after treatment), red–orange discoloration of urine (lasts 1-2 days after administration), radiation recall skin reaction. Drug interactions: Incompatible with dexamethasone and heparin; precipitate will form.
Anthracycline antibiotic:	Acute myelogenous leukemia, acute	Dosing varies with protocol.	Cog: ++ S: ++	DLT: Cardiotoxicity; acute, chronic, and late onset. Acute; ST wave changes,

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
Idarubicin (Idamycin)	lymphoblastic leukemia, chronic myelogenous leukemia in blast crisis, myelodysplastic syndromes (MDS)	Extensive tissue binding with half-life of 20-30 h; levels detectable months after administration. Metabolized by liver; metabolites are excreted in bile. Reduce dose with elevated bilirubin levels.	A: 0 Motor: 0 D: +++ Com: + F: ++	tachycardia, and PVC can occur with dose. Chronic cardiomyopathy can limit cumulative doses >550 mg/m ² ; 50% incidence with doses >1000 mg/m ² . Late onset (5-20 yr after treatment); progressive left ventricular dysfunction, arrhythmias, and sudden death. Preventative IV administration of dexrazoxane reduces cardiotoxicity. Monitoring of ejection fraction is recommended. Small weekly doses or continuous infusion for 2-4 days markedly decrease cardiotoxicity. Myelosuppression with WBC nadir at 10-14 days; recovery by day 21. Mucositis and diarrhea may be dose limiting in infusion protocols. Others: Moderate to severe nausea and vomiting (80-90%; premedicate for nausea and vomiting), alopecia (occurs in all; reversible), photosensitivity, mucositis and diarrhea (common but not severe), reversible effects on liver enzymes, red discoloration of urine in first 1-2 days of dose, radiation recall skin reaction. Drug interactions: Avoid combining with probenecid or sulfinpyrazone to avoid uric acid nephropathy. Incompatible with heparin; precipitates can form.
Anthracycline antibiotic: Epirubicin (Ellence)	Breast cancer, metastatic breast cancer, gastric cancer	Dosing varies with protocol. Extensive tissue binding with half-life of 20-30 h; levels detectable months after administration. Metabolized by liver; metabolites are excreted in the bile and urine. Reduce dose with elevated bilirubin levels.	Cog: ++ S: ++ A: 0 Motor: 0 D: ++ Com: + F: ++	DLT: Myelosuppression with WBC nadir at 8-14 days; recovery by day 21. Cardiotoxicity; acute, chronic, and late onset. Acute; ST wave changes, tachycardia, PVC, chest pain, and myopericarditis can occur within 24-48 h of dose. Chronic can limit cumulative dose >550 mg/m ² ; 50% incidence with doses >1000 mg/m ² . Chronic form of cardiotoxicity presents as a dilated cardiomyopathy with congestive heart failure. Risk increases significantly with cumulative doses >900 mg/m ² . Late onset (5-20 yr after treatment); progressive left ventricular dysfunction, arrhythmias, and sudden death. Preventative IV administration of dexrazoxane reduces cardiotoxicity. Monitoring of ejection fraction is recommended. Continuous infusion and weekly schedules decrease risk of cardiotoxicity. Others: Mild nausea and vomiting (premedicate for nausea and vomiting),

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
				mild mucositis and diarrhea (common and dose dependent), alopecia (25%-50%; occurs within 10 days of dose; reverses with discontinuance), red-orange discoloration of urine for 24 h after dose, radiation recall skin reaction. Potent vesicant. Extravasation is associated with significant tissue damage. Apply ice. Drug interactions: Incompatible with heparin; precipitates can form. Increased myelosuppression when used with 5-FU or cyclophosphamide. Cimetidine reduces levels and effects by 50%.
Anthracenedione: Mitoxantrone (Novantrone)	Hodgkin's disease, non-Hodgkin's lymphoma	Dosing varies with protocol.	Cog: ++ S: ++ A: 0 Motor: 0 D: + Com: + F: +	DLT: Myelosuppression with WBC and platelet nadirs at day 7-10; recovery by day 21. Severe nausea and vomiting can be dose limiting in first 3 h after drug administration and last 4-24 h. Premedicate for nausea and vomiting. Others: Pain, inflammation, and necrosis at injection site. Reduced cardiotoxicity and less ulceration with extravasation. Nausea, vomiting, alopecia, and mucositis are less severe than with the anthracycline antibiotics. Powerful vesicant.
Alkylating agents: Highly reactive alkyl groups; covalently bind with nucleic acids in proteins, causing cross-linking of DNA and inhibition of DNA synthesis. Nitrogen mustard derivatives and nitrosoureas that transform into alkylating agents.				
Nitrogen mustard alkylating agent: Cyclophosphamide (Cytoxan)	Breast cancer, non-Hodgkin's lymphoma, chronic lymphocytic leukemia, ovarian cancer, bone and soft-tissue sarcoma, rhabdomyosarcoma, neuroblastoma, Wilms' tumor	Dosing varies with protocol. Activated by hepatic oxidase enzymes; half-life is 7 h; 15% eliminated unchanged in the urine. Reduce dose for renal dysfunction with creatinine clearance <25 ml/min. Cleared with hemodialysis.	Cog: + S: + A: 0 Motor: 0 D: + Com: + F: +	DLT: Myelosuppression with WBC. Leukopenia nadir at 7-14 days; recovery by day 21. Dose-limiting hemorrhagic cystitis (5%-10% of patients). Time of onset is variable and may begin within 24 h of therapy or may be delayed for up to several weeks. Usually reversible upon discontinuation of drug. Minimized with prehydration with at least 3 L of fluid before the dose (low-dose regimens) or with prehydration and Mesna administration (high-dose regimens; mandatory to prevent bladder toxicity). Continuous bladder irrigations may also be useful. Others: Dose-related nausea and vomiting (severe with high-dose regimens; onset is within 2-4 h of dose and lasts up to 24 h; premedicate for nausea and vomiting), dose-related alopecia (severe with high-dose regimens; occurs 2-3 wk after dose), hyperpigmentation of skin and nails,

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
				<p>anorexia, cardiotoxicity (observed with high-dose therapy), immunosuppression, SIADH, hypersensitivity reaction (rhinitis, irritation of the nose and throat), thrombocytopenia (usually with high-dose therapy), nephrotoxicity (may occur with high-dose regimens).</p> <p>Drug interactions: Phenobarbital, phenytoin, and other drugs that stimulate the liver P450 system increase the rate of metabolic activation of cyclophosphamide to its toxic metabolites.</p> <p>Increases the effect of anticoagulants; may need to decrease dose of anticoagulants depending on coagulation parameters.</p> <p>Decreases plasma levels of digoxin by activating its metabolism in the liver.</p> <p>May increase risk of doxorubicin-induced cardiotoxicity.</p>
Nitrogen mustard alkylating agent: Ifosfamide (Mitoxana, Ifex)	Recurrent germ cell tumors, soft-tissue sarcoma, osteogenic sarcoma, non-Hodgkin's lymphoma, Hodgkin's disease, non-small-cell and small-cell lung cancers, bladder cancer, head and neck cancer, cervical cancer, Ewing's sarcoma	<p>Dosing varies with protocol. Reduce dose for renal dysfunction with creatinine clearance <25 ml/min.</p> <p>Activated by hepatic oxidase enzymes; half-life is 7 h; 20%-50% eliminated unchanged (not metabolized) in the urine.</p> <p>Distributes into the CNS so is useful in eradicating CNS metastases or tumors.</p>	<p>Cog: +++</p> <p>S: +++</p> <p>A: ++</p> <p>Motor: +++</p> <p>D: +++</p> <p>Com: ++</p> <p>F: +++</p>	<p>DLT: Myelosuppression with WBC nadir at 10-14 days; recovery in 21 days.</p> <p>Dose-limiting toxicity is hemorrhagic cystitis; prehydrate and administer Mesna. Minimize dose-limiting side effect of hemorrhagic cystitis. Continuous bladder irrigations may also be useful.</p> <p>Others: Dose-related nausea and vomiting (severe with high-dose regimens; occurs within 3-6 h of dose and may last up to 3 days; premedicate for nausea and vomiting), CNS toxicity (lethargy, confusion, seizure, cerebellar ataxia, weakness, hallucinations, cranial nerve dysfunction, and, rarely, stupor and coma; risk increased with high-dose therapy and renal impairment), alopecia (>80% of patients; dose related and severe with high-dose regimens), SIADH.</p> <p>Drug interactions: Phenobarbital, phenytoin, and other drugs that induce CYP450 enzymes, increase the rate of metabolic activation of ifosfamide to its toxic metabolites and increase its toxicity. Cimetidine and allopurinol increase the formation of ifosfamide metabolites and its toxicity.</p> <p>Cisplatin increases renal toxicity.</p> <p>Increases anticoagulant effects and toxicity of warfarin (Coumadin).</p>

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
Nitrosourea: Carmustine (BiCNU—IV)	Brain tumors, Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma. Transforms into an alkylating agent and to isocyanate compound toxic to tumor cells.	Dosing varies with protocol. 30% of blood levels penetrate CNS, so useful in treatment of cancer or metastases in the CNS. Reduce dose for renal insufficiency.	Cog: ++ S: ++ A: 0 Motor: + D: ++ Com: ++ F: ++	DLT: Dose-limiting interstitial lung disease and pulmonary fibrosis (cough, dyspnea, pulmonary infiltrates, respiratory failure) with cumulative doses >1400 mg/m ² . Pulmonary symptoms treated with steroids. Myelosuppression is dose limiting; involves all blood elements; delayed, prolonged, and cumulative. Lasts 6-8 wks. Affects WBCs and platelets. Platelet nadir is 4-6 wk after dose and lasts 1-3 wk. Others: Severe nausea and vomiting (occurs within 2 h of dose and lasts 4-6 h; premedicate for nausea and vomiting), facial flushing, burning sensation at injection site with faster rates of administration, hepatotoxicity with elevated liver enzymes (90%) within 1 wk of therapy, hepatic veno-occlusive disease with high doses (5%-20%). Skin contact with drug may cause brownish discoloration and pain. Drug interactions: Cimetidine increases toxicity. Amphotericin B increases cellular levels of carmustine, increasing toxicity (including renal toxicity). Decreases digoxin and phenytoin levels.
Nitrosourea: Lomustine (CeeNU—oral)	Brain tumors, Hodgkin's disease, non-Hodgkin's lymphoma	Dosing varies with protocol.	Cog: ++++ S: ++++ A: ++ Motor: +++ D: +++ Com: ++ F: +++	DLT: Myelosuppression is dose-limiting toxicity; delayed, cumulative, and prolonged; lasts 6-8 wk; affects all elements. Platelet nadir is 4-6 wks after dose and lasts 1-3 wks. Renal toxicity with cumulative doses >1,000 mg/m ² (azotemia, decreased kidney size, renal failure, glomerulosclerosis, severe tubular loss, interstitial fibrosis). Others: Nausea and vomiting (occurs 2-6 h after dose and lasts up to 24 h; premedicate for nausea and vomiting), neurotoxicity (confusion, lethargy, dysarthria, ataxia). Drug interactions: Cimetidine increases levels and toxicity. Avoid alcohol for at least 1 h before and after dose.
Nitrosourea: Dacarbazine (DTIC—IV)	Metastatic malignant melanoma, Hodgkin's disease, soft-tissue sarcomas,	Dosing varies with protocol. Half-life is 5 hrs; 50% of dose is eliminated unchanged (not	Cog: ++++ S: +++ A: + Motor: ++++ D: +++ Com: ++	DLT: Myelosuppression with WBC and platelet nadir at 21-25 days. CNS toxicity (paresthesias, neuropathies, ataxia, lethargy, headache, confusion, seizures). Others: Pain or burning at injection site,

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
	neuroblastoma	metabolized) by kidneys.	F: ++++	severe nausea and vomiting (occurs within 1-3 h and lasts up to 12 h; pretreat with antiemetic therapy), anorexia, flu-like syndrome (fever, chills, malaise, myalgias, arthralgias) for several days after therapy, increased risk of photosensitivity. Drug interactions: Incompatible with heparin, lidocaine, and hydrocortisone. Phenytoin and phenobarbital decrease levels by increasing CYP450 metabolism.
Nitrosourea: Temozolomide (Temodar—oral)	Brain tumors, metastatic melanoma	Dosing varies with protocol. Half-life is 1.8 h; readily crosses the blood–brain barrier, so useful in treatment of CNS tumors or metastases.	Cog: ++ S: ++ A: 0 Motor: ++++ D: + Com: + F: ++	DLT: Myelosuppression affecting WBC and platelets. Mild to moderate nausea and vomiting (occurs 1-3 h after dose and lasts up to 12 h), headache (25%; can be severe), fatigue, flu-like symptoms (occur several days after dose administration), constipation, photosensitivity. Drug interactions: None known.
Alkylating agent: Busulfan (Myleran—oral)	Drug of choice for palliative treatment of chronic myelogenous (CML). Remission rate ~90% after one dose. Used in bone marrow ablation prior to bone marrow transplant.	Dosing varies with protocol. Selective action in treatment of cancers involving the bone marrow.	Cog: ++ S: ++ A: 0 Motor: + D: +++ Com: + F: +	DLT: Severe myelosuppression. Others: Nausea and vomiting is mild with standard doses, but can be severe with high dose regimens; pretreat for nausea and vomiting. Associated with hyperpigmentation and pulmonary fibrosis. Use prophylactic anticonvulsants to prevent seizures with high-dose regimens. Use allopurinol to prevent hyperuricemia.
Procarbazine (Matulane—oral)	Hodgkin's lymphoma, non-Hodgkin's lymphoma, brain tumors, cutaneous T-cell lymphoma	Dosing varies with protocol.	Cog: ++ S: ++ A: 0 Motor: + D: +++ Com: + F: +	DLT: Myelosuppression, nausea and vomiting is mild with standard doses, but can be severe with high dose regimens—pretreat for nausea and vomiting. Others: Disulfiram reaction when combined with alcohol, CNS effects (depression, headache, mania, insomnia, hallucinations).
Nitrogen mustard: Chlorambucil (Leukeran—oral)	Leukemia's drug of choice for CLL and lymphomas	Dosing varies with protocol.	Cog: ++ S: ++ A: 0 Motor: + D: +++ Com: + F: +	DLT: Severe myelosuppression; conduct weekly blood counts. Others: Nausea and vomiting is mild with standard doses, but can be severe with high dose regimens; pretreat for nausea and vomiting; known carcinogen in humans; mutagenic and teratogenic, use contraception.

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
Nitrogen mustard: Melphalan (Alkeran—oral) (L-PAM, L-phenylalanine—IV)	Multiple myeloma, breast cancer, ovarian cancer, polycythemia vera, and in transplant setting	Dosage varies with protocol.	Cog: + S: + A: 0 Motor: + D: +++ Com: + F: +	DLT: Myelosuppression with WBC and platelet nadir at 4-6 wks; delayed and prolonged nadir. Nausea and vomiting may be severe and dose limiting with high dose therapy. Others: Hypersensitivity reactions with IV form (rare), alopecia (uncommon; skin reactions at injection site (uncommon) secondary malignancies, teratogenic. Drug interactions: Cimetidine decreases levels and effects by 30%, steroids enhance antitumor effects; cyclosporine enhances renal toxicity secondary to melphalan.
Nitrogen mustard: Mechlorethamine (Mustargen, nitrogen mustard)	Hodgkin's lymphoma, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma (topical use), treatment of pleural effusions caused by metastatic disease	Dosage varies with protocol.	Cog: ++ S: ++ A: 0 Motor: + D: +++ Com: + F: +	DLT: Myelosuppression with WBC and platelet nadir at 7-10 days, recovery by day 21. Nausea and vomiting within first 3 h, lasts for 4-8 h and up to 24 h. Others: Potent vesicant (use central line and running IV to administer), alopecia, amenorrhea, azoospermia, hyperuricemia, weakness, sleepiness, headache, hypersensitivity reactions (rare), secondary malignancies. Drug interactions: Sodium thiosulfate inactivates effects of mechlorethamine.
Thiotepa (Triethylenethio-phosphoramidate Thioplex—IV)	Breast cancer, ovarian cancer, superficial bladder cancer, Hodgkin's and non-Hodgkin's lymphoma, transplant setting for ovarian and breast cancer	Dosing varies with protocol.	Cog: ++ S: ++ A: 0 Motor: + D: +++ Com: + F: +	DLT: Myelosuppression; WBC nadir at 7-10 days; recovery by day 21. Platelet nadir at day 21 with recovery by day 28-35. Mucositis may be dose limiting; allergic reactions (rare); nausea and vomiting is mild with standard doses, but can be severe with high dose regimens, pretreat for nausea and vomiting; chemical or hemorrhagic cystitis after bladder instillation; skin reactions; teratogenic, carcinogenic with secondary malignancies.
Heavy metal compounds: Platinum products are alkylating compounds that bind to DNA and form cross-links and bending of DNA with impaired tumor cell synthesis.				
Cisplatin (Platinol)	Testicular cancer, ovarian cancer, bladder cancer, head and neck cancer, esophageal cancer, small-cell and non-small-cell lung cancers, non-Hodgkin's lymphoma, trophoblastic	Dosing varies with protocol. Binds to erythrocytes and protein. Eliminated in 3 phases: Free drug eliminated in 20-30 min, protein-bound drug eliminated in 1 hr, and	Cog: ++ S: ++ A: 0 Motor: ++++ D: ++++ Com: ++ F: ++++	DLT: Severe dose-limiting nausea and vomiting; acute and delayed. Acute occurs within 1 h of dose and lasts 8-12 h; delayed can last 3-5 days and cause severe dehydration and electrolyte losses. Pretreat nausea and vomiting with corticosteroids and serotonin-receptor agents such as ondansetron (Zofran). Dose-related electrolyte disturbances associated with starting with first dose; wasting of potassium and magnesium and reduction of creatinine clearance,

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
		erythrocyte-bound drug eliminated in 1-3 days.		<p>hypomagnesemia, hypocalcemia, and hypokalemia common.</p> <p>Myelosuppression in 25-30%. White blood cells, platelets, and red blood cells equally affected (dose related). Anemia can be severe; manage with erythropoietin and iron supplementation. Hemolytic anemia can also occur. Nephrotoxicity is dose-limiting toxicity; progressive (35%-40%). Incidence of nephrotoxicity is decreased by careful diuresis with mannitol and aggressive hydration with saline.</p> <p>Neurotoxicity is dose limiting; cumulative toxicity, irreversible ototoxicity, vestibular damage, peripheral neuropathy (distal stocking glove distribution); post dose pain and paresthesias reverse within 1 yr.</p> <p>Ototoxicity: High-frequency hearing, tinnitus.</p> <p>Ocular toxicity: Optic neuritis, papilledema, cerebral blindness, disturbances in color perception.</p> <p>Others: Raynaud's phenomenon, SIADH, hypersensitivity reactions with dose (facial edema, wheezing, bronchospasm, hypotension), myelosuppression (25%-30%), metallic taste of food, loss of appetite.</p> <p>Radiosensitizing agent.</p> <p>Drug interactions: Decreases effect of phenytoin.</p> <p>Directly inactivated by amifostine and mesna.</p> <p>Increases nephrotoxicity from aminoglycosides and amphotericin B.</p> <p>Increases levels and toxicity of etoposide, methotrexate ifosfamide, and bleomycin, increasing accumulation of each drug.</p> <p>May enhance antitumor activity of etoposide.</p> <p>Administer after paclitaxel when used in combination to reduce toxicity.</p> <p>Risk of ototoxicity is increased when used with aminoglycosides and loop diuretics.</p>
Carboplatin (Paraplatin)	Ovarian cancer, germ cell tumors, head and neck cancer, small-cell and non-small-cell lung cancer, bladder cancer, relapsed and refractory acute	Dosing varies with protocol.	<p>Cog: +</p> <p>S: +</p> <p>A: 0</p> <p>Motor: ++</p> <p>D: ++</p> <p>Com: +</p> <p>F: ++</p>	<p>DLT: Myelosuppression is dose limiting, dose-dependent, cumulative toxicity. Platelet nadir at day 21.</p> <p>Others: Significantly less nausea and vomiting and renal toxicity than seen with cisplatin. Hypocalcemia, hypokalemia, hypomagnesemia, hyponatremia, peripheral neuropathy (<10%), allergic</p>

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
	leukemia, endometrial			reaction (25%; skin rash, urticaria, pruritus). Skin testing may be helpful in identifying patients at risk for allergic reactions; mild and reversible elevation of LFTs.
Oxaliplatin (Eloxatin, Iproplatin, Ormaplatin)	Metastatic colorectal cancer, component of the chemotherapy protocols 5-FU/LV and FOLFOX4	Dosing varies with protocol.	Cog: + S: + A: 0 Motor: +++ D: +++ Com: + F: +++	DLT: Neurotoxicity is dose limiting; peripheral sensory neuropathy with distal paresthesias; worsened by cold; usually reversible after 3-4 months. Laryngopharyngeal dysesthesias can cause difficulty breathing or swallowing immediately or 1-3 days after dose. >50% risk of neurotoxicity with cumulative doses of 1200 mg/m ² . Others: Nausea and vomiting (65% with oxaliplatin, 90% when combined with 5-FU/LV; well controlled with antiemetic therapy), diarrhea (30% with oxaliplatin, 80%-90% when combined with 5-FU/LV), myelosuppression (mild thrombocytopenia, anemia). Drug interactions: None known.
Antitumor antibiotic: From <i>Streptomyces</i> fungus; causes breakage of tumor cell DNA strands and formation of free radicals after binding with iron; active against cells in the second gap phase of the cell cycle.				
Bleomycin (Blenoxane)	Hodgkin's disease and non-Hodgkin's lymphoma, germ cell tumors, head and neck cancer, squamous cell carcinomas. Sclerosing agent for malignant pleural effusion and ascites.	Dosing varies with protocol. 40%-70% renal elimination; half-life is 2-4 hrs (increases to 20 hrs with renal dysfunction). Reduce dose with renal dysfunction.	Cog: + S: + A: 0 Motor: + D: ++ Com: + F: +	DLT: Pulmonary toxicity is dose limiting (10%). Increased risk with patients >70 yr of age and with cumulative doses >450 units. Presents with cough, dyspnea, dry inspiratory crackles, and infiltrates on chest X-ray. Risk of pulmonary side effects increased with previous lung disease, advanced age, chest irradiation, and renal dysfunction. Radiation therapy enhances pulmonary toxicity. Pulmonary function tests (PFTs) with specific focus on diffusing capacity (DL _{CO}) and vital capacity is the most sensitive approach for detecting pulmonary toxicity. A decrease of 15% or more in PFT mandates immediately stopping the drug. Fatal fibrosis (1%). Others: Hypersensitivity reactions (25%; fever and chills), fever (25%-50%) within 1 hr up to 2 days after dose, mild nausea and vomiting, common mucocutaneous reactions (mild stomatitis; hyperpigmentation of the elbows, knees, hand joints; thickened nail beds; alopecia; skin erythema; and edema). Drug interactions: Oxygen therapy at high concentrations may enhance pulmonary toxicity. Fraction of inspired oxygen (FIO ₂) should be maintained at <25%.

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
				Phenothiazines increase levels and toxicity by reducing metabolism of liver P450 enzymes. Cisplatin decreases renal clearance, increasing levels and toxicity.
Enzyme produced by <i>Escherichia coli</i> bacteria: Degrades the nonessential amino acid L-asparagine, reducing protein synthesis.				
L-asparaginase (Elspar, Oncospar)	Acute lymphocytic leukemia	Dosing varies with protocol and product dosage form. Half-life is about 1 day for Elspar and 6 days for Oncospar PEG, a long-acting form that requires lower doses and less-frequent administration. Side effect profile is similar for both products.	Cog: +++ S: +++ A: ++ Motor: +++ D: +++ Com: ++ F: +++	DLT: Liver toxicity (common, dose limiting), mild elevation in LFTs (including serum bilirubin and liver enzymes), hemorrhage and thrombosis due to impaired synthesis of clotting factors and anticoagulants with risk of bleeding and clotting (50%), decreased production of lipoproteins and albumin. Life-threatening allergic reactions (bronchospasm, respiratory distress, hypotension; resuscitation drugs and equipment required at bedside), fever, chills, nausea, vomiting (50%); skin testing is helpful for identifying patients with increased risk of allergy. Neurologic toxicity (25%; lethargy, confusion, agitation, hallucinations; coma requires discontinuance). Others: Mild hypersensitivity (25%; skin rash, urticaria), pancreatitis (up to 10% of patients; reverses with discontinuance), hyperglycemia (decreased insulin production). Drug interactions: Reduces effects of methotrexate; administer these drugs 24 hrs apart. Increases effects of vincristine; administer vincristine 12-24 hrs before L-asparaginase.
Tyrosine kinase inhibitors: Decrease production of cancer cells.				
Imatinib mesylate (Gleevec—oral)	Chronic myelogenous leukemia, acute lymphoblastic leukemia, gastrointestinal stromal tumors	Dosing varies with protocol.	Cog: + S: + A: 0 Motor: ++ D: ++ Com: + F: ++	Side effects are well tolerated due to selectivity for cancer cells. Myelosuppression with neutropenia and thrombocytopenia. Nausea and vomiting (50%; reduced by taking with meal), diarrhea, pleural effusion, ascites, pulmonary edema (5%), muscle cramps, rash, diarrhea, fluid retention (dose related; pleural effusion, ascites, pulmonary edema, weight gain), transient ankle and periorbital edema, mild elevation of liver enzymes; skin reactions which can be severe (Stevens-Johnson syndrome). Drug interactions: Dilantin, carbamazepine, rifampicin, phenobarbital, and St. John's

From L. Carl, J. Gallo, and P. Johnson, 2014, *Practical Pharmacology in Rehabilitation: Effect of Medication on Therapy* (Champaign, IL: Human Kinetics).

Medication	Indications	Dosing	Side effects affecting rehab	Dose-limiting toxicities (DLT) and other side effects or considerations
				<p>wort increase rate of metabolism and decrease effects.</p> <p>Ketoconazole, itraconazole, erythromycin, and clarithromycin inhibit CYP3A4 metabolism, increasing levels and toxicity. Reduces metabolism of warfarin (Coumadin), increasing levels and toxicity.</p>

Cog = cognition; S = sedation; A = agitation or mania; Motor = discoordination; D = dysphagia; Com = communication; F = falls; CNS = central nervous system; DLT = dose-limiting toxicities; DNA = deoxyribonucleic acid; IV = intravenous; LV = left ventricular; SIADH = syndrome of inappropriate antidiuretic hormone; INR= international normalized ratio; PVCs = premature ventricular contractions; ST = ST portions of the electrocardiogram reflecting cardiac contraction; WBC = white blood count; GI = gastrointestinal; CHF = congestive heart failure.

The likelihood rating scale for encountering the side effects is as follows: 0 = Almost no probability of encountering side effects. + = Little likelihood of encountering side effects. +/++ = Low probability of encountering side effects; however, probability increases with increased dosage. ++ = Medium likelihood of encountering side effects. +++ = High likelihood of encountering side effects, particularly with high doses. ++++ = Highest likelihood of encountering side effects; best to avoid in at-risk patients.