



**Southwest  
Oncology Group**  
A National Clinical Research Group

## MEMORANDUM

**DATE:** November 1, 2003

**TO:** All Member and CCOP Head Nurse Oncologists/CRAs

**FROM:** Siu Fun Wong, Pharm. D and Pam Williams, RN, MSN, CCRP

**SUBJECT:** Southwest Oncology Group Nursing Drug Manual

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Enclosed please find an update to the manual referenced above. We hope that this information is useful to you.

cc: Charles A. Coltman, Jr., M.D.  
Marjorie A. Godfrey

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## MEMORANDUM

**DATE:** February 16, 2001

**TO:** All Member and CCOP Head Nurse Oncologists/CRAs

**FROM:** Siu Fun Wong, Pharm. D and Pam Williams, RN, MSN, CCRP

**SUBJECT:** Southwest Oncology Group Nursing Drug Manual

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This manual is a collaborative project of the Nurse Oncologist Committee and the Pharmacy Committee of the Southwest Oncology Group (SWOG). The purpose of the drug monographs in this manual is to provide the clinicians a quick reference on the pertinent information of the drugs being used in Group protocols. This will be a one-time mailing to each Member Institution and CCOP. Subsequent updates to the manual will be available on the Southwest Oncology Group website. As Head Nurse of your institution, it will be your responsibility to keep the manual current and provide copies for anyone who may want one.

Thank you for your assistance with this new and important manual.

cc: Charles A. Coltman, Jr., MD  
Marjorie A. Godfrey

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<b>Generic Name</b>	<b>Amifostine</b> (WR-2721, Ethiofos)
<b>Trade Name</b>	Ethyol (MedImmune)
<b>NSC #</b>	296961 (under Ethiofos)
<b>Classification</b>	an organic thiophosphate compound
<b>Action</b>	Amifostine is a prodrug that is converted by the plasma membrane-bound enzyme alkaline phosphatase to the active compound WR-1065. WR-1065 exerts the ability to scavenge both free radicals and reactive drug derivatives to protect against the adverse effects of chemotherapy and radiation. WR-1065 has demonstrated selective uptake by the normal cells than the malignant cells. This is possibly due to the decreased activity of alkaline phosphatase in tumor cells, decreased vascularity of tumors, and the pH dependence of WR-1065 uptake.
<b>Indication</b>	Amifostine decreases cumulative nephrotoxicity of cisplatin and is radioprotective of xerostomia (FDA). Amifostine is also being studied in decreasing and preventing neurotoxicity, ototoxicity, myelosuppression (multiple lineage), & cardiotoxicity associated with chemotherapy and radiation.
<b>Dose Form</b>	500 mg lyophilized powder with 500 mg mannitol.
<b>Storage/Stability</b>	Intact vials should be stored under refrigeration. After reconstituted with 9.5 ml NS (conc. 50 mg/ml), the solution is stable for 5 hrs at rm temp and 24 hrs under refrigeration. Further dilution with NS to concentration range 5 –40 mg/ml provides stability of 5 hrs at rm temp and 24 hrs under refrigeration in PVC bags.
<b>Dose/Administration</b>	740mg/m <sup>2</sup> IVPB infuse over 15 mins, to be given 30 mins prior to chemo(may repeat dose 2 hrs after administration in some regimens). Consult specific protocol for dosage and dosage adjustment guidelines.
<b>Kinetics</b>	200 mg IVPB before each dose of radiation (appears to be the most commonly used dose). The plasma elimination half-life is 8.76 mins. Small volume of distribution with low plasma protein binding. Concentrations in a majority of tissues declined within the first 30 mins. These properties suggest that amifostine is rapidly dephosphorylated and enters cells as WR-1065. Because of the observed rapid decline of drug levels in normal tissues, repeated doses of amifostine may be required in patients receiving cytotoxic agents with long half-life or require long infusion time.
<b>Adverse Effects</b>	<ol style="list-style-type: none"> <li>1. Hypotension – more frequent with infusions longer than 15 mins and dose higher than 740 mg/m<sup>2</sup> (62%). Most of the hypotension were asymptomatic and self-limiting, less than 3% required discontinuation of the treatment. Prophylactic hydration, supine positioning of the patient, and blood pressure monitoring are recommended. Interrupt infusion if &gt;20% decrease in SBP.</li> <li>2. Nausea/Vomiting – usually sudden in onset, last 5 to 30 mins, and resolve spontaneously. Nausea often starts 15 mins after the initiation of infusion and emesis is reported more often in longer infusions and higher doses.</li> <li>3. Allergic reactions – there are no reports of anaphylactic shock; skin rashes and rigors have been reported in less than 1% of the patients.</li> <li>4. Others – clinically significant hypocalcemia (&lt;1%) occurring 4 hrs after administration and return to normal in 7 days. Administration of oral calcium and vitamin D appeared to show benefits. Minor effects include flushing, feeling of warmth or coldness, dizziness, somnolence, hiccups, and sneezing have been reported.</li> </ol>
<b>Nursing Implications</b>	Avoid prolonged infusion and monitor vital signs. Additional prophylactic antiemetics.

<b>Generic Name</b>	Anti-thymocyte Globulin (Rabbit), ATG
<b>Trade Name</b>	Thymoglobulin® (SangStat Medical Corporation)
<b>Classification</b>	A polyclonal mixture of IgG and IgM immunoglobulin solution produced by the immunization of rabbits with human thymocytes
<b>Action</b>	The mechanism by which polyclonal antilymphocyte preparations suppress immune responses is not fully understood. Possible mechanism may be due to the variety of antibodies in ATG that recognize key receptors on T-cells causing inactivation and death of these of T-cells, thus reversing the rejection process.
<b>Indication</b>	Anti-thymocyte Globulin (Rabbit) is indicated for the treatment of renal transplant acute rejection, in conjunction with concomitant immunosuppression. ATG can also be used in cardiac, liver, and kidney-pancreas transplantation. ATG has been shown to be effective in reversing steroid-resistant rejection in approximately 80-90% of cases.
<b>Dose Form</b>	Anti-thymocyte Globulin (Rabbit) [Thymoglobulin] is available as sterile, lyophilized powder to be reconstituted with sterile diluent. Each package contains one 7-ml vial consisting of a freeze-dried Thymoglobulin Formulation (25 mg) and one vial of diluent of Sterile Water for Injection, USP (> 5ml).
<b>Storage/Stability</b>	The package should be stored under refrigeration (2-8 <sup>o</sup> C) and protected from light. Do not freeze. Each vial should be reconstituted with 5 ml of the diluent provided and should be used within 4 hours. Further dilution with NS or D5W to 0.5 mg/ml must be performed prior to administration.
<b>Dose/Administration</b>	1.5 mg/kg/lean body weight IVPB over 4-6 hrs q day x 7-14 days A 0.22-micron filter through a high-flow vein must be used for the administration. Prophylactic antiviral therapy is recommended. Premedication with hydrocortisone 50-100 mg, acetaminophen 650 mg, and diphenhydramine 25-50 mg 1 hour prior to infusion is recommended. <b>Consult the specific protocol for doses and dosage adjustment guidelines</b>
<b>Kinetics</b>	Anti-thymocyte Globulin (Rabbit) has a long half-life in human plasma. After multiple administrations, the clearance decreases resulting in an extended half-life. Rabbit immune globulin can be detected in the serum of recipients up to 40 to 50 days after the last dose. The apparent volume of distribution of Anti-thymocyte Globulin (Rabbit) is about two times of the plasma volume indicating that it remains within the plasma and extravascular fluid, and does not enter the lipophilic compartment of the body.

#### Adverse Effects

- 1) Contraindications: ATG is contraindicated in patients with history of allergy or anaphylaxis to rabbit proteins, or who have an acute viral illness.
- 2) Infusion-related reactions - fever (63%) and chills (57%), slow infusion rate and premedications are helpful in alleviating these symptoms.
- 3) Infections - Prolonged use and overdosage of ATG in association with other immunosuppressive agents may cause over-immunosuppression resulting in severe infections (5-15%) and may increase the incidence of lymphoma or post-transplant lymphoproliferative disease or other malignancies. CMV infection (13%), sepsis (12%), urinary tract infection (18%) herpes simplex (4.9%), gastrointestinal moniliasis (4.9%), oral moniliasis (3.7%), & other (17%).
- 4) Hematologic – Leukopenia (47%), & thrombocytopenia (37%)
- 5) Neurologic – Headache (40%), & dizziness (8.5%)
- 6) Gastrointestinal - Abdominal pain (38%), diarrhea (30%), nausea (37%), & gastritis (1.2%)
- 7) Cardiovascular – Hypertension (37%), & tachycardia (27%)
- 8) Metabolic – Hyperkalemia (27%)
- 9) Miscellaneous - Peripheral edema ( 34%), dyspnea (28%), malaise (13%), & asthenia (27%).

#### Nursing Implications

Premedications for infusion.(See Dose Administration section) Do not shake drug solution. Use 0.22-micron filter for administration Patient education on hematologic and infection-related signs and symptoms.

<b>Generic Name</b>	Bryostatin 1
<b>Trade Name</b>	Not yet available
<b>NSC</b>	339555
<b>Classification</b>	A naturally occurring macrocyclic lactone originally isolated from the marine invertebrate animal, Bryozoan, <i>Bugula neritina</i> .
<b>Action</b>	Bryostatin 1 activates the protein kinase C in tissue culture cells, causing the translocation of this enzyme to the membrane and the phosphorylation of specific protein substrates. Bryostatin 1 has both antitumor and immunomodulatory activity.
<b>Indication</b>	Bryostatin 1 possesses anti-tumor activity <i>in vitro</i> and <i>in vivo</i> against a variety of tumors including leukemia, melanoma, and lung cancer. Preclinical studies also suggest that bryostatin-1 induced the differentiation of various human B-cell NHL cell lines and of chronic B-cell leukemia cell lines. Bryostatin 1 has been reported to potentiate the <i>in vitro</i> apoptosis induced by a variety of cytotoxic agents in a number of tumor cell lines.
<b>Dose Form</b>	Bryostatin 1 is supplied by the NCI as a two-part formulation. The kit includes a 6 ml flint vial containing 0.1 mg bryostatin 1 as a white lyophilized cake or powder with 5 mg povidone USP (as a bulking agent) lyophilized from 40% t-butanol. The second two ml flint vial contains 1 ml of sterile PEG diluent (60% polyethylene glycol 400, 30% dehydrated ethyl alcohol, and 10% polysorbate 80).
<b>Storage/Stability</b>	The intact vials should be stored under refrigeration (2-8°C). Shelf life evaluation of the intact vials is ongoing. The lyophilized powder should be reconstituted with 1 ml of the PEG diluent. After complete dissolution of the content, the resulting solution must be further diluted with 9 ml of 0.9% NaCl to a concentration of 10 mcg/ml and is physically and chemically stable for at least 24 hrs. The drug should be further diluted with benzyl alcohol preserved 0.9% NaCl to a concentration between 1 and 10 mcg/ml prior to administration and is stable for 14 days at room temp in glass or polyolefin container. <b>Use of PVC (polyvinylchloride) bags is not recommended due to leaching of the plasticizer.</b>
<b>Dose/Administration</b>	25 mcg/m <sup>2</sup> IVPB over 1 hr or continuous infusion over 24 hrs q week x 3 weeks to be repeated every 4 weeks. 40 mcg/m <sup>2</sup> /day x 3 days continuous infusion every 2 weeks. Consult specific protocol for dosage and dosage adjustment guidelines.
<b>Kinetics</b>	The plasma half-life is 1.05 hr and the terminal half-life is 22.96 hrs. Urinary excretion represents the major pathway of elimination for the first 12 hrs and the fecal excretion becomes the major pathway 12 hrs after administration. The drug is widely distributed in the liver, bone marrow, lung, spleen, kidney, and gastrointestinal tracts.
<b>Adverse Effects</b>	<ol style="list-style-type: none"> <li>1. Neurologic – myalgia, dose-limiting toxicity, cumulative and dose-related. Usually affect the calves and thigh muscles and the muscles of the extraocular movements. Persist over 3-5 days and resolve over 2 days. Can be managed with bed rest and regular analgesia, and in some cases myalgia has been reported to be relieved by exercise. The affected muscles were tender on palpation, but the serum creatinine kinase and the erythrocyte sedimentation rate are normal. Headache in association with lethargy, fever, sweats, rigors, rhinitis accounted for most of the clinical toxicity.</li> <li>2. Dermatologic - phlebitis is a frequent and dose related problem (44% at 25 mcg this dose level) and associated with the formulation of the drug. Concomitant infusion or dilution with normal saline appeared to decrease the incidence and severity of reaction.</li> <li>3. Hematologic – immediate decrease in hemoglobin values was observed in the first 4 hrs after treatment and is more prominent in higher dose treatments. Unlike decreases in platelet, neutrophil, and lymphocyte counts, recovery of the hemoglobin values was not noted up to 2 weeks after administration. There was no clinical evidence of bleeding and the patients showed no evidence of hemodynamic compromise.</li> <li>4. Others – nausea/vomiting (mild and infrequent), diarrhea, constipation, increased liver function tests, acute reaction (shortness of breath, flushing, hypotension, bradycardia), and rash have been reported.</li> </ol>
<b>Nursing Implications</b>	<ol style="list-style-type: none"> <li>1. Use non-PVC container and supplies for preparation and administration of bryostatin</li> <li>2. Dilute drug prior to administration to minimize phlebitis complications.</li> <li>3. Educate patients on management of myalgia.</li> </ol>

<b>Generic Name</b>	Bupropion
<b>Trade Name</b>	Zyban Wellbutrin (GlaxoSmithKline)
<b>Classification</b>	Aminoketone-derivative antidepressant
<b>Action</b>	Precise mechanism of antidepressant action is unclear, but appears to affect the nonadrenergic system.
<b>Indications</b>	Smoking cessation, depressive affective disorders, other uses include bipolar depression and attention-deficient hyperactivity disorder.
<b>Dose Form</b>	Extended-release film-coated oral tablet (ET) in 100 mg & 150 mg Film-coated conventional tablet (CT) in 75 mg & 100 mg
<b>Storage</b>	Bupropion should be stored at room temperature in a tight, light- and moisture-resistant container.
<b>Dose/Administration</b>	Smoking cessation: 150 mg q day (ET) for three days to begin 1-2 weeks prior to discontinuation of cigarette smoking, then increase to a maximum dose of 150 mg twice daily. Therapy should be continued for a total of 7-12 weeks. Depression: starting dose is 100mg twice daily (CT) or 150 mg once daily (ET) for several weeks, then titrate to a maximum daily dose at 450 mg(CT) or 400 mg (ET) as needed. Bupropion should be used in caution in patients with organ failure, especially hepatic dysfunction. Consult the specific protocol for doses and dosage adjustment guidelines. <i>Avoid taking evening dose at bedtime to decrease insomnia.</i>

**Kinetics** 5-20% absorbed orally. Food does not appear to affect absorption. bupropion is extensively metabolized in the liver. The half-life is about 14 hrs (single dose) and 21 hrs (multiple dosing). Unchanged drug comprised 0.5% of the dose excreted. The effect of age, gender, or end organ functions on the metabolism and/or elimination of bupropion is unclear. Bupropion may induce hepatic enzymes. Drugs that inhibit CYP2B6 may affect bupropion metabolism, for example MOA inhibitors should be discontinued for two weeks prior to initiating bupropion. Levodopa. may enhance the toxicity of bupropion. The drug is distributed in breast milk.

**Side effects**

- Central Nervous System effects: seizures (1% in patients with other risk factors, 0.4% in general population) agitation (32%), insomnia (19%), anxiety (6%), confusion (8%) and delusions (1%) Headache/migraine (26%), dizziness (26%), depression (1%) suicidal ideation (incidence unknown)
- Metabolic: weight loss (28%), weight gain (14%),
- GI: Dry mouth (28%), constipation (26%), nausea/vomiting (23%), anorexia (18%), abdominal pain (9%), diarrhea (7%), appetite (4%)
- Cardiovascular: tachycardia (11%) palpitations (6%) hypertension, chest pain and flushing (4%) EKG abnormalities (<1%)
- Dermatologic: excessive sweating (22%) rash (5-8%), pruritus (4%), urticaria (2%)
- Ocular: blurred vision (15%) amblyopia (3%)
- Skeletal/Muscular: myalgia (6%), arthralgia (5%), arthritis (3%), muscle spasm or twitch (2%), neck pain (2%)
- GU: Menstrual complaints (5%), impotence and decreased libido (3%), urinary frequency (5%), urinary urgency or retention (2%), vaginal hemorrhage (2%)
- Others: infection (9%). hot flashes (3%), fever/chills (2%), flu-like symptoms (1%), SIADH, hepatitis, leukocytosis, & leukopenia have been reported.

**Nursing Implications:**

1. Patients should be screened and counseled to notify their physician, if they are taking or plan to take any over the counter products due to the potential for drug interactions.
2. Patients should be cautioned to avoid alcoholic beverages.

**Generic Name** Busulfan injection

**Trade Name** Busulfex

**NSC Number** 750

**Classification** – Alkylating agent

**Mechanism of Action** – Busulfan acts as a bifunctional alkylating agent that is hydrolyzed to release two methanesulfonate groups producing reactive carbonium ions that alkylate DNA, preventing replication.

**Indication** – Busulfan injection is approved as part of a conditioning regimen (in combination with cyclophosphamide) prior to allogeneic hematopoietic progenitor cell transplantation in patients with chronic myelogenous leukemia. As used in its oral dosage form, busulfan injectable is also active in acute lymphocytic leukemia.

**Dose Form** – 60mg/10ml (6mg/ml) busulfan solution in a clear glass ampoule

**Storage and Stability** – Busulfan solution in glass ampoules should be stored between 2°-8° C. After appropriate dilution (0.5mg/ml), busulfan is stable at 25°C in 0.9% Sodium Chloride or Dextrose 5% in Water for 8 hours; and at 2°-8°C in 0.9% Sodium Chloride for 12 hours.

**Administration** – Busulfan is administered via central venous access by IV infusion over 2 hours.

**Dosage** – Busulfan injection is dosed 0.8mg/kg (IBW or Actual BW, whichever is less) every 6 hours for 4 days (16 doses). Concomitant seizure prophylaxis with phenytoin is recommended. Consult specific protocol for dosage and dosage adjustment guidelines.

**Kinetics** – Busulfan achieves concentrations in the cerebrospinal fluid nearly equal to plasma and is approximately 30% bound to plasma elements; busulfan has a half-life of 2-3 hours and is metabolized via conjugation with glutathione, then further extensive oxidative metabolism; approximately 30% of busulfan is excreted into the urine over 48 hours. Drug interactions that affect busulfan clearance include itraconazole (decreases clearance by up to 25%), phenytoin (increases clearance by 15% or more), however all busulfan kinetics were studied with patients on phenytoin, and acetaminophen (may reduce clearance due to reduced glutathione levels).

**Adverse effects** –

**Hematologic:** profound myelosuppression in 100% of patients (ANC <500cells/ $\mu$ L, 100%; thrombocytopenia <25,000/mm<sup>3</sup> or requiring platelet transfusion, 98%; hemoglobin <8.0g/dl, 69%).

**Gastrointestinal:** nausea (7% severe, 92% mild to moderate), stomatitis (26% grade 3, 71% grade 1-2), and vomiting (95% mild to moderate)..

**Other:** Grade 3-4 hyperbilirubinemia (30%, 5% life-threatening) Hyperbilirubinemia was associated with VOD in 5 patients and GVHD in 6 patients. Hyperglycemia, electrolyte abnormalities, edema, elevated serum BUN/creatinine, insomnia, anxiety, rhinitis, mild or moderate dyspnea, and rash. One patient developed a seizure during the clinical trial. Three patients developed alveolar hemorrhage.

**Nursing implications** –

- This drug must be administered over 2 hours through central venous access, flushing the line before and after infusion.
- Seizure prophylaxis with phenytoin is recommended; acetaminophen use less than 72 hours prior to busulfan is discouraged.



<b>Generic Name</b>	Celecoxib
<b>Trade Name</b>	Celebrex (Pzifer)
<b>Classification</b>	NSAID (nonsteroidal anti-inflammatory drug)
<b>Action</b>	Inhibits prostaglandin synthesis by primarily inhibiting cyclooxygenase-2 (COX-2) isoenzyme at therapeutic concentration
<b>Indication</b>	<b>Familial Adenomatous Polyposis (FAP):</b> to reduce the number of adenomatous colorectal polyps <b>Osteoarthritis (OA):</b> for the relief of signs and symptoms <b>Rheumatoid Arthritis (RA):</b> for the relief of signs and symptoms
<b>Dose Form</b>	100 mg and 200 mg capsules, oral
<b>Storage/Stability</b>	Store at room temperature 25°C (77°F)
<b>Dose/Administration</b>	<b>Familial Adenomatous Polyposis:</b> 400 mg PO bid with food <b>Osteoarthritis:</b> 200 mg PO once qd or 100 mg bid <b>Rheumatoid Arthritis:</b> 100-200 mg PO bid Consult specific protocol for dosage and dosage adjustment guidelines.

**Contraindications:** Celecoxib should not be used in patients with known hypersensitivity to celecoxib and should not be given to patients who are allergic to sulfonamides (e.g. trimethoprim/sulfamethoxazole, sulfasalazine, nitrofurantoin). In addition, celecoxib should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAID's. The use of celecoxib is NOT recommended in patients with advanced renal disease. The daily dose should be reduced by 50% in patients with mild hepatic impairment and is not recommended in patients with severe hepatic impairment.

**Kinetics:** Peak Plasma levels occur approximately 3 hours after oral dose (under fasting conditions peak, plasma levels ( $C_{max}$ ) and AUC area dose proportional up to 400 mg daily; with doses 400mg daily there are less than proportional increases in  $C_{max}$  and AUA. Co-administration with an aluminum or magnesium containing antacid reduce celecoxib plasma concentrations (10% decrease in AUC; 37% decrease in  $C_{max}$ ) Steady state concentrations are achieved on or before day 5. The effective  $t_{1/2}$  of celecoxib is 11.2 hr and it is ~97% protein bound. Mechanism is primarily mediated through cytochrome P450 2C9 to inactive metabolites. Celecoxib is excreted predominantly through hepatic metabolism with <3% unchanged drug recovered in urine and feces.

#### Adverse Effects

**Gastrointestinal:** Dyspepsia (8.8%); Diarrhea (5.6%); Abdominal Pain (4.1%); Nausea (3.5%)

**Central and Peripheral Nervous System:** Headache (15.8%)

**Respiratory:** Upper Respiratory Tract Infection (8.1%); Sinusitis (5%)

**Hematologic:** Anemia (0.6%); if patients on long term celecoxib therapy exhibit blood loss or signs and symptoms of anemia. Hct/Hgb levels should be checked.

**Hepatic:** AST & ALT increases of  $\geq 3$  x upper normal limits (0.2%), rare cases of fatal fulminant hepatitis, liver necrosis and hepatic failure; patients should be carefully monitored and celecoxib should be discontinued if s/s of liver disease occur.

#### Nursing Implications

- Educate patient on s/s of bleeding (hematuria, ecchymosis, epistaxis)
- Educate patient on s/s of GI ulceration, bleeding and perforation (epigastric pain, dyspepsia, nausea, vomiting, bloating), skin rash, edema & unexplained weight gain.
- Inform patient of warning signs and symptoms of hepatotoxicity (nausea, fatigue, lethargy, pruritus, jaundice, right upper quadrant tenderness, "flu-like" symptoms)
- Contraindication: Patient who has allergy to sulfa drugs may have allergic reaction to celecoxib.

<b>Generic Name</b>	Cephalexin
<b>Trade Name</b>	Keflex
<b>Dose Form</b>	Oral suspension; 250 & 500 mg capsules
<b>Classification</b>	semi-synthetic cephalosporin, first generation oral cephalosporin antibiotic
<b>Action</b>	Cephalosporins are bactericidal and exert their activity through inhibition of mucopeptide synthesis interfering with cell wall synthesis of bacteria.
<b>Indications</b>	Infection by gram-positive cocci including penicillinase producing and non-penicillinase-producing Staphylococcus aureus, S epidermidis, Group A -hemolytic streptococci and group B streptococci.
<b>Storage</b>	Cephalexin should be stored at room temperature in tight container.
<b>Dose/Administration</b>	Dosage is 250mg to 500mg four times daily. Consult the specific protocol for doses and dosage and dosage adjustment guidelines.
<b>Kinetics:</b>	Well absorbed orally. Cephalexin is acid-stable Food does not appear to affect absorption. Cephalexin is renally eliminated with 90% eliminated in the first 8-12hr following administration. The drug is excreted in breast milk.
<b>Side effects:</b>	<p><u>GI</u>: nausea/vomiting (&lt;8%), diarrhea, pseudomembranous colitis.</p> <p><u>Hypersensitivity</u>: Hypersensitivity reactions occur in &lt; 5% of patients. Rash, fever, chills, eosinophilia, serum sickness Stevens-Johnson syndrome,</p> <p><u>Hematologic</u>: Positive direct and indirect Coombs' test (3%) transient neutropenia (&lt;1%),</p> <p><u>Renal and GU</u>: increased BUN and serum creatinine, renal dysfunction</p> <p><u>Central Nervous System effects</u>: headache, dizziness ,seizures</p> <p><u>Cardiovascular</u>:. chest pain and flushing,</p>

**Nursing Implications:**

- Cephalexin should not be administered to patients with known history of allergic reaction to cephalosporins. Patients who are allergic to penicillins may be cross-allergic to cephalexin. Caution should be used in patients who have a history of allergy to penicillins.
- No reports of adverse effects to the fetus to have been reported in pregnant mothers taking cephalosporin. However, the safety of cephalosporins are not established in pregnancy. Cephalexin dose should be reduce in renal dysfunction.

<b>Generic Name</b>	CI-980
<b>Trade Name</b> <b>NSC #</b>	(Not available, investigational use only) Parke-Davis Pharmaceuticals 635370
<b>Classification</b>	Mitotic inhibitor
<b>Action</b>	Binds to the colchicine binding site on tubulin and inhibits the tubulin polymerization, blocking the formation of the mitotic spindle. M-phase specific drug
<b>Indication</b>	Spectrum of activity is similar and superior to that of vincristine, has favorable cross-resistance profile with the vinca alkaloids. Synergistic effect seen with taxanes in vitro.
<b>Dose Form</b>	10 mg preservative-free, lyophilized powder in 6 ml amber glass vial
<b>Storage/Stability</b>	The intact vial should be stored at room temp and protected from light. Reconstituted with 5 ml sterile water for injection to a concentration of 2 mg/ml is stable for 24 hrs at room temp and protect from light. Further dilution in D5W (conc. 0.04 to 0.5 mg/ml) is stable for 24 hrs at room temp. <b>Dilution in 0.9% NaCl is not recommended due to precipitation.</b>
<b>Dose/Administration</b>	4.5 mg/m <sup>2</sup> /day IV continuous infusion D1-3 q 21 days. Extravasation precautions. Recommend to use peripheral line for infusion. Avoid central venous catheters containing polyurethane or silicone (PICC line) due to occurrence of phlebitis and requiring the removal of the catheter.
<b>Kinetics</b>	90% protein bound. Terminal half-life is 15.9 hours at 0.4-4 mg/kg in mice and 4.8 hrs at 0.06-0.3 mg/kg in dogs due to higher systemic plasma clearance. The presence of CI-980 in breast milk is not known.

#### Adverse Effects

1. Neurotoxicity - coma, confusion, expressive aphasia, cerebellar dysfunction, hand tremors, headache, fever, mood changes, and loss of consciousness. Neurocortical events are more prone to occur around the end of infusion. Parathesias has also been reported. All events were reversible.
2. Hematologic - dose-related leukopenia and granulocytopenia, thrombocytopenia is less common.
3. Gastrointestinal - nausea, vomiting, reflux, GI bleeding (in the absence of thrombocytopenia), constipation, diarrhea, and stomatitis.
4. Phlebitis - infusion through peripheral veins
5. Cardiovascular - transient hypertension during or shortly after completion of infusion
6. Fatigue

#### Nursing Implications

1. Infusion device for administration
2. Vesicant, extravasation precautions
3. Monitoring - neurotoxicity and phlebitis

<b>Generic Name</b>	Docetaxel
<b>Trade Name</b>	Taxotere (Aventis)
<b>NSC Number</b>	628503
<b>Classification</b>	a semisynthetic taxoid
<b>Action</b>	Docetaxel (similar to Taxol) binds to free tubulin and promotes assembly of stable microtubules, interfering with mitosis and cell replication.
<b>Indication</b>	Locally advanced or metastatic breast cancer (FDA), also possesses activity in non-small cell lung, ovarian, and head and neck ca.
<b>Dose Form</b>	20 mg and 80 mg powder with accompanying diluent (13% ethanol in water)
<b>Storage/Stability</b>	The intact vials should be refrigerated and protected from bright light. Slowly inject the <u>entire</u> diluent solution (1.83 ml in 20 mg and 7.33 ml in 80mg) to reconstitute the vials which is stable for 8 hrs at rm. temp or refrigerated. Rotate vial gently for approx. 15 seconds and allow reconstituted clear solution to stand for 5 minutes. Withdraw appropriate amount of final solution (10 mg/ml) and diluent in NS or D5W to a final concentration of 0.3 to 0.9 mg/ml prior to administration. The final solution is stable for 4 hrs at rm. temp.
<b>Dose/Administration</b>	Single agent: 100 mg/m <sup>2</sup> IVPB infuse over 1 hour every 3 weeks. Pt with hepatic dysfunction should be treated with 75 mg/m <sup>2</sup> . May be given in combination with doxorubin or vinorelbine. <b>Pre-medication of oral dexamethasone 4-8 mg bid x 3-5 days, starting one day prior to treatment is required. Non-PVC tubing and container should be used for drug infusion.</b> Consult specific protocol for dosage and dosage adjustment guidelines.
<b>Kinetics</b>	The peak concentration and AUC are dose related. Elimination half-life is 12 hrs. Highly protein bound and metabolized in the liver and primarily excreted in the feces with 48 hrs of an infusion. Watch for CYP3A4 potential drug interactions.
<b>Adverse Effects</b>	
	<ol style="list-style-type: none"> <li>1. Hematologic- grade IV neutropenia occurred in 95% of pts treated with 100 mg/m<sup>2</sup> (overall 57%) with recovery with 15 days.</li> <li>2. Arthralgia (0.5%), asthenia (11.2%)</li> <li>3. Fluid retention- cumulative at dose 746 mg/m<sup>2</sup>, severe in 5% and 2% required discontinuation of therapy (490 mg/m<sup>2</sup>, 22% and 34%, respectively in pts who did not received corticosteroids)</li> <li>4. Hypersensitivity reaction - significantly lowered with prophylactic corticosteroids</li> <li>5. Liver dysfunction - lower initial dose to 60-75 mg/m<sup>2</sup> to decrease severity of neutropenia.</li> <li>6. GI - nausea/vomiting is moderate and common, prophylactic antiemetic(s) recommended</li> <li>7. Dermatologic - Alopecia; cutaneous reaction manifested as rash can occur, corticosteroids can be helpful in lessening the incidence and severity of this reaction.</li> <li>8. Neurologic: paresthesias, stomatitis</li> </ol>
<b>Nursing Implications</b>	
	<ol style="list-style-type: none"> <li>1. Ensure patient compliance with dexamethasone pre-medications.</li> <li>2. Use non-PVC tubing for administration (similar to Taxol)</li> <li>3. Final solution for administration is only stable for 4 hours after preparation.</li> <li>4. Prophylactic antiemetics prior to administration .</li> </ol>

<b>Generic Name</b>	Sterically stabilized liposomal doxorubicin, Stealth-liposomal doxorubicin
<b>Trade Name</b>	Doxil (OrtoBiotech)
<b>NSC Number</b>	620212
<b>Classification</b>	Liposomal-encapsulated cytotoxic anthracycline antibiotic

**Action** Has an inhibitory effect on nucleic acid synthesis and interacts with the enzyme topoisomerase II. The liposomes are microscopic vesicles composed of phospholipid bilayer that encapsulate the active drug. The liposomes are formulated with surface bound methoxypolyethylene glycol (MPEG), which protects the liposomes from detection by the mononuclear phagocyte system and therefore increases blood circulation time. The exact mechanism of release is not understood.

**Indication** FDA Approved for treatment of AIDS-related Kaposi's sarcoma (KS). Also used in ovarian carcinoma.

**Dose Form** 2mg/ml single dose vial. (20mg/vial)

**Storage/Stability** Store refrigerated between 2° C to 8° C (36° F to 46° F). Do not freeze for longer than 1 month. Prolonged freezing may adversely affect liposomal drug products. No preservatives or bacteriostatic agents are present in Doxil. Diluted Doxil should be refrigerated between 2° C to 8° C (36° F to 46° F) and administered within 24 hours.

NOTE: Doxil is not a clear solution but a translucent, red liposomal dispersion; however, parental drug products should be inspected visually for particulate matter whenever solution and container permit. Do not use if a precipitate or foreign matter is present.

**Administration** The recommended dose of liposomal doxorubicin for patients with AIDS-related KS is 20mg/m<sup>2</sup> administered IVPB over 30 minutes q 3 week s . The recommended dose for ovarian carcinoma is 40-50mg/m<sup>2</sup> IVPB over 1-2 hours q 4 wks. (**Not to exceed 90mg total**) The appropriate dose must be diluted in 250ml of 5% Dextrose, USP prior to administration. Consult the specific protocol for doses and dosage adjustment guidelines. **Do not use with an in-line filter.**

**Rapid infusion may increase the risk of infusion-related reactions but DOXIL MUST NOT BE GIVEN BY CONTINUOUS INFUSION, intramuscular, or subcutaneous use. Doxil must not be given by the intramuscular or subcutaneous route.** Doxil is considered an irritant and precautions should be taken to avoid extravasation. Extravasation may occur with or without an accompanying stinging or burning sensation. In case of extravasation, perform institutional guidelines for management and apply ice over the site.

**Kinetics** The steady-state volume of distribution of liposomal doxorubicin indicates it is confined mostly to the vascular fluid volume. Protein binding of liposomal doxorubicin has not been determined, but the active ingredient, doxorubicin, binds extensively to tissue. Half-life for a 20 mg\m<sup>2</sup> squared dose is approximately 55 hours. Elimination of liposomal doxorubicin is slow, 5.5% of a dose was recovered in urine after 72 hours. Patients with hepatic impairment have not been studied, however, standard doxorubicin is eliminated in large part by the liver, therefore, appropriate reduction in doses should be made in patients with elevated bilirubin levels.

#### **Adverse Effects**

1. Hematologic--In AIDS-related Kaposi's sarcoma patients, neutropenia is common and dose-limiting; thrombocytopenia, anemia
2. Gastrointestinal--nausea (17%),stomatitis (7%)
3. Other--acute infusion reactions (7 to 20%), asthenia, alopecia, (9%), palmer-plantar erythrodysesthesia (3%), fever, cardiomyopathy/heart failure (1%), and occasional hepatic dysfunction.

#### **Nursing Implications**

- Advise Patient that the urine will be red for 1 to 2 days and of reversible complete alopecia.
- Drug is an irritant. Monitor site during administration.

<b>GENERIC NAME</b>	ETOPOSIDE (VP-16, VP-16-213)
<b>TRADE NAME</b>	VePesid (Bristol-Myers Oncology)
<b>CLASSIFICATION</b>	Plant Alkaloid (Podophyllotoxin), cell cycle specific
<b>ACTION</b>	Etoposide causes metaphase arrest and inhibits cells from entering mitosis. Etoposide interacts with DNA topoisomerase II resulting in increased DNA scission and the inhibition of rejoining. Cells are most sensitive to the cytotoxic effects of Etoposide during the G2 phase.
<b>INDICATION</b>	Use in combination therapy or as single agent. Etoposide exhibits a broad spectrum for use in both solid tumors and hematologic malignancy. (ie: testicular cancers, lung cancer, lymphomas, Kaposi's sarcoma )
<b>DOSE FORM</b>	SOLUTION FOR INJECTION 20mg/ml 5ml vials CAPSULES 50mg oil-filled capsules
<b>STORAGE/STABILITY</b>	Store unopened vials for injection at room temperature. Dilute with 0.9% NaCl to a concentration of 0.2mg/ml stable at room temperature 96 hours, or at concentration 0.4mg/ml stable 48 hours room temperature in either glass or plastic. May be mixed with cisplatin and floxuridine in the same container at following concentrations: cisplatin 0.186mg/ml, etoposide 0.286mg/ml, floxuridine 0.714mg/ml stable 7 days room temperature. Capsules stored under refrigeration stable 2 years, at room temperature stable 3 months. For patients unable to swallow capsules, injectable form may be used po at same dose as capsules. Undiluted solution for injection stable in plastic syringe 3 days at room temperature. Further dilution to mask taste of injectable solution in orange juice, apple juice, or lemonade is recommended at concentration 0.4mg/ml; stability 3 hours at room temperature after dilution.
<b>DOSE/ADMINISTRATION</b>	IV INFUSION - 50 to 150 mg/m <sup>2</sup> /day infused over at least 1-3 hours x 3-5 days or 15-30 mg/m <sup>2</sup> /day as a continuous infusion over 5 days every 3-4 weeks. PO - oral dose form may be used at twice IV dose rounded to nearest 50mg or use alternating dose schedule. May take in divided doses. For use in small cell lung cancer current chronic oral dose is 50 mg/m <sup>2</sup> /day on days 1-21 every 28 days.
<b>KINETICS</b>	Mean oral bioavailability 50% (range 25-75%). Etoposide does not undergo first-pass metabolism with oral dosing. Following IV administration, Etoposide exhibits a terminal half-life of 3-20 hours. Etoposide is highly protein bound (97%). Elimination is 40-60% by renal excretion with 2-16% hepatic metabolism and biliary excretion.
<b>ADVERSE EFFECTS</b>	<ol style="list-style-type: none"> <li>1. MYELOSUPPRESSION is most often dose limiting with granulocyte nadirs (at 7-14 days), and platelet nadirs (at 9-16 days) after administration. Bone marrow recovery is usually by day 20 with no cumulative toxicity. In the case of chronic oral dosing, the nadir may occur around day 21 with recovery by day 28. Anemia is usually not significant. Treatment may be repeated at 3-4 week intervals.</li> <li>2. GASTROINTESTINAL - (30-40%) mild-moderate nausea/vomiting which responds to standard antiemetic therapy. Also diarrhea, anorexia, stomatitis.</li> <li>3. ALOPECIA - (66%) Reversible hair loss.</li> <li>4. HYPOTENSION - Temporary hypotension following rapid IV administration secondary to propylene glycol vehicle. Stop infusion and after normalization of blood pressure restart at half the initial rate. May slowly escalate rate.</li> <li>5. ANAPHYLACTOID REACTION - (0.7-2%) presenting with fever, chills, bronchospasm.</li> </ol>
<b>NURSING</b>	<ol style="list-style-type: none"> <li>1. Hypotension - management (see adverse effects section).</li> <li>2. Phlebitis - hardening of veins use for administration may persist for months.</li> <li>3. Do not break apart or withdraw contents of capsule with syringe since oil-filled and difficult to obtain entire contents for accurate dosing.</li> </ol>

<b>GENERIC NAME</b>	Granulocyte Colony Stimulating Factor (G-CSF, Filgrastim)
<b>TRADE NAME</b>	Neupogen <sup>R</sup> (Amgen)
<b>NSC NUMBER</b>	613795
<b>CLASSIFICATION</b>	Biological Response Modifiers – cytokines
<b>MECHANISM OF ACTION</b>	A glycoprotein that regulates normal hematopoiesis by binding to specific cell surface receptors and stimulating proliferation, differentiation commitment, and some end-cell functional activation of neutrophils.
<b>INDICATIONS</b>	Chemotherapy induced neutropenia, bone marrow transplant patients, severe chronic neutropenia (FDA approved indication). Also used in myelodysplastic syndrome, aplastic anemia, cyclical neutropenia etc.
<b>DOSAGE FORM</b>	300 mcg/1ml and 480 mcg/1.6 ml single dose preservative-free vial.
<b>DOSE &amp; ADMINISTRATION</b>	G-CSF starting dose 5-10 mcg/kg/day, max 30 mcg/kg/day daily subcutaneously until ANC at desired level (usual duration of treatment 7-14 days depending on cytotoxic chemotherapy regimen). G-CSF should not be given 24 hours prior to and/or following antineoplastic treatment. Consult specific protocol for dosage and dosage adjustment guidelines.
<b>CONTRAINDICATIONS</b>	Known hypersensitivity reaction to GCSF or E.Coli derived products.
<b>STORAGE AND STABILITY</b>	Intact vials should be stored under refrigeration until ready to use. May store in room temperature for 24 hours. Storage of undiluted drug in plastic syringe is stable up to 24 hours at room temperature and 7 days under refrigeration. Manufacturer provided temperature indicator is available in container for patient to monitor proper storage. Avoid shaking. Use D5W for dilution, do not use saline.
<b>KINETICS</b>	Onset of clinical effect 5 to 7 days. Plasma distribution half-life = 15 mins, elimination half-life = 3.5 hrs. Route of elimination - not known.
<b>ADVERSE EFFECTS</b>	<ol style="list-style-type: none"> <li>1. Bone pain (24%) - usually precurs the recovery of neutrophil counts, dose related, reversible, prophylactic administration of analgesic helpful.</li> <li>2. Inflammation and/or transient bruising at injection sites.</li> <li>3. Transient decrease of WBC with blood samples collected within 4-6 hours after subcutaneous injections of GCSF.</li> <li>4. Decrease in platelet counts up to 25% at dose level of 30-60 mcg/kg.</li> </ol>
<b>NURSING IMPLICATIONS</b>	<ol style="list-style-type: none"> <li>1. Do not shake or freeze the drug.</li> <li>2. Rotate injection sites and limit injection volume to 2 ml per site.</li> <li>3. Monitor CBC routinely for desired response.</li> </ol>

<b>Generic Name</b>	Gemcitabine HCl For Injection (2',2'-difluorodeoxycytidine)
<b>Trade Name</b>	Gemzar (Eli Lilly )
<b>NSC Number</b>	613327
<b>Classification</b>	A deoxycytidine analog antimetabolite, structurally related to cytosine arabinoside.
<b>Action</b>	Gemcitabine is metabolized intracellularly by nucleoside kinases to the active diphosphate and triphosphate nucleosides that cause inhibition of DNA polymerase activity. Evidence indicated that gemcitabine also inhibit RNA synthesis as well as induce apoptosis.
<b>Indication</b>	Pancreatic cancer (FDA approved); Lung, ovarian, and GU cancers.
<b>Dose Form</b>	Dry powder 200 mg and 1000 mg vials.
<b>Storage/Stability</b>	Intact vials can be stored at room temp. When reconstituted to 40 mg/ml with 0.9% NaCl, the solution is stable for 24 hours at rm temp and <b>should not be refrigerated</b> to avoid crystallization. The drug should be further diluted to 0.1 mg/ml with 0.9% NaCl prior to administration and is stable for 24 hrs at rm temp and should not be refrigerated.
<b>Dose/Administration</b>	1000 mg/m <sup>2</sup> IVPB over 30 mins once weekly for 7 weeks, followed by a week of rest. Subsequent cycles should be given once weekly for 3 weeks, and repeat every 4 weeks.
<b>Kinetics</b>	Gemcitabine is rapidly distributed but the volume of distribution is smaller in women and elderly, and with shorter infusions. Clearance is slower in women and elderly pts and the elimination half-life ranged from 32 to 94 mins in short infusions and 356 mins to 638 mins in long infusions. Terminal elimination half-life is 14-22.4 hrs; urinary excretion is the major route of elimination.

#### Adverse Effects

1. Hematological – dose-limiting toxicity, mild and transient neutropenia (6-51%), thrombocytopenia (0.2-51%), and anemia (1-14%).
2. GI – Nausea and vomiting occur frequently but are severe in only 15% of patients. Diarrhea is mild and infrequent (1-36%).
3. Dermatological – transient rash (0-25%) during therapy and tend to be macular, erythematous, and pruritic. They can be managed symptomatically with topical corticosteroids or systemic antihistamine. The rashes usually remain stable or improve with continued gemcitabine therapy. Alopecia is infrequent (0-23%).
4. Flu-like symptoms – frequent side effect (23-100%), Symptoms such as low-grade fever, fatigue, malaise, myalgia, and arthralgia usually start the evening after gemcitabine infusion and last up to several days. Acetaminophen is effective except in high dose gemcitabine therapy where reduction of doses may be necessary.
5. Others - edema (26-58%), lethargy (23-38%), fever (0-32%), elevated transaminases (10-23%), dyspnea (0-19%), mucositis (0-1%), neuropathy (1%). In addition, proteinuria, hematuria, hypotension, and bronchospasm have been reported. These effects are usually mild and resolve within 24 hrs after the infusion.

#### Nursing Implications

1. Do not refrigerate reconstituted or diluted solutions of gemcitabine,
2. Beware of dosing schedule at the first 2 cycles of treatments.
3. Prophylactic antiemetic.
4. Inform and educate patients on management of flu-like symptoms and rash.



<b>GENERIC NAME</b>	HYDROXYUREA
<b>TRADE NAME</b>	HYDREA (Bristol Myers Oncology)
<b>NSC NUMBER</b>	32065
<b>CLASSIFICATION</b>	Miscellaneous, cell cycle specific
<b>ACTION</b>	The exact mechanism of action for hydroxyurea is unknown. Hydroxyurea causes immediate inhibition of DNA synthesis without interference of RNA or protein synthesis. Hydroxyurea interferes with DNA synthesis in part by inhibiting the enzyme conversion of ribonucleotides to deoxyribonucleotides.
<b>INDICATION</b>	Used in melanoma, acute and chronic myelocytic leukemia, ovarian cancer, epidermoid carcinoma of the head and neck, AML, MDS
<b>DOSE FORM</b>	CAPSULES 500mg powder filled pink and green capsules
<b>STORAGE/STABILITY</b>	Store capsules at room temperature.
<b>DOSE/ADMINISTRATION</b>	Dose calculated on lesser of actual weight or ideal body weight. PO - continuous : 800-2000mg/m <sup>2</sup> daily as single dose PO - intermittent : 3200mg/m <sup>2</sup> every 3 days as single dose Daily dose must be adjusted by close monitoring of blood counts. Consult specific protocol for dosage and dosage adjustment guidelines.
<b>KINETICS</b>	Hydroxyurea is readily absorbed from the gastrointestinal tract with peak serum levels within 2 hours. Serum concentration at zero within 24 hours. No cumulative effect with repeated administration. 50% degradation in the liver with elimination as respiratory carbon dioxide and urea in the urine. Remaining excreted unchanged in the urine.
<b>ADVERSE EFFECTS</b>	<ol style="list-style-type: none"> <li>1. <b>HEMATOLOGIC</b> - Myelosuppression (nadir 10-17 days) leukopenia is dose related in severity. Thrombocytopenia and anemia less common. Self-limiting megaloblastic erythropoiesis with fatigue, muscle weakness, nausea, diarrhea, paresthesias (unrelated to vitamin B-12 or folic acid deficiency) is often seen with initiation of therapy and lessens with continuation of therapy.</li> <li>2. <b>GASTROINTESTINAL</b> - Nausea, diarrhea, anorexia, constipation usually mild. Seen in &gt;80% of patients receiving doses around 3000mg/m<sup>2</sup>.</li> <li>3. <b>NEUROLOGIC</b> These symptoms are seldom seen . Headache, hallucinations, disorientation.</li> <li>4. <b>OTHER</b> - Renal impairment (increase in serum creatinine, BUN ) reversible. Also seen fever, chills, malaise, rash, alopecia(rare).</li> <li>5. Due to excretion of hydroxyurea in breast milk, breast feeding is not recommended.</li> </ol>
<b>NURSING</b>	<ol style="list-style-type: none"> <li>1. Oral use of this medication generally well tolerated without the need for premedication with antiemetics. In patients receiving doses around 3000mg/m<sup>2</sup> premedication with oral compazine may be given as needed. Increased fluid intake recommended.</li> </ol>

**Generic Name:** Ibritumomab tiuxetan

**Trade Name:** Zevalin (IDEC Pharmaceuticals)

**NSC Number:** 710085

**Classification:** Monoclonal antibody directed against CD20 antigen

**Mechanism of Action:** Ibritumomab binds to the CD20 antigen on B lymphocytes inducing apoptosis in CD20+ B-cell lines. The chelate tiuxetan binds to In-111 or Y-90. In-111-labeled antibody is used for dosimetry studies to estimate radiation absorbed doses of Y-90 ibritumomab tiuxetan. The beta emissions from Y-90 cause cell damage by forming free radicals in the target and surrounding cells.

**Indication:** Ibritumomab tiuxetan is approved for the treatment of relapsed or refractory low-grade follicular or transformed B-cell non-Hodgkin's lymphoma, including Rituximab refractory follicular non-Hodgkin's lymphoma.

**Dose Form:** The kits for the preparation of a single dose of In-111 Zevalin or Y-90 include 4 vials: one Zevalin vial containing 3.2 mg of Ibritumomab tiuxetan in 2 mL of 0.9% sodium chloride solution; one 50 mM Sodium Acetate vial; one Formulation Buffer vial; one empty Reaction vial and four identification labels.

**Storage and Stability:** Store kits at 2-8° (36-46°F). Do not freeze. Prepared doses of In-111 Zevalin should be stored at 2-8° (36-46°F) until use and administered within 12 hours of radiolabeling. Prepared doses of In-90 Zevalin should be stored at 2-8° (36-46°F) until use and administered within 8 hours of radiolabeling.

**Administration and Dosage:** Zevalin administration is a two-step process. Step 1 is a 250 mg/m<sup>2</sup> infusion of Rituximab followed by a fixed dose of 5 mCi (1.6 mg total antibody dose) In-111 as a 10 minute IV push. Step 2 occurs seven to nine days later and includes a 250 mg/m<sup>2</sup> infusion of Rituximab followed by a 0.4 mCi/kg dose of Y-90 Zevalin as an IV push over 10 minutes. (Note: Step 2 will only occur if adequate distribution is demonstrated after In-111 dosimetry studies.)

**Kinetics:** The mean effective half-life in blood was 30 hours and the mean area under the fraction of injected activity (FIA) vs. time was 39 hours. Over seven days, 7.2% of the injected activity was excreted in the urine.

**Adverse Effects: Body as a whole:** asthenia (43%), infection (29%), fever (17%), abdominal pain (16%), pain (13%), headache (12%), back pain (8%), sever/life-threatening allergic reaction (1%), sever/life-threatening tumor pain (1%) **Cardiovascular System:** hypotension (6%) **Digestive System:** nausea (31%) vomiting (12%), diarrhea (9%), anorexia, (8%), sever/life-threatening gastrointestinal hemorrhage (1%), sever/life-threatening melena (1%) **Hematologic:** thrombocytopenia (95%), neutropenia (77%), anemia (61%), ecchymosis (7%), sever/life-threatening pancytopenia (2%) **Metabolic disorders:** peripheral edema (8%), angioedema (5%) **Musculoskeletal:** arthralgia (7%), myalgia (7%) **Nervous System:** dizziness (10%), insomnia (5%) **Respiratory:** dyspnea (14%), increased cough (10%), rhinitis (6%), bronchospasm (5%), sever/life-threatening apnea (1%) **Skin and Appendages:** pruritis (9%), rash (8%)

Hematologic toxicities were usually severe and prolonged while non-hematologic toxicities were mild in severity. (NOTE: Since Zevalin dosing includes the use of Rituximab, see the prescribing information for the adverse effects associated with Rituximab)

**Nursing Implications:**

- Consider acetaminophen and diphenhydramine as premedication for Rituximab dosing.
- Proper aseptic technique and precautions for handling radioactive materials should be used when handling Zevalin.
- Vial and syringe shields should be used when handling this agent.
- Product contains albumin

<b>Generic Name</b>	Idarubicin
<b>Trade Name</b>	Idamycin (Pfizer Pharmaceuticals)
<b>NSC Number</b>	256439
<b>Classification-</b>	anthracycline antibiotic
<b>Mechanism of Action</b>	A DNA-intercalating analog of daunorubicin which has an inhibitory effect on nucleic acid synthesis and interacts with the enzyme topoisomerase II.
<b>Indications</b>	AML in adults, ALL and myelodysplastic syndrome
<b>Dose Form</b>	Available as single use 5mg/5ml, 10mg/10ml and 20mg/20ml vials
<b>Storage and Stability</b>	Idarubicin should be stored under refrigeration 2° – 8° C ( 36° to 46° F), and protected from light. The vials are preservative-free and are for single use only. Follow own institution's sterility policy regarding products that do not contain a preservative. Prolonged contact in an alkaline pH will degrade Idarubicin.
<b>Administration</b>	Given intravenously over 10-15 minutes; Idarubicin is a potent vesicant, care should be taken to avoid extravasation. Idarubicin should never be administered by IM or SC routes. Do not mix with other drugs. Precipitation occurs with heparin.
<b>Dosage</b>	Induction therapy in patients with AML: 12mg/m <sup>2</sup> daily for 3 days in combination with Ara-C. Dose reduction should be considered for hepatic impairment. Consult protocol for specific doses and dose adjustments.
<b>Kinetics</b>	Idarubicin undergoes extensive extrahepatic metabolism and a rapid distribution phase. Idarubicin has a very high volume of distribution. Elimination occurs predominantly by biliary and to a lesser extent by renal excretion. The mean terminal t <sub>1/2</sub> is 22 hours when used as a single agent and 20 hours when used in combination. Elimination exceeds 45 hours.

#### **Adverse Effects**

Severe Myelosuppression (95%) Severe infection (95%), Hemorrhage (63%).

GI: Nausea and Vomiting (82%), Mucositis (50%), Abdominal Pain and Diarrhea (73%) (severe <5%)  
Dermatologic (46%), including: generalized rash, urticaria and a bullous erythrodermatous rash of palms and soles, Alopecia (77%)

Renal and Hepatic: changes in renal and hepatic function tests have been observed with severe changes occurring in <1% and <5% respectively

Cardiovascular (16%): CHF, serious arrhythmias including atrial fibrillation, chest pain, myocardial infarction and asymptomatic declines in LVEF have occurred. Myocardial insufficiency and arrhythmias were usually reversible and occurred in the setting of sepsis, anemia and aggressive IV fluid administration. These occurred more frequently in patients over 60 years old and in patients with pre-existing cardiac disease.

#### **Nursing Implications**

1. **VESICANT**-Idarubicin should be administered over 10-15 minutes into a freely flowing line of NS or D5W. Extravasation can cause severe local tissue necrosis. Extravasation may occur with or without an accompanying burning sensation. If extravasation occurs terminate infusion immediately. Treat extravasation per institutional guidelines. For more information see package insert and seek further medical treatment as deemed necessary.
2. Monitor CBCs and liver/kidney function. Neutropenic and thrombocytopenic precautions may be necessary.
3. Monitor mucous membranes.
4. Inform patient of reddish-orange urine discoloration.

<b>GENERIC NAME</b>	IFOSFAMIDE
<b>TRADE NAME</b>	IFEX (Bristol Myers Oncology)
<b>NSC NUMBER</b>	10974
<b>CLASSIFICATION</b>	Alkylating agent, cell cycle nonspecific
<b>ACTION</b>	Ifosfamide is activated by hepatic microsomal enzymes forming the unstable intermediate 4-hydroxyifosfamide, which is in equilibrium with aldoifosfamide. Aldoifosfamide splits into active alkylating ifosfamide and acrolein. The active metabolite, ifosfamide mustard, covalently binds to protein and DNA causing chain scission.
<b>INDICATION</b>	Ifosfamide is active in testicular cancer (salvage therapy), sarcomas, lung cancer, ovarian cancer, melanoma, as well as Non-Hodgkin's lymphoma, acute and chronic lymphocytic leukemia.
<b>DOSE FORM</b>	POWDER FOR INJECTION (white) 1 gm/vial
<b>STORAGE/STABILITY</b>	Store powder at room temperature. Reconstitute with 20ml bacteriostatic water for injection to final concentration 50mg/ml. The resulting solution is stable 7 days at room temperature, 21 days refrigerated. Further dilution in D5W, 0.9%NaCl (0.6-20mg/ml) is stable 7 days room temperature, 21 days refrigerated (glass/plastic).
<b>DOSE/ADMINISTRATION</b>	IV INFUSION: over 30 minutes with intermittent dosing of mesna to 24 hours continuous infusion concurrently with mesna. 1.2gm/m <sup>2</sup> /day daily x 5 days every 21 days (VIP-testicular cancer) 1.2-3.4gm/m <sup>2</sup> /day daily x 3-5 days every 21-28 days (sarcoma) 5.0-8.0gm/m <sup>2</sup> over 24 hours day 1 every 21-28 days (sarcoma) Consult specific protocol for dosage and dosage adjustment guidelines.
<b>KINETICS</b>	Ifosfamide is extensively metabolized by the liver with saturation of metabolic pathways at high doses. Excretion is primarily renal. The half-life is dose dependent: 1.6-2.4gm/m <sup>2</sup> half-life approximately 7 hours, 3.8-5.0gm/m <sup>2</sup> half-life approximately 15 hours.
<b>ADVERSE EFFECTS</b>	<ol style="list-style-type: none"> <li>1. <b>HEMATOLOGIC</b> - Myelosuppression is both dose limiting and dose related. Leukopenia (50%) and thrombocytopenia (20%) occurs at 1.2gm/m<sup>2</sup>/day x 5 days. Anemia is usually insignificant. Nadir occurs at day 7-14 with recovery within 5-10 days. Fractionated dosing of ifosfamide produces less myelosuppression than a single high dose schedule.</li> <li>2. <b>URINARY TRACT TOXICITY</b> - Irritation to the bladder mucosa is believed to be due in part to the acrolein metabolite. Urotoxicity (50%) including hemorrhagic cystitis, dysuria, urinary frequency, and other symptoms of bladder irritation. Hematuria (6-92%) may be greatly reduced by use of vigorous hydration and frequent urination for a dilutional effect and to minimize contact of metabolites with the urothelium. Since toxicity is related to higher doses of ifosfamide, use of a fractionated dosing schedule may reduce urotoxicity. Hematuria may also be reduced by the concurrent use of mesna (uroprotector). Mesna is administered IV bolus at 20% dose of ifosfamide 15 minutes prior to and 4 and 8 hours after ifosfamide administration or concurrent with continuous infusion ifosfamide at 1:1 ifosfamide:mesna dose. (A bolus dose of mesna should be given prior to initiation of ifosfamide and continue for 8-12 hours after ifosfamide infusion complete.) For outpatient use or when IV route is unavailable, injectable mesna may be given orally at 40% dose of ifosfamide (twice the IV dose) 2 hours prior to and 4 and 8 hours after ifosfamide administration. Dispense mesna for oral use in plastic syringe. Have patient mix contents of syringe in orange juice, apple juice, or cola and drink at above dosing schedule. (stable 24 hours room temperature or refrigerated)</li> <li>3. Reversible renal toxicity (6%) seen as transient elevations in serum creatinine, blood urea nitrogen.</li> <li>4. <b>CENTRAL NERVOUS SYSTEM</b> - CNS toxicity (12-20%) includes somnolence, confusion, hallucinations, coma, seizures, depressive psychosis, and death. Neurotoxicity may be related to the metabolite chloroacetaldehyde. Symptoms may occur within 2 hours of administration and may persist up to 3 days after completion of therapy. Emotional instability, decreased short-term memory, and a flattened affect may persist for 4-10 weeks after treatment. The incidence of neurotoxicity appears to increase with doses of 3-10gm/m<sup>2</sup> and in patients with decreased renal function. Fractionated dosing schedules over 3-5 days may decrease both the severity and frequency of neurotoxicity.</li> <li>5. <b>GASTROINTESTINAL</b> - Nausea/vomiting (58-95%) is dose related in severity and incidence, and usually begins within 3-24 hours after administration. Transient diarrhea (1%) also reported.</li> <li>6. <b>OTHER</b> - 1) Alopecia (83%) is reversible. 2) Hypersensitivity reaction has occurred in less than 1% patients treated with ifosfamide. 3) Reversible liver dysfunction (3%) seen as increases in liver function tests and/or bilirubin.</li> </ol>
<b>NURSING</b>	<ol style="list-style-type: none"> <li>1. Urotoxic - Adequate hydration to maintain good urine output, and concurrent use of the uroprotector mesna to reduce risk of urotoxicity. Check urine dipstick for hematuria daily during ifosfamide administration. Encourage frequent urination.</li> <li>2. Prophylactic pre/and or post antiemetics should be available.</li> <li>3. CNS toxicity - Ifosfamide induced neurotoxicity may be masked by narcotic analgesics, benzodiazepines, phenothiazines, sedatives, and metoclopramide which may also produce CNS side effects. Concurrent use of these agents may be temporarily discontinued during therapy if symptoms of neurotoxicity occur, or prior to initiation of therapy in patients at increased risk, or in patients receiving high doses of ifosfamide (&gt;3gm/m<sup>2</sup>).</li> </ol>

<b>Generic Name</b>	Irinotecan (CPT-11)
<b>Trade Name</b>	Camptosar (Pfizer Pharmaceuticals)
<b>NSC #</b>	6116348
<b>Classification</b>	Topoisomerase I inhibitor, a semisynthetic analog of the alkaloid camptothecin, derived from the <i>Camptotheca acuminata</i> tree
<b>Action</b>	Irinotecan and its active metabolite, SN-38 inhibit the topoisomerase I enzyme which is required for the elongation phase of DNA replication and RNA transcription
<b>Indication</b>	Metastatic colorectal cancer that recurred or progressed on 5-fluorouracil based therapy, activities also seen in breast, lung, ovarian, and gastric cancers
<b>Dose Form</b>	100 mg/5 ml vial
<b>Storage/Stability</b>	Intact vial should be stored at room temp and protect from light. Dilution in D5W (preferred) or NS to concentration 0.12 - 1.1 mg/ml is stable for 24 hrs in room temp. Dilution in D5W can be stored under refrigeration and is stable for 48 hrs. <b>Refrigeration of admixture using NS is not recommended due to incidence of visible particulates. Freezing of intact vials or admixture should be avoided due to precipitation.</b>
<b>Dose/Administration</b>	125 mg/m <sup>2</sup> IVPB infuse over 90 min q week x 4 weeks, repeat every 6 weeks. Other dosing regimens are also used. Consult the specific protocol for doses and dosage and dosage adjustment guidelines.
<b>Kinetics</b>	Terminal half-life of irinotecan is 6 hours whereas SN-38 is 10 hours; irinotecan is about 50% protein bound and SN-38 is about 95% protein bound; both irinotecan and SN-38 are metabolized with the cumulative biliary and urinary excretion over a period of 48 hours ranged from 25% -50% (dose-dependent). Pharmacokinetic data in pediatric is not known. Dose modification in hepatic or renal disease is not recommended at this time.

#### Adverse Effect

- 1) Gastrointestinal - early cholinergic diarrhea (8%) and late diarrhea (31%). Early diarrhea usually occur during or within 24 hours of administration of irinotecan, presentation can be severe but is usually transient. It may be preceded by complaints of diaphoresis and abdominal cramping. Administration of 0.25 to 1 mg of intravenous atropine is recommended. Late diarrhea usually occur more than 24 hours after treatment and can be prolonged. Symptoms should be treated with loperamide (Imodium) **promptly**. Patients should be instructed to begin 4 mg of loperamide at the first onset of diarrhea followed by 2 mg every 2 hours until patient is diarrhea-free for at least 12 hours. Patient may modify dose to 4 mg every 4 hours during sleeping hours. Premedication with loperamide is not recommended. Refer to package insert for irinotecan dose modification recommendations. Nausea (17%) and vomiting (13%) can be severe (grade 3 &4), prophylactic antiemetic(s) are highly recommended. Abdominal cramping or pain had been reported at 16.4%.
- 2) Hematologic - Grade 3 & 4 leukopenia (28%) and anemia (6.9%) can occur. Refer to package insert for irinotecan dose modification recommendations.
- 3) Grade 3 &4 asthenia (12.2%), fever (45.5% overall) had been reported.
- 4) Dermatologic - alopecia (60.5% grade 1-4). Rash (12.8%) have been reported but did not result in discontinuation of treatment.
- 5) Hepatic - grade 3 or 4 liver enzyme abnormalities were observed in fewer than 10% of patients, usually associated with liver metastasis.
- 6) Respiratory - grade 3 or 4 dyspnea (3.6%) were infrequent and is usually associated with lung metastasis.
- 7) Neurologic - Mild insomnia (19.4%) and dizziness (14.8%) had been reported.
- 8) Cardiovascular - Flushing was observed during administration of irinotecan but has not required intervention.

#### Nursing Implications

- 1) Familiarize with the use and administration of atropine for the onset of acute early diarrhea.
- 2) Instruct patients to have loperamide readily available and reinforce compliance.
- 3) Avoid concurrent use of drugs with laxative properties.
- 4) Prophylactic antiemetic(s) should be given.
- 5) Do not use 0.9% NaCl as diluent if possible.

**GENERIC NAME** JM-216 (BMS-182751), (Bristol-Myers Squibb)

**NSC NUMBER** **NEED**

**CLASSIFICATION** JM-216 is a novel platinum complex that has shown anti-tumor activity when administered orally.

**ACTION** JM-216 functionally acts as an alkylating agent.

**INDICATIONS** JM-216 is being investigated in non small cell lung cancer, small cell lung cancer, ovarian cancer, prostate cancer and cervical cancer.

**DOSE FORM** 10mg, 50mg, and 200mg capsules (oral)

**STORAGE** should be stored at 2-30° C, be protected from light.

**DOSE/ADMINISTRATION** JM-216 is administered orally on an empty stomach. The MTD is 140mg/m<sup>2</sup>/day x 5 days. The recommended dose being used in current trials is 100-120mg/m<sup>2</sup>/day x 5 days.

**KINETICS** Single dose studies have revealed that JM-216 exhibits saturable absorption. Studies were stopped at single doses of 700mg/m<sup>2</sup> when MTD's could not be reached. When JM-216 is given on a daily x 5 schedule the kinetics of absorption and elimination did not appear to change with increasing dose or repeated administration. Plasma concentrations peak 2 hours after a dose and are detectable at 24 hours when the next dose is due.

**ADVERSE EFFECTS**

- Gastrointestinal: nausea(66%), vomiting (66%), diarrhea. (66%)
- Hematologic: neutropenia (85%), thrombocytopenia (85%)- dose limiting toxicity
- At 120mg/m<sup>2</sup>/day x 5 days grade III/IV neutropenia occurred in 25 and 17% of patients respectively. Thrombocytopenia occurred in 30 and 33% of patients. (Grade-III N/V occurred in 8% of patients-no grade-IV)
- No significant cardiac, pulmonary, renal or neurologic toxicities occurred.

**NURSING IMPLICATIONS**

- Should be administered on an empty stomach
- Anti-emetics should be given.
- Diarrhea may occur, but is of short duration and responds to medication.

<b>GENERIC NAME</b>	MELPHALAN (L-PAM)
<b>TRADE NAME</b>	ALKERAN (GlaxoSmithKline.)
<b>NSC NUMBER</b>	8806
<b>CLASSIFICATION</b>	Alkylating agent, cell cycle nonspecific
<b>ACTION</b>	Melphalan is a bifunctional alkylating agent which is active against resting and rapidly dividing tumor cells. It exerts its cytotoxic activity by interstrand cross-linking of DNA.
<b>INDICATION</b>	Melphalan is active in multiple myeloma, breast cancer, and ovarian cancer.
<b>DOSE FORM</b>	TABLET white, scored 2mg POWDER FOR INJECTION 50mg/vial with 10ml provided sterile diluent
<b>STORAGE/STABILITY</b>	Store tablets at room temperature.

Store powder for injection at room temperature. Reconstitute by rapidly injecting 10ml provided sterile diluent and shake vigorously. Resulting clear solution (5mg/ml) is stable at room temperature for 30 minutes. Do not refrigerate reconstituted solution to avoid precipitation. Immediately further dilute dose in 0.9%NaCl (0.1-0.45mg/ml) which is stable 60 minutes at room temperature. The reconstituted/diluted solutions of melphalan are highly unstable and administration must be complete within 60 minutes of reconstitution.

**DOSE/ADMINISTRATION** PO - 8mg/m<sup>2</sup>/day po days 1-4 with prednisone 40mg/m<sup>2</sup>/day po days 1-7 or 6mg single daily dose x2-3 weeks with careful monitoring of blood counts. Following recovery of counts, when white blood cell (WBC) and platelet counts are rising a maintenance dose of 1-4mg po daily is initiated with careful monitoring of blood counts. Optimal response may be seen gradually over several months of repeated or continuous therapy to maintain WBC 3000-3500/mm<sup>3</sup>. (multiple myeloma) 0.2mg/kg/day po days 1-5 every 4-5 weeks (ovarian cancer)

IV - indicated in patients for whom oral therapy is not appropriate. 16mg/m<sup>2</sup> in 0.9%NaCl (0.1-0.45mg/ml) IVPB over 15 minutes day 1 every 14 days x 4 doses. Following adequate recovery of bone marrow, a maintenance dose of 16mg/m<sup>2</sup> IVPB every 4 weeks is initiated with close monitoring of blood counts. (multiple myeloma). The manufacturer recommends consideration of up to 50% dose reduction in patients with renal insufficiency as measured by blood urea nitrogen (BUN) = or > 30mg/dl. Consult specific protocol for dosage and dosage adjustment guidelines.

**KINETICS** Oral absorption of melphalan is erratic and incomplete. Interaction with food can cause up to a 39% decrease in the area under the plasma-time curve. Patients should be instructed to take melphalan on an empty stomach to maximize absorption. Highly variable plasma levels following oral administration may be a result of incomplete intestinal absorption, variable "first pass" hepatic metabolism, and rapid hydrolysis. The area under the plasma concentration-time curve for oral melphalan ranges from 25-89% of the IV dose. Melphalan is 60-90% bound to plasma proteins with a half-life of approximately 70-90 minutes. Elimination is primarily by metabolism to monohydroxye and dihydroxymelphalan hydrolysis products. Urinary excretion is approximately 10%.

#### **ADVERSE EFFECTS**

1. **HEMATOLOGIC** - myelosuppression is dose-limiting toxicity with both leukopenia and thrombocytopenia nadir at 14-21 days. Recovery can be delayed up to 4-6 weeks following treatment. Anemia is usually less significant. Severe myelotoxicity is more common with IV dosing (28%) than with oral dosing (11%). Irreversible bone marrow failure has been reported. Patients with decreased bone marrow reserve secondary to prior chemotherapy or radiation therapy and patients with impaired renal function are at increased risk for severe to irreversible bone marrow toxicity. In one study, increased myelosuppression was associated with poor renal function as measured by blood urea nitrogen levels at or above 30mg/dl. A 50% decrease in dose reduced the incidence of severe bone marrow suppression from 50% to 11% in these patients. Monitoring of complete blood counts with differentials should be obtained prior to each IV dose as well as periodically during treatment. Acute nonlymphocytic leukemia and myeloproliferative syndromes occur as second malignancy from long-term administration of melphalan. At cumulative doses less than 600mg there is < 2% risk of second malignancy. At cumulative doses 730-9652mg a ten year study indicates 11-20% second malignancy.
2. **GASTROINTESTINAL** - Nausea/vomiting, mucositis, and diarrhea are mild and occur infrequently. However, at high doses used in pretreatment for bone marrow transplant gastrointestinal toxicity becomes dose-limiting.
3. **HYPERSENSITIVITY REACTIONS** - acute hypersensitivity reactions (2.4%) especially with the IV formulation include urticaria, pruritis, edema, bronchospasm, dyspnea, tachycardia, hypotension, and anaphylaxis.
4. **OTHER** - Rarely reported pulmonary fibrosis, interstitial pneumonitis, and dermatitis associated with long-term administration.
5. Alopecia is rare and generally only seen at high doses used in pretreatment for bone marrow transplant.

#### **NURSING**

1. Oral formulation is well tolerated and antiemetics are generally not necessary. Melphalan should be taken on an empty stomach.
2. Close monitoring of blood counts.

<b>GENERIC NAME:</b>	MITOXANTRONE
<b>TRADE NAME:</b>	Novantrone (Amgen)
<b>NSC NUMBER</b>	301739
<b>CLASSIFICATION :</b>	Anthracenediones, a synthetic agent
<b>MECHANISM OF ACTION :</b>	Chemical structure similar to anthracyclines but exact action remains unclear. Cell-cycle nonspecific. Inhibit both DNA and RNA synthesis.
<b>STORAGE AND STABILITY :</b>	The dark blue solution contains mitoxantrone in 2 mg/ml concentration in vials of 10 ml, 12.5 ml, and 15 ml with pH 3.7. The intact vials can be stored at room temperature and is stable for 2 years. The concentrate must be diluted to at least 50 ml D5W or NS prior to administration and be used within 24 hours because the product contains no preservative <u>Mitoxantrone is not compatible with heparin.</u>
<b>DOSE &amp; ADMINISTRATION:</b>	10-12 mg/m <sup>2</sup> /day x 1-3 days slow IVP or IVPB. Mitoxantrone is also being used via intracavitary route for malignant effusions ( 17-40 mg single dose, max 80 mg cumulative dose intraperitoneally; 10-40 mg single dose, max 220 mg cumulative dose intrapleurally; and 20 mg single dose, max 60 mg cumulative dose intrapericardially).
<b>PHARMACOKINETICS :</b>	Rapid distribution to tissues and highly protein bound with large volume of distribution. The mean terminal half-life is about 40 hours. Mitoxantrone is metabolized in the liver and less than 10% excreted unchanged in the urine.
<b>ADVERSE EFFECTS :</b>	<ol style="list-style-type: none"> <li>1. Myelosuppression - esp. leukopenia, increase risk in hepatic impaired patients. Nadir in 10-14 days and recovery by day 19-21. Thrombocytopenia and anemia have been reported.</li> <li>2. Cardiotoxicity - CHF and decreased LVEF occurred in 3-6% of adults and children. 3-4% incidence of cardiac failure during treatment and generally associated with cumulative dose exceeding 120 mg/m<sup>2</sup>, particularly if therapy is continued for 9-12 months. Risk factors include previous treatment with anthracyclines, age, and history of cardiac disease.</li> <li>3. Gastrointestinal - mild nausea/vomiting (50%) &amp; severe N/V(&lt;9%) as single agent. Mucositis (4-50%).</li> <li>4. Alopecia - mild (11%)</li> <li>5. Erythematous eruptions</li> <li>6. Blue-green urine can occur within 24 hours after administration of therapy.</li> <li>7. Others - <b>Not classified as a vesicant, but case reports of tissue necrosis following extravasation.</b> Elevation in liver enzymes, renal dysfunction (hematuria, proteinuria, and mild renal failure), and neurological toxicity (weakness, headaches, and mood changes). Edema during therapy has been reported.</li> </ol>
<b>NURSING IMPLICATIONS:</b>	<ol style="list-style-type: none"> <li>1. Monitor cumulative dose for cardiotoxicity.</li> <li>2. Inform patient of blue-green urine.</li> <li>3. Monitor blood counts.</li> </ol>



**GENERIC NAME** MECHLORETHAMINE HYDROCHLORIDE (NITROGEN MUSTARD)  
**TRADE NAME** MUSTARGEN (Merck & Co.)  
**NSC NUMBER** 762  
**CLASSIFICATION** Alkylating agent, cell cycle nonspecific  
**ACTION** Mechlorethamine is a polyfunctional alkylating agent. In neutral or alkaline solution, the drug undergoes ionization to produce a carbonium ion which attaches to the DNA nucleoside, guanine. The cytotoxic effects of this interaction include miscoding of base pairs, structural cleavage of guanine, depurination of DNA, and cross-linking of DNA by guanine-guanine pairs.  
**INDICATION** Primary use in combination chemotherapy for Hodgkin's disease. Mechlorethamine is also active in lymphosarcoma, bronchogenic carcinoma, and mycosis fungoides. Although mechlorethamine has been used intrapleurally and intrapericardially for malignant effusions, it has generally been replaced for use in this manner by other agents such as doxycycline or bleomycin.  
**DOSE FORM** POWDER FOR INJECTION 10mg/vial  
**STORAGE/STABILITY** Store vials at room temperature. Reconstitute with 10ml nonpreserved sterile water for injection or nonpreserved 0.9%NaCl to concentration 1mg/ml. The resulting clear, colorless solution is highly unstable and will decompose on standing. Solution in the vial or plastic syringe is stable 60 minutes at room temperature.  
**DOSE/ADMINISTRATION** IV - 6mg/m<sup>2</sup> IVP day 1 every 28 days (MOPP/ABV hybrid - Hodgkin's) 6mg/m<sup>2</sup> IVP day 1, day 8 (every 28 days MOPP alternating w/ABVD every other month, MVPP every 42 days - Hodgkin's)  
CUTANEOUS - desensitization to prevent delayed hypersensitivity reaction to topical application (100mcg IV weekly x 5 weeks). This is followed by 10mg in 45-60ml water topically applied daily to 3 times per week to both involved and uninvolved skin. (mycosis fungoides) Consult specific protocol for dosage and dosage adjustment guidelines.  
**KINETICS** Mechlorethamine is a highly reactive drug and rapidly undergoes chemical transformation in water or bodily fluids. Within minutes the drug is no longer present in blood. Less than 0.01% active drug is recovered in urine. However, greater than 50% inactive metabolites are excreted in the urine in the first 24 hours after administration.  
**ADVERSE EFFECTS**  
1. HEMATOLOGIC - cumulative, dose-limiting myelosuppression with leukopenia and thrombocytopenia nadir occurring around day 7-14. Recovery is within 7-10 days and anemia is less significant.  
2. NAUSEA/VOMITING - moderate to severe (close to 100%) Onset is rapid within 30 minutes to 2 hours after administration, persisting up to 8 hours.  
3. VESICANT - pain and tissue necrosis upon extravasation. Chemical neutralization with 1/6 molar solution of sodium thiosulfate as follows: 1) To prepare 1/6 molar solution, combine 4ml (10%) sodium thiosulfate with 6ml sterile water for injection. 2) Inject 5ml IV through existing line. Administer multiple injections subcutaneously into extravasation site. May repeat over several hours as per physician's order. 3) Apply cold compresses for 6-12 hours.  
4. CUTANEOUS - local vein discomfort followed by thrombophlebitis may occur with IV administration. Also, brown discoloration of veins used for administration. Topical skin contact with the undiluted powder form or concentrated solution (1mg/ml) can result in ulceration and tissue damage. Irrigate exposed skin with copious amounts of water x 15 minutes followed by 2% sodium thiosulfate. For eye exposure irrigate the eye x 15 minutes with water followed immediately by an ophthalmology consult.  
5. SECOND MALIGNANCY - (1-6%) Non-Hodgkin's lymphoma and non lymphocytic leukemia have been reported.  
6. OTHER - Delayed menses and temporary or permanent amenorrhea occurs in females. Impaired spermatogenesis occurs in males and may persist for several years after treatment. Azoospermia and total germinal aplasia have been reported in males.  
7. Alopecia, usually diffuse thinning.  
8. Cutaneous hypersensitivity reactions occur in nearly 100% patients treated with repeated topical application. Symptoms include hyperpigmentation of the skin, urticaria, and generalized pruritis. Desensitization with minute IV doses has been shown to prevent this delayed hypersensitivity reaction. Hypersensitivity reactions related to systemic administration including respiratory distress, hypotension and anaphylaxis are rare but have been reported.  
**NURSING**  
1. Vesicant - POTENT VESICANT, use extravasation precautions. Also, see above for chemical neutralization.  
2. Prophylactic pre and/or post antiemetics for nausea/vomiting should be available.

<b>Generic Name</b>	Nilutamide
<b>Trade Name</b>	Nilandron (Hoechst Marion Roussel)
<b>NSC Number</b>	Not available
<b>Classification</b>	Anti-Androgen
<b>Action</b>	Blocks the effects of testosterone at the androgen receptor level and interacts with the androgen receptor preventing the normal androgenic response.
<b>Indication</b>	For use in combination with surgical castration for the treatment of metastatic prostate cancer.
<b>Dose Form</b>	50mg tablets (oral)
<b>Storage/Stability</b>	Store at room temperature (15-30°C) and protect from light
<b>Dose/Administration</b>	Recommended dosage is 6 tablets (50mg each) once a day (for a total daily dose of 300mg) for 30 days followed thereafter by 3 tablets once a day (for a total daily dosage of 150mg). Nilutamide can be taken without regard to meals. Although no dosing change appears to be warranted for nilutamide in patients with renal dysfunction, its use in patients with hepatic function impairment is not recommended. <b>NOTE: It is important to consult the specific protocol for doses and dosage adjustment guidelines.</b> Nilutamide has been shown to inhibit the activity of cytochrome P-450 isoenzymes, and therefore, may reduce the metabolism of compounds requiring these systems. Drugs with a low therapeutic margin could have delayed elimination and increases in their serum half-life, leading to toxic levels. The dosage of these drugs may need to be modified. Consult specific protocol for dosage and dosage adjustment guidelines.
<b>Kinetics</b>	Absorption: Rapid and complete Distribution: Moderate binding to plasma proteins and low binding to erythrocytes Metabolism: Extensive, mainly via the liver P450 system Half-life: 38-59 hours Elimination: Primarily in the urine (62%)
<b>Adverse Effects</b>	<ul style="list-style-type: none"> <li>• <i>Body as a Whole:</i> pain (26.8%), headache (13.9%), asthenia (19.1%), back pain (11.5%), abdominal pain (10.0%), chest pain (7.2%), flu syndrome (7.2%), fever (5.3%)</li> <li>• <i>Cardiovascular System:</i> hypertension (9.1%)</li> <li>• <i>Digestive System:</i> nausea (23.9%), constipation (19.6%), anorexia (11.0%), dyspepsia (6.7%), vomiting (5.7%)</li> <li>• <i>Endocrine System:</i> hot flashes (66.5%), impotence (11.0%), libido decreased (11.0%)</li> <li>• <i>Hemic &amp; Lymphatic System:</i> anemia (7.2%)</li> <li>• <i>Metabolic &amp; Nutritional System:</i> increased AST (12.9%), peripheral edema (12.4%), increased ALT (9.1%)</li> <li>• <i>Musculoskeletal System:</i> bone pain (6.2%);</li> <li>• <i>Nervous System:</i> insomnia (16.3%), dizziness (10.0%), depression (8.6%), hypesthesia (5.3%)</li> <li>• <i>Respiratory System:</i> dyspnea (10.5%), upper respiratory infection (8.1%), pneumonia (5.3%)</li> <li>• <i>Skin &amp; Appendages:</i> sweating (6.2%), body hair loss (5.7%), dry skin (5.3%), rash (5.3%)</li> <li>• <i>Special Senses:</i> impaired adaptation to dark (56.9%), chromatopsia (8.6%), impaired adaptation to light (7.7%), abnormal vision (6.2%)</li> <li>• <i>Urogenital System:</i> testicular atrophy (16.3%), gynecomastia (10.5%), urinary tract infection (8.6%), hematuria (8.1%), urinary tract disorder (7.2%), nocturia (6.7%)</li> </ul>
<b>Nursing Implications</b>	<ul style="list-style-type: none"> <li>• Because of the possibility of interstitial pneumonitis, patients should be told to report immediately any dyspnea or aggravation of pre-existing dyspnea.</li> <li>• Because of the possibility of hepatitis, patients should also be told to report nausea, vomiting, abdominal pain, or jaundice.</li> <li>• Patient counseling for hot flashes</li> </ul>

<b>Generic Name</b>	O <sup>6</sup> -Benzylguanine (Chemical name: 6-(Phenylmethoxy)-1H-purin-2-amine)
<b>Trade Name</b>	None
<b>NSC</b>	637037
<b>Classification</b>	Undetermined
<b>Action</b>	O <sup>6</sup> -benzylguanine is a selective and direct inhibitor of O <sup>6</sup> -alkylguanine-DNA alkyltransferase (AGT), a DNA repair protein that plays an important role in protecting cells from the lethal effects of chloroethylnitrosourea and thiazines.
<b>Indication</b>	Still in trials (currently for: colon cancer, brain tumors, lung cancer, breast cancer, rhabdomyosarcoma, acute myeloid leukemia)
<b>Dosage Form</b>	Dual pack with diluent-100 mg active drug, with 670 mg mannitol USP, and sodium hydroxide. The diluent is a 30 ml vial consisting of 40% polyethylene glycol 400 in pH 7 phosphate
<b>Storage/Stability</b>	Dual packs or intact vials should be stored under refrigeration. Shelf-life undetermined. Reconstituted drug is stable for at least 24 hrs when stored at room temperature; however, <b>the single use lyophilized dosage form contains no antibacterial preservative. Therefore, vials should be discarded within 8 hours of the initial entry.</b>
<b>Dose/Administration</b>	IV (usually as a one-hour infusion) Consult specific protocol for dosage and dosage adjustment guidelines.
<b>Kinetics</b>	Not yet reported in humans
<b>Adverse Effects</b>	Neutropenia, renal toxicity, gastrointestinal toxicity, hepatic toxicity <b>O<sup>6</sup> may be susceptible to interactions with inhibitors and inducers of p450 metabolism.</b>
<b>Nursing Implications</b>	Use of O <sup>6</sup> in clinical trials is limited, thus the nursing implications are yet to be reported.

<b>Generic Name</b>	Octreotide, SMS 201-995
<b>Trade Name</b>	Sandostatin, (Novartis)
<b>NSC #</b>	685403
<b>Classification</b>	A synthetic, D-amino acid-substituted derivative of the natural tetradecapeptide somatostatin, a hypothalamic releasing factor inhibitor. This synthetic product sustains a longer half-life of 2 hours and becomes more active.
<b>Action</b>	Octreotide acts directly to inhibit the growth of the somatotropin-release inhibiting factor (SRIF) receptor positive tumors by triggering signal transduction pathways which negatively control growth. Octreotide also inhibits the SRIF receptor negative tumors by down regulating stimuli of tumor growth such as hormones and growth factors
<b>Indication</b>	lipomas, metastatic carcinoid and the carcinoid syndrome, radiation or chemo induced chronic diarrhea. Used concurrently with antineoplastic agents due to its potential additive or synergistic effects in pancreatic cancer. Chronic therapy in acromegaly.
<b>Dose Form</b>	Available as 0.05, 0.1, and 0.5 mg/ml preservative-free ampules; LAR depot 10,20,30 mg vial
<b>Storage/Stability</b>	Intact ampule should be stored under refrigeration and protect from light. Stable at room temperature up to 24 hours
<b>Dose/Administration</b>	<p><b>Carcinoid Syndrome</b> - 50 mcg SQ qd or bid, titrate over 2 weeks to 100-600 mcg/day bid or tid according to symptom suppression. Pediatric doses of 1-10 mcg/kg have been used and well tolerated. Dosage adjustment for severe renal dysfunction is recommended.</p> <p><b>Pancreatic Cancer in conjunction with antineoplastic drug(s)</b> - 160 mg IM every other week for 4 doses, then every 4 weeks thereafter.</p> <p><b>Chronic diarrhea:</b> 150 mg mcg subq bid-tid; LAR depot 20-40 mg q month</p>
<b>Kinetics</b>	Bioavailability of 100% reported following subcutaneous injection, with peak concentration at 0.4 hours. Plasma half-life averages at 1.5 hours, may increase with age due to decreased drug clearance. About 65% of the drug is protein bound. Octreotide is slowly catabolized to inactive peptide fragments but about 32% is excreted unchanged into the urine. Effect of hepatic dysfunction on drug clearance is unknown.
<b>Adverse Effects</b>	<p><b>Gastrointestinal</b> - nausea (8%), abdominal pain (9%), loose stool (4-6%), diarrhea (7%, not dose-related), fat malabsorption (&lt;3%), other rare reports include constipation, flatulence, rectal spasms, and a bloated stomach sensation.</p> <p><b>Dermatologic</b> - local injection site reaction with pain (7.5%), local wheal or erythema (1%), hair loss, skin flaking or thinning, pruritus, rash, bruising or bleeding from a superficial wound were also reported.</p> <p><b>CNS</b> - headache (6%), dizziness, fatigue and weakness (1-4%), anxiety, anorexia, depression, hyperesthesia, decreased libido, nervousness and shaking, syncope, insomnia, and tremor were reported.</p> <p><b>Endocrine</b> - hypo- or hyperglycemia (1-2%), galactorrhea, hypothyroidism (low total and free thyroxine but high thyroid-stimulating hormone) were also reported.</p> <p><b>Hepatic</b> - jaundice and/or liver enzyme elevation were reported</p> <p><b>Drug-drug interactions</b> - decrease cyclosporin level</p> <p><b>Drug-food interactions</b> - change absorption of dietary fats, decrease B12 levels</p>

### Nursing Implications

1. Patient education for self-administration, home administration kits are commercially available.

**Generic Name:** oxaliplatin

**Trade Name:** Eloxitan (Sanofi-Synthelabo Inc.)

**NSC Number:** 266046

**Classification:** Organoplatinum

**Mechanism of Action:** Oxaliplatin undergoes nonenzymatic conversion forming reactive species, which form DNA crosslinks. The crosslinks inhibit DNA replication and transcription.

**Indication:** Used in combination with 5-FU/LV to treat patients with metastatic colon cancer whose disease has progressed or recurred within 6 months of first-line treatment with bolus 5-FU/LV and irinotecan.

**Dose Form:** 50 mg or 100 mg of oxaliplatin as a sterile, preservative-free, lyophilized powder in single use vials.

**Storage and Stability:** Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). After reconstitution the contents of the original vial may be stored up to 24 hours under refrigeration at 2-8° (36-46°F). The final diluted 250-500 mL infusion solution is stable for 6 hours at room temperature or up to 24 hours under refrigeration at 2-8° (36-46°F). **NOT compatible with NS**

**Administration:** Intravenous infusion over two hours. Note nursing implications for extravasation precautions.

**Dosage Regimen:** DAY 1: 85 mg/m<sup>2</sup> Oxaliplatin in 250-500 mL D5W and Leucovorin 200 mg/m<sup>2</sup> IV infusion in D5W both given over 2 hours at the same time in separate bags using a Y-line, followed by 5-FU 400 mg/m<sup>2</sup> IV bolus given over 2-4 minutes, followed by 5-FU 600 mg/m<sup>2</sup> IV infusion in 500 mL D5W (recommended) as a 22 hour continuous infusion.

DAY 2: Leucovorin 200 mg/m<sup>2</sup> IV infusion over 2 hours followed by 5-FU 400 mg/m<sup>2</sup> IV bolus given over 2-4 minutes, followed by 5-FU 600 mg/m<sup>2</sup> IV infusion in 500 mL D5W (recommended) as a 22 hour continuous infusion.

**Kinetics:** After a two-hour infusion of Oxaliplatin, approximately 15% of the administered platinum is present in the systemic circulation while 85% is rapidly distributed in the tissues or eliminated in the urine. Plasma protein binding is irreversible and is greater than 90%.

**Adverse Events: Body as a whole:** fatigue (61%), abdominal pain (31%), fever (25%), back pain (11%), pain (14%), dehydration (5%), allergic reaction (3%), rigors (9%), hypersensitivity reactions/anaphylactic shock (<1%) *can be fatal (see nursing guidelines for premed recommendations)* **Gastrointestinal:** diarrhea (46%), nausea (64%), vomiting (37%), stomatitis (14%), anorexia (20%), gastroesophageal reflux (1%), constipation (13%), dyspepsia (7%), taste perversion (5%), mucositis (2%) **Hematologic:** epistaxis (2%), anemia (64%), leucopenia (13%), neutropenia (7%), thrombocytopenia (30%) **Renal:** elevation of serum creatinine (10%) **Hepatic:** SGOT (36%), SGPT (54%), total bilirubin (13%) **Respiratory:** dyspnea (13%), cough (11%), rhinitis (6%), upper respiratory infection (7%), pharyngitis (2%) **Metabolic disorders:** edema (10%), hypokalemia (3%), peripheral edema (5%) **Skin and appendages:** injection site reaction (9%), Hand-Foot syndrome (1%), flushing (3%), rash (5%), alopecia (3%) **Cardiovascular:** thromboembolism (2%), chest pain (5%) **Nervous System:** acute neuropathy (65%), persistent neuropathy (43%) (*neuropathies can be exacerbated by cold temperatures*), dizziness (7%), insomnia (11%) **Musculoskeletal:** arthralgia (7%) (NOTE: please see prescribing information for adverse effects associated with 5-FU and Leucovorin)

**Nursing implications:**

- Extravasation may cause pain and inflammation at the injection site and lead to severe complications including necrosis. Redness and swelling at the injection site have been reported with oxaliplatin administration.
- Oxaliplatin is not compatible with alkaline solutions (i.e. 5-FU) and must not be administered through the same IV line.
- The infusion line should be flushed with D5W prior to administration of any concomitant medications.
- Do not use any aluminum containing needles or administration sets when administering Oxaliplatin.
- Premedication with antiemetics including 5-HT<sub>3</sub> blockers with or without dexamethasone is recommended.

<b>GENERIC NAME</b>	PACLITAXEL,
<b>TRADE NAME</b>	TAXOL (Bristol-Myers Oncology) (generic preparations are now available)
<b>NSC NUMBER</b>	673089
<b>CLASSIFICATION</b>	Diterpene plant product, taxane, cell cycle nonspecific
<b>ACTION</b>	Microtubules are structures within the cell necessary for many vital functions as well as cell division. Taxol promotes the assembly of excessively stable microtubules. This stability inhibits the normal reorganization of these structures, resulting in abnormal bundles of nonfunctional microtubules.
<b>INDICATION</b>	The primary indication for Taxol is use in refractory ovarian cancer. In current studies Taxol has demonstrated activity in non-small cell lung cancer, breast cancer, melanoma, head and neck cancer, and use as a radiosensitizer in astrocytoma cell lines.
<b>DOSE FORM</b>	SOLUTION FOR INJECTION in Cremophor EL 6 mg/ml vials (30 mg and 100 mg)
<b>STORAGE/STABILITY</b>	Store vials under refrigeration or rm temp. Taxol must be diluted prior to administration in D5W or 0.9% NaCl to a final concentration of 0.3-1.2mg/ml. The resulting solution is stable at room temperature for 52 hours. The plasticizer [di-(2-ethylhexoyl)phthalate] DEHP may be leached from polyvinyl chloride (PVC) infusion bags and sets by Taxol. Prepare and store Taxol in glass or polypropylene bottles or non-PVC plastic bags (polypropylene or polyolefin) and infuse through polyethylene-lined administration sets (non-PVC tubing). Use an in-line filter not larger than 0.22 microns. (attach filter to end of tubing if no in-line filter)
<b>DOSE/ADMINISTRATION</b>	IV INFUSION - 30 mg/m <sup>2</sup> /day IV over 96 hrs, up to 135mg/m <sup>2</sup> IV over 24 hours, up to 350 mg/m <sup>2</sup> over 3 hrs, and up to 200 mg/m <sup>2</sup> over 1 hr every 3 to 4 weeks All patients should be premedicated prior to Taxol administration to prevent hypersensitivity reactions. Recommended premedications include: dexamethasone 20mg IVP, diphenhydramine 50mg (or equivalent) IVP, cimetidine 300mg (or ranitidine 50mg or famotidine 20 mg) IVPB 30-60 minutes before Taxol. INTRAPERITONEAL (IP) - 25-125mg/m <sup>2</sup> (investigational) Consult specific protocol for dosage and dosage adjustment guidelines.
<b>KINETICS</b>	Taxol is highly protein bound (95-98%). Mean elimination half-life range from 5-17 hours. The precise mechanism of systemic clearance of Taxol is not known. It is suggested that hepatic metabolism, biliary excretion, and extensive tissue binding are responsible for the bulk of systemic clearance.
<b>ADVERSE EFFECTS</b>	1) MYELOSUPPRESSION - dose-limiting toxicity. Neutropenia is dose related, non cumulative, and mean nadir occurs at 10-14 days with recovery within 7 days. Thrombocytopenia and anemia are not significant. 2) HYPERSENSITIVITY REACTIONS - Despite recommended premedications, reactions ranging from mild (39%) with flushing, rash to severe reactions (2%) with hypotension, dyspnea, and chest pain requiring interruption of infusion have occurred. Patients with a history of prior severe hypersensitivity reactions to Taxol or other drugs formulated in Cremophor EL (ie: cyclosporin, teniposide) should be treated with extreme precautions. 3) CARDIOVASCULAR - Hypotension and transient bradycardia not requiring treatment occurs most often (39%). Severe cardiovascular events including arrhythmias and AV block have been reported (<2%). Cardiac monitoring is required for patients with serious conduction abnormalities. Frequent vital sign monitoring, especially during the first hour of infusion recommended. Patients at greater risk for cardiovascular events include those with a history of prior cardiac abnormalities and patients taking medications which can alter cardiac conducton.(ie: Digoxin, calcium channel blockers) 4) NEUROTOXICITY - Peripheral neuropathy is dose related and cumulative, most often presenting as mild paresthesia at lower doses. At doses 250mg/m <sup>2</sup> and above, peripheral neuropathy may be dose-limiting. 5) GASTROINTESTINAL - Nausea, vomiting, diarrhea and mucositis (except at higher doses) is mild to moderate. 6) OTHER - Alopecia is complete and reversible(total body hair loss occurs with Taxol). Arthralgia and myalgia is dose dependent and more common in doses >170mg/m <sup>2</sup> . Presentation as pain in large joints noted 2-3 days after treatment, resolving within 5 days.

**POTENTIAL DRUG INTERACTIONS: CYP2C8 & CYP3A4**

**NURSING IMPLICATIONS**

**Hypersensitivity reactions** can be severe. Premedicate prior to Taxol.(see Dose and Administration above)

**Cardiovascular** - Taxol infusion should be stopped and physician should be consulted if patient experiences any signs and symptoms of cardiovascular and/or hypersensitivity reactions.

<b>Generic Name</b>	Pamidronate
<b>Trade Name</b>	Aredia (Novartis)
<b>Classification</b>	Bisphosphonates, a bone resorption inhibitor
<b>Action</b>	pamidronate adsorbs to calcium phosphate (hydroxyapatite) crystals in bone and may directly block dissolution of this mineral component of bone. It does not inhibit bone formation and mineralization.
<b>Indication</b>	Hypercalcemia of malignancy, Paget's disease, and osteolytic bone metastases of breast cancer and osteolytic lesions of multiple myeloma.
<b>Dose Form</b>	30mg & 90 mg sterile lyophilized powder with mannitol.
<b>Storage/Stability</b>	The dose should be diluted to a concentration not to exceed 0.35 mg/ml. The drug may be further diluted in D5W, NS, and _ NS and is stable for up to 24 hours at room temperature. The rate of administration should not exceed a rate of 1 mg/minute. Pamidronate should not be mixed with Ca++ containing solutions.
<b>Dose/Administration</b>	<b>Hypercalcemia</b> – 60-90 mg (corrected serum Ca <13.5 mg/dL); 90 mg (corrected serum Ca >13.5 mg/dL) IVPB over 2-4hrs. may repeat in 7 days if etiology of hypercalcemia not corrected. <b>Paget Disease</b> – 30 mg/day x 3 days, may repeat as clinically indicated. <b>Osteolytic Bone Lesions of Multiple Myeloma and Osteolytic Bone Metastases of Breast Cancer</b> – 90 mg IVPB over 90 min. Consult specific protocol for dosage and dosage adjustment guidelines.
<b>Kinetics</b>	Parenterally administered pamidronate is selectively accumulated in the skeleton, liver and spleen. The drug is eliminated unmetabolized, primarily via the urine. The terminal elimination half-life is 27 hours. The rate of elimination from bone has not been determined. At the recommended therapeutic dose, dose adjustment is not required in pts with renal impairment.
<b>Adverse Effects</b>	<ol style="list-style-type: none"> <li>1. Transient elevation of temperature by at least 1<sup>o</sup> C 4 to 24 hrs after administration (34% compared to 18% in placebo trial).</li> <li>2. Drug-related local soft tissue reaction (18% for 90 mg dose) manifested by redness, swelling or induration and pain on palpation at the site of infusion.</li> <li>3. Asymptomatic hypophosphatemia and hypomagnesiumia.</li> <li>4. Acute exacerbation of bone pain in Paget's Disease.</li> <li>5. Hypocalcemia may lower seizure threshold in patients with malignant disease and brain metastasis (3% reported in three US hypercalcemia trials)</li> </ol>
<b>Nursing Implications</b>	<ol style="list-style-type: none"> <li>1. Avoid calcium containing intravenous solution.</li> <li>2. Council patient of transient temperature elevations.</li> </ol>

<b>Generic Name</b>	Pentoxifylline, 1-(5-oxohexyl)-3,7-dimethylxanthine
<b>Trade Name</b>	Trental (Aventis)(generic formulations now available)
<b>NSC</b>	Not available
<b>Classification</b>	a synthetic xanthine derivative
<b>Action</b>	Improves blood flow by reducing blood viscosity & improving erythrocyte flexibility. Has been shown to increase leukocyte deformability & to inhibit neutrophil adhesion and activation.
<b>Indication</b>	Symptomatic treatment of intermittent claudication on the basis of chronic occlusive arterial disease of the limbs, acute and chronic cerebrovascular insufficiency. Has been studied in other conditions including: diabetic angiopathies and neuropathies, transient ischemic attacks, leg ulcers, sickle cell thalassemias, strokes, high-altitude sickness, asthenozoospermia, acute and chronic hearing disorders, severe idiopathic recurrent aphthous stomatitis, eye circulation disorders, Raynaud's phenomenon infectious diseases and as adjuvant therapy in oncology.
<b>Dose Form</b>	400 mg extended-release, film coated oral tablet in bottle of 100's
<b>Storage/Stability</b>	Store at room temp and protect from light
<b>Dose/Administration</b>	For the management of intermittent claudication, the usual adult dose is 400 mg po three times a day with meals. May reduce dose to 400 mg twice a day in the presence of GI and/or CNS effects. Further dose reduction due to toxicity will call for discontinuation of the drug. Onset of action occur in 2-4 weeks, allow at least 8 weeks of therapy to determine efficacy.
<b>Kinetics</b>	Rapid (within 1 hour) and complete oral absorption, food intake can delay absorption. Extensive first-pass metabolism in the liver. Elimination half-life is dose dependent and is significantly prolonged in patients with hepatic disease. Approximately 95% of the drug and its metabolite is excreted in the urine within the first 24 hrs

#### Adverse Effects

1. Gastrointestinal – dyspepsia(2.8%), nausea(2.2%), vomiting(1.2%); belching ,flatus/bloating (<1%),anorexia, cholecystitis, constipation, dry mouth/thirst (<1%)
2. CNS - dizziness (2%), headache(1.2), tremor (0.3%), anxiety, confusion, depression, seizures (<1%)
3. Cardiovascular – angina/chest pain (<1%), arrhythmia, tachycardia, palpitation, flushing, dyspnea, edema, hypotension (<1%)
4. Respiratory- epistaxis, flu-like s/s, laryngitis, nasal congestion (<1%)
4. Broad spectrum of other adverse effects had been reported with the administration of pentoxifylline, no direct attribution has been established. Fatal aplastic anemia has been reported in at least 2 patients receiving pentoxifylline, although a causal relationship to the drug has not been clearly established.
5. Pentoxifylline is **contraindicated** in patients who have a history of intolerance to the drug or to xanthine derivatives such as caffeine, theophylline, or theobromine.

#### Nursing Implications

- 1) Do not crush tablet for administration.
- 2) Patients receiving warfarin (coumadin) should have more frequent PT time monitoring.
- 3) Close monitoring of blood pressure is recommended in patients receiving pentoxifylline and antihypertensive agents.



<b>Generic Name</b>	PSC 833
<b>Trade Name</b>	None
<b>NSC</b>	41322
<b>Classification</b>	A non-immunosuppressive analog of cyclosporin
<b>Action</b>	PSC833 overcomes multi-drug resistance by inhibiting efflux and allowing antineoplastic drugs to accumulate within the resistance tumor cells by decrease oversuppression of P-glycoprotein and MDR1 gene
<b>Indication</b>	A drug resistance modifying agent (RMA) to be used concurrently with antineoplastic drug(s)
<b>Dose Form</b>	5000 mg/100 ml bottle micro-emulsified oral solution 50 mg/ml injectable ampule (60% cremophor EL)
<b>Storage/Stability</b>	Stored at room temperature (15-25C). Oral formulation is emulsified with ethanol, therefore bottle should not be used 2 weeks after initial entry to prevent excessive evaporation causing unstable emulsion.

**Dose /Administration**

**PO:**5 mg/kg po qid x 12 doses starting at least 24 hours prior to administration of cytotoxic agent(s). The drug should be taken on an empty stomach. The PSC833 solution should be diluted 1:10 in orange or apple juice, or non-alcoholic drinks e.g. soda and administer within 10 minutes after preparation. **Avoid grapefruit juice because the flavonoids in the grapefruit juice can slow down metabolism of the PSC833 and increase its level.**

**IV:** loading dose 1 mg/kg over 1 hr followed by 12 mg/kg/day continuous infusion (MTD). Dilute in D5W and use non-PVC administration products.

**Kinetics** Metabolized by P450 enzyme. Plasma level >2000 mcg/ml desirable for maximum therapeutic effect.

**Adverse Effects**

**Neurologic** - Cerebellar ataxia (dose-limiting toxicity, 100% when dose >12mg/kg/day, begins 36-48hrs after initiation of infusion and resolved 3-5 wks after completion of treatment),dizziness, light-headedness, headache, peripheral neuropathy (25%, dose- related, numbness and tingling of lips, tongue, and fingers).

**Gastrointestinal-** nausea/vomiting primarily associated with oral administration.

**Cardiovascular** - chest tightness, urge to cough, hypotension with progressive syncope, hypertension, no anaphylactic reaction reported.

**Hepatic** - asymptomatic elevated bilirubin and transaminase (83%, incidence increased with PSC levels, usually occurs 48 hrs after completion of PSC infusion and resolved with 7 days).

**Hyperglycemia** - mild, ? associated with use of D5W solution

**Drug/Drug Interactions:** May increase bone marrow toxicities of concurrent antineoplastic agent(s) by altering the pharmacokinetic properties. Follow drug-interaction information of cyclosporin.

**Drug/Disease Interaction:** Liver disease

**Nursing Implications:**

1. Take on empty stomach.
2. Dilute with juice or soda within 10 minutes prior to administration
3. Do not use oral solution bottle 2 weeks after opening
4. Conduct concurrent medication history to advise drug/drug interactions
5. Advise patient to avoid alcohol and sedative-hypnotics medications due to increase risk of neurologic symptoms, avoid driving or operating heavy machinery
6. Use non-PVC administration products when administer PSC parenterally.

<b>Generic Name</b>	R115777 (B)-6-[amino(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-4-(3-chlorophenyl)-1-methyl-2(1H)-quinolinone
<b>Trade Name</b>	Not available
<b>NSC Number</b>	58359
<b>Classification</b>	Farnesyl Protein Transferase Inhibitor
<b>Action</b>	R115777 exerts its anti-tumor activity at least in part by preventing post-translational membrane anchorage of ras proteins by preventing their farnesylation. Ras mutations have been implicated in up to 90% of patients with pancreatic cancer, 50% of patients with colon cancer and in 25 to 30% of human cancers in general.
<b>Indications</b>	At this time the therapeutic indication is Ras-dependent tumors. The most likely indications to be studied are pancreatic and colon cancer.
<b>Dose Form</b>	R115777 is currently available as a 50mg and 100mg capsule filled with pellets.
<b>Storage/Stability</b>	R115777 capsules should be stored at room temperature and protected from light.
<b>Dose/Administration</b>	R115777 is administered orally twice daily after a meal in previous studies. Total daily dose and frequency of administration has not been established. Consult the specific protocol for doses and dosage adjustment guidelines
<b>Kinetics</b>	<p>Preliminary results of the first Phase I trial indicate that R115777 is rapidly absorbed after oral administration. The median terminal half-life is about 16 hours. Urinary excretion of R115777 is negligible.</p> <p><b>In-vitro R115777 inhibits the metabolism of specific CYP3A4, CYP2D6, and CYP2C8/9/10 substrates indicating the possibility of clinically relevant interactions with co-medicated drugs that are mainly metabolized by these cytochrome P-450 forms.</b></p>

**Adverse Effects** (*Incidence of frequency of adverse effects is not available*)

- 1) Hematologic - Animal data from dogs suggest that reversible myelosuppression can occur at high dose levels; however, no Grade 3 or 4 hematological toxicity has been observed to date in humans receiving 1300mg of R115777 for 3 cycles of 5 days. One patient developed grade 4 leukopenia after 20 days of treatment of 300mg bid.
- 2) Ocular - Animal data from rats indicate that cataracts can occur. Rhodopsin kinase is known to be farnesylated. There is no current information as to whether a farnesyltransferase inhibitor can affect rhodopsin kinase in the human eye. Strongly recommend ophthalmology follow-up (including slit-lamp biomicroscopy) to be carried out on a regular basis.
- 3) Gastrointestinal - Nausea and vomiting were the most common adverse events related to the liquid formulation of R115777 administration to patients, but are very likely to be related to the taste of the solution. The current formulation has been replaced by the oral capsule formulation.
- 4) Renal - One case of non-life-threatening renal failure was noted at 1300mg bid.
- 5) Dermatologic - A grade 3 exanthema has been reported after 12 days of treatment with R115777 at 150mg bid.

**Nursing Implications**

1. Carefully monitor all medications for possible drug interactions.
2. Take R115777 after a meal
3. Routine monitoring by an ophthalmologist.

<b>Generic Name</b>	Rituximab
<b>Trade Name</b>	Rituxan™ (Genetech)
<b>NSC Number</b>	687451
<b>Classification</b>	A genetically engineered chimeric murine/human monoclonal antibody against the CD20 antigen found on the surface of normal and malignant B lymphocytes.
<b>Action</b>	The Fab domain of rituximab binds specifically to the antigen CD20, a transmembrane protein located on pre-B and mature B lymphocytes. The antigen is expressed in >90% of B-cell non-Hodgkin's lymphoma and chronic lymphocytic leukemia. The Fc domain of rituximab recruits immune effector functions to mediate B-cell lysis <i>in vitro</i> .
<b>Indication</b>	Treatment of patients with relapsed or refractory low-grade or follicular, CD20 positive, B-cell non-Hodgkin's lymphoma. Combination therapy of rituximab with CHOP chemotherapy is being studied in an attempt to improve the incidence and duration of response.
<b>Dose Form</b>	100 mg/10 ml and 500 mg /50 ml preservative-free single dose vials.
<b>Storage/Stability</b>	The intact vials of Rituxan should be stored under refrigeration and protected from direct sunlight. The recommended dose of rituximab should be diluted in 0.9% NaCl or D5W to a final concentration of 1 to 4 mg/ml prior to administration. The final solution for infusion is stable at 2-8°C for 24 hours and at room temperature for 12 hours. Rituxan™ can be placed in PVC or polyethylene bags for administration.
<b>Dose/Administration</b>	375 mg/m <sup>2</sup> IVPB q weekly for 4 doses. The first infusion should be initiated at 50 mg/hr and be escalated at 50 mg/hr increments every 30 mins, to a maximum of 400 mg/hr. Subsequent infusion can be initiated at 100 mg/hr and increased by 100 mg/hr increments every 30 mins, to a maximum of 400 mg/hr. In the event of hypersensitivity or infusion-related event, interrupted the infusion and restarted the infusion at 2 the previous rate upon resolution of the patient symptoms. Consult specific protocol for dosage and dosage adjustment guidelines.
<b>Premedication with acetaminophen 500-650 mg and diphenhydramine 25-50 mg po/IVP are recommended. Anti-hypertensive medications should not be administered within 12 hours prior to rituximab infusion</b>	

**Kinetics** The half-life is dose-related. At 375 mg/m<sup>2</sup> as IVPB, the mean serum half-life was 59.8 hrs (11.1-104.6 hrs) after the first dose and 174 hrs (26-442 hrs) after the 4<sup>th</sup> dose, probably reflective of the tumor burden and the CD20 B-cell population among patients and repeated administrations. Rituximab was detectable in the serum of patients 3 to 6 months after completion of treatment. The co-administration of CHOP chemotherapy did not alter the pharmacokinetic profile of rituximab.

**Adverse Effects**

1. Infusion-related events: fever (49%), chills/rigors (32%, severe 1.6%), asthenia (16%, severe 0.3%), headache(14%, severe 0.6%), nausea(18%, severe 0.3%), vomiting (7%, severe 0.3%), hypotension (10%, severe 1%), angioedema (13%, severe 0.3%), bronchospasm (8%, severe 1%), dyspnea (<5%, severe 0.3%), rhinitis (8%, severe 0.3%), pruritus (10%, severe 0.3%), rash (10%, severe 0.3%) , urticaria (8%, severe 1%), flushing and pain at disease sites (<5%) generally occurred within 2-2 hrs after initiation of the first infusion. The incidence of infusion-related events decreased from 80% to 40% from first infusion to subsequent infusions.
2. Immunologic: deplete B-cell (immunoglobulins) in 70-80% of patients but no increase incidence of infection. Only 15% of patients will develop hypogammaglobulinemia.
3. Hematologic: thrombocytopenia ( overall 8%, severe 1.3%); neutropenia (overall 7%, severe 1.9%; severe anemia 1%. A single case of transient aplastic anemia and 2 cases of hemolytic anemia were reported.
4. Cardiac : arrhythmias occurred in 4 out of 275 pts (0.6%)during Rituxan infusion. One of 4 discontinued treatment due to ventricular tachycardia and supraventricular tachycardias. Angina was reported during infusion and MI occurred 4 days post-infusion in one subject with a prior history of MI.
5. Others - abdominal pain (6%, severe 0.6%), Myalgia (7%, severe 0.3%), dizziness (7%).

*Patients who received retreatment experienced similar adverse effects in incidence and severity except increased incidence in the following events: asthenia, throat irritation, flushing, tachycardia, anorexia, leukopenia, thrombocytopenia, anemia, peripheral edema, dizziness, depression, respiratory symptoms, night sweats, and pruritis.*

*Patients with lesions >10 cm experienced increased incidence of dizziness, neutropenia, thrombocytopenia, myalgia, anemia, chest pain, hypotension, and dyspnea.*

**Nursing Implications**

1. Premedication of all patients are highly recommended, especially those who are at high risk.
2. Gradual titration of the infusion rate during administration of Rituxan.
3. Understand the infusion-related events and know the appropriate management

<b>Generic Name</b>	L-Selenomethionine
<b>Classification</b>	Essential non-metallic trace element
<b>Action:</b>	Unknown
<b>Indication:</b>	No current FDA indications. Potential chemopreventive agent for cancer of the esophagus, breast, prostate, colon, lung, and skin.
<b>Dose Form:</b>	Available from NCI as capsules containing 25, 50, 100, 200, and 400 µg Selenium as L-selenomethionine
<b>Storage/Stability</b>	Stored at room temperature.
<b>Dose/Administration</b>	200-400 µg/day by mouth. Consult the specific protocol for doses and dosage adjustment guidelines.
<b>Kinetics</b>	Approximately 75% of an oral dose is absorbed. Half-life estimates range from 70 to 300 days.
<b>Adverse Effects</b>	Nausea, fatigue, irritability, dermatitis, hair loss and nail tenderness/loss have been reported. Incidence of adverse effects is not available.
<b>Nursing Implications</b>	None.

<b>Generic Name</b>	<b>Tirapazamine</b>
<b>Trade Name</b>	Tirazone (Sanofi)
<b>NSC Number</b>	130181
<b>Classification</b>	Benzotriazine hypoxic cytotoxic agent.
<b>Action</b>	Tirapazamine is a potent and selective hypoxic cytotoxic agent. The cytotoxic species is thought to be the one-electron reduction product, an oxidizing radical anion that causes extensive single- and double-strand breaks in DNA.
<b>Indication</b>	As an adjunct to radiation therapy or chemotherapy in treatment of tumor cells. Has been studied primarily in combination with cisplatin. Has been investigated in cervical, NCSLC, malignant melanoma and platinum-resistant malignancies.
<b>Dose Form</b>	Intravenous formulation: Tirapazamine is supplied in clear glass 20ml ampules and 100ml bottles containing 0.7mg/ml in an isotonic citrate buffer. Oral formulation: Tirapazamine is supplied in soft gelatin capsules containing 50mg of tirapazamine.
<b>Storage/Stability</b>	Tirapazamine drug supplies should be stored at 59 to 86 degrees F (15-30 degrees C) in the light-proof packaging provided.
<b>Dose/Administration</b>	Dose has not been established. Intravenous doses of 260-450mg/m <sup>2</sup> every 3 week have been used. It is recommended that infusion be administered via a central line due to yellow tracking of the veins when administered into a peripheral line. Consult specific protocol for dosage and dosage adjustment guidelines.
<b>Kinetics</b>	Tirapazamine follows linear kinetics. After single IV dosing, total systemic exposure to tirapazamine increased with dose, with individual AUC values ranging from 18.6mcg x min/ml at 18mg/m <sup>2</sup> to 1165mcg x min/ml at 390mg/m <sup>2</sup> . Clearance values of tirapazamine were independent of dose and ranged from 0.496 to 2.11 L/min. The half-life of tirapazamine ranged from 19.9 to 58.0 minutes. Tirapazamine is metabolized in the liver & in tumor tissue to its 2- and 4- electron bioreductive products and is eliminated mainly by renal excretion. Oral bioavailability is 65% or greater.

### **Adverse Effects**

*Frequently observed adverse effects.*

1. Gastrointestinal symptoms: Nausea, vomiting, diarrhea .
2. Muscle cramps, fever, headache, fatigue, and anemia.

*Less frequent adverse effects.*

1. Myelosuppression which is largely related to concomitant anticancer medication.
2. Acute, reversible hearing loss, which is the dose limiting toxicity, has been seen in patients who received a dose of 450mg/m<sup>2</sup>. At lower dose levels (330 and 390 mg/m<sup>2</sup>), ototoxicity may occur sporadically.
3. Dermatological: skin rash (maculopapular and pruritic or erythematous..

### **Nursing Implications**

1. If tirapazamine is infused into a peripheral vein, it may cause yellow tracking of the veins. In an attempt to alleviate this condition, several sites have opted to administer the drug via central lines.
2. Caution patient about hearing loss and tinnitus.

**Generic Name** Iodine I-131 Tositumomab, Iodine-131 Anti B1 Antibody  
**Trade Name** Bexxar®  
**NSC Number** Not available  
**Classification** Radioimmunotherapeutic Monoclonal Antibody

**Action** Biodistribution studies have demonstrated that radiolabeled anti-B1 antibody reacts with the CD20 cell surface antigen present on normal B cells and most B-cell lymphomas and leukemias

**Indication** For the treatment of low grade non Hodgkin's Lymphoma (NHL), transformed low grade NHL, and other CD 20-expressing B-cell malignancies

**Dose Form** Iodine-131 anti B1 antibody is a sterile, colorless liquid in a glass vial. The dosimetric dose is provided in a 10 ml vial and contains not less than 1.4 ml of solution with a calibrated activity of 8-12 mCi. The therapeutic vial contains not less than 20 ml of solution in a 30 ml vial with a calibrated activity of 112-168 mCi.

**Storage/Stability** Store in the freezer until it is thawed for administration to the patient. The product must be administered to the patient within 72 hours of the calibration date and time specified on the product label.

**Dose/Administration** Patients receiving non-myeloablative doses of Iodine-131 Anti B-1 Antibody will undergo two phases of drug administration. The first phase, termed "dosimetric dose", involves the intravenous administration of 450 mg of Anti B1 Antibody followed by an IV infusion of a low radioactive dose (5 mCi) of Iodine-131-Anti-B1 Antibody for the purpose of determining the rate of whole body clearance of radioactivity (residence time) so that a whole body radiation dose can be calculated. The second phase, termed "therapeutic dose", involves the IV administration of 450 mg of Anti-B1 Antibody followed by an IV infusion of the patient-specific dose of Iodine-131 Anti-B1 Antibody to deliver a specified total body dose. Consult specific protocol for dosage and dosage adjustment guidelines.

**Kinetics** After IV administration, a two compartmental model best fit the data with a median terminal half-life of 70.4 hours. The mean clearance was  $97.9 \pm 109.2$  ml/hr. Dose dependent pharmacokinetics were observed with a larger AUC, slower clearance, longer terminal half-life, and a smaller volume of distribution at steady state observed with increasing predose levels of anti-B1 antibody. The route of excretion was renal with  $65 \pm 13\%$  of the injected dose recovered in the urine over the initial 5 day time period.

#### **Adverse Effects**

- Common (20-90%) Flu like syndrome consisting of fever and chills, nausea, asthenia, headache, WBC  $<2000$  cells/mm<sup>3</sup>, ANC  $<1000$  cells/mm<sup>3</sup>, plt count  $<50,000$  cells/mm<sup>3</sup>
- Less common (10-20%) Rash, anorexia, infection, pain, myalgia, arthralgia, pruritis, abdominal pain, vomiting, pharyngitis, diarrhea, increase in cough, Hgb  $<8$  g/dl
- Infrequent s/e (1-10%) ANC  $<100$  cells/mm<sup>3</sup>, plt count  $<10,000$  cells/mm<sup>3</sup>, Hgb  $<6.5$  g/dl, elevated TSH
- Safety is unknown in pregnant or lactating women

#### **Nursing Implications**

1. Antibody must be administered by personnel authorized to deliver therapeutic doses of a radionuclide to patients.
2. Supportive care for flu-like syndromes.
3. Patient precautions for radiolabeled agents.

<b>Generic Name</b>	Trastuzumab, recombinant humanized anti-HER2 antibody, RhuMAb HER2,
<b>Trade Name</b>	Herceptin (Genentech)
<b>NSC Number</b>	688097
<b>Classification</b>	Monoclonal immunoglobulin G1 kappa antibody
<b>Action</b>	Acts as a mediator of antibody-dependent cellular cytotoxic (ADCC) agent through its high affinity, high specificity binding to extracellular domain of HER2 Receptor . HER2 is a proto-oncogene that encodes a transmembrane receptor protein which is structurally related to the epidermal growth factor receptor.
<b>Indication</b>	As a single agent in the treatment of patients with metastatic breast cancer whose tumors overexpress HER2 protein and who have received at least one chemotherapy regimen for their metastatic disease. In combination with paclitaxel in chemo-naive patients with metastatic breast cancer whose tumors overexpress HER2 protein. Is being investigated in Stage I-III breast cancer, and in other tumors that overexpress HER2.
<b>Dose Form</b>	Lyophilized, sterile powder containing 440 mg trastuzumab per vial under vacuum. Each carton contains one vial of 440 mg trastuzumab and one 30 ml vial of bacteriostatic water for injection, USP, 1.1% benzyl alcohol.
<b>Storage/Stability</b>	Prior to reconstitution: store at 2-8 °C (36-46 °F). Each vial of trastuzumab should be reconstituted with 20 ml of BWFI, USP, 1.1% benzyl alcohol preserved, as supplied (note that BWFI is supplied in a 30 ml vial). The resulting solution will contain trastuzumab 21 mg/ml and should not be used more than 28 days beyond the date of reconstitution with refrigeration. Do not freeze reconstituted trastuzumab. Diluted trastuzumab in polyvinylchloride or polyethylene bags containing 0.9% NaCl maintains both stability and sterility up to 24 hours refrigerated (2-8 °C). Trastuzumab should not be administered or mixed with dextrose solution. For patients with known hypersensitivity to benzyl alcohol, trastuzumab may be reconstituted with sterile water for injection and must be used immediately.
<b>Dose/ Administration</b>	Usual loading dose: Trastuzumab 4 mg/kg administered as a 90-minute infusion. Usual maintenance dose: Trastuzumab 2 mg/kg as a 30-minute infusion once weekly as tolerated. Consult the specific protocol for doses and dosage adjustment guidelines. Trastuzumab may increase the probability of cardiac dysfunction when used concurrently with anthracyclines. Information on trastuzumab compatibility with other medications is not available. Trastuzumab should not be administered or mixed with dextrose solution.
<b>Kinetics</b>	Dose-dependent. In studies using a loading dose of 4 mg/kg followed by a weekly maintenance dose of 2 mg/kg, a mean $t_{1/2}$ of 5.8 days was observed. The volume of distribution is equivalent to the serum volume. The disposition of trastuzumab is not altered based on age or serum creatinine. Administration of trastuzumab with paclitaxel resulted in reduction in trastuzumab clearance. Serum levels of trastuzumab in combination with cisplatin, doxorubicin, or epirubicin plus cyclophosphamide did not suggest any interactions.

#### Adverse Effects

1. Cardiac failure/dysfunction (class III-IV): 5% (single agent) to 19% (with anthracycline and cyclophosphamide); discontinuation of trastuzumab should be considered in patients with clinical CHF. Risk may increase in geriatric patients and patients with pre-existing cardiac dysfunction or prior cardiotoxic treatments. The probability of cardiac dysfunction is highest in patients who received herceptin concurrently with anthracyclines.
2. Infusion-associated symptoms: 40% chills and/or fevers primarily with initial infusion; possible severe reactions, including anaphylaxis and pulmonary events. In some cases, symptoms occur during or within 24 hours of administration. Post-marketing severe infusion reactions leading to fatal outcome have been reported.
3. Pulmonary: Severe pulmonary events (dyspnea, pulmonary infiltrates, pleural effusion, non-cardiogenic pulmonary edema, pulmonary insufficiency and hypoxia and ARDS) leading to death have been reported. Patients with symptomatic intrinsic lung disease or with extensive tumor involvement of the lungs may be at greater risk of severe reactions. Pneumonitis and pulmonary fibrosis have also been reported in postmarketing settings.
4. Hematologic: Anemia and leukopenia- 3% (single agent); if given with AC-anemia -36% and leukopenia - 52%-- severity primarily mild to moderate.
5. Diarrhea: 25%; severity primarily mild to moderate. Increased risk in combination therapy.
6. Infection: 20%; primarily mild upper respiratory infections or catheter infections. Increased risk in combination therapy

#### Nursing Implications

1. Monitor for chills, fever, nausea, rigors, headache, hypotension, or pulmonary events during infusion.
2. Do not use dextrose-containing solution with trastuzumab administration.
3. Monitor for signs and symptoms of clinical CHF.

<b>GENERIC NAME</b>	VINBLASTINE (VLB)
<b>TRADE NAME</b>	VELBAN (Lilly)
<b>NSC NUMBER</b>	49842
<b>CLASSIFICATION</b>	Plant alkaloid, cell cycle specific
<b>ACTION</b>	Vinblastine is an alkaloid obtained from the periwinkle plant. It is believed to act similarly to Vincristine causing mitotic inhibition and arresting the cell cycle in metaphase. Vinblastine also interferes with metabolic pathways of amino acids. By blocking utilization of glutamic acid Vinblastine inhibits purine synthesis and urea formation via the citric acid cycle.
<b>INDICATION</b>	Use as single agent and in combination therapy for Hodgkin's disease, lymphomas, advanced breast cancer, testicular germ-cell cancers, and choriocarcinomas.
<b>DOSE FORM</b>	POWDER FOR INJECTION 10mg/vial SOLUTION FOR INJECTION 1mg/ml in 10ml vials
<b>STORAGE/STABILITY</b>	Store vials under refrigeration. Reconstitute with 10ml preserved 0.9%NaCl to a concentration of 1mg/ml. The resulting clear, colorless solution is stable in the vial for 30 days refrigerated. Further dilution (0.02mg/ml) in NS or D5W stable 7 days room temperature, 21 days refrigerated (glass/plastic).
<b>DOSAGE/ADMINISTRATION</b>	IV use only. <b>***NOT FOR INTRATHECAL ADMINISTRATION***</b> IVP - usual adult weekly dosage range 4-8mg/m <sup>2</sup> 1.5-1.7mg/m <sup>2</sup> /day by continuous infusion may be given for 5 days every 28 days 4-6mg/m <sup>2</sup> on days 1, 2 every 21-28 days 50% dose reduction recommended by the manufacturer for patients with direct serum bilirubin > 3mg/dl.
<b>KINETICS</b>	Consult specific protocol for dosage and dosage adjustment guidelines. Vinblastine undergoes rapid, extensive tissue binding (>75% protein bound). The plasma half-life is approximately 24 hours. Vinblastine undergoes hepatic metabolism with excretion in the bile and in the urine.
<b>ADVERSE EFFECTS</b>	<ol style="list-style-type: none"> <li>1. MYELOSUPPRESSION - primarily leukopenia, dose-related, dose limiting toxicity with nadir at day 4-10 with recovery in 7-14 days. Thrombocytopenia and anemia usually not significant.</li> <li>2. VESICANT - pain and tissue necrosis upon extravasation.</li> <li>3. NEUROTOXICITY - less frequent than with Vincristine. Constipation and paralytic ileus may occur with high doses (above 20mg) and are rarely seen with doses below 10mg. Also, paresthesias, peripheral neuropathy, jaw pain, and urinary retention may occur in patients receiving prolonged therapy or in patients receiving high individual doses.</li> <li>4. GASTROINTESTINAL - Nausea and vomiting is mild, usually lasting less than 24 hours, stomatitis.</li> <li>5. OTHER - Alopecia is mild and reversible.</li> </ol>
<b>NURSING</b>	<ol style="list-style-type: none"> <li>1. Vesicant- Manufacturer recommends local injection of hyaluronidase and application of warm compress to disperse the drug. Upon extravasation consult extravasation policy and procedure.</li> <li>2. For IV use only.</li> <li>3. NOT FOR INTRATHECAL USE.</li> </ol>



<b>GENERIC NAME</b>	VINCRIStINE (VCR, LCR)
<b>TRADE NAME</b>	ONCOVIN (Lilly), VINCASAR PFS (Adria)
<b>NSC NUMBER</b>	67574
<b>CLASSIFICATION</b>	Plant alkaloid, cell cycle specific
<b>ACTION</b>	Vincristine is an alkaloid derived from the periwinkle plant. Its precise mechanism of action is unknown. The cytotoxic effects of vincristine are believed to be due to a reversible binding of the drug to the microtubule and spindle proteins in the S phase. In this way it arrests mitotic division at the stage of metaphase.
<b>INDICATION</b>	Use in combination with other oncolytic agents in acute leukemia, Wilm's tumor, small cell lung cancer, lymphomas, sarcomas, neuroblastoma, Kaposi sarcoma.
<b>DOSE FORM</b>	SOLUTION FOR INJECTION 1mg/ml 1,2,5 ml vials and 1,2 ml disposable syringes
<b>STORAGE/STABILITY</b>	Store vials and syringes under refrigeration. Solution is stable 30 days refrigerated after opening. Further dilution in D5W, NS (0.02mg/ml) stable 7 days room temperature, 21 days refrigerated.
<b>DOSE/ADMINISTRATION</b>	For IV use only <b>**NOT FOR INTRATHECAL ADMINISTRATION**</b> 0.4-1.4mg/m <sup>2</sup> one dose per week IVP over 1 minute into freely flowing IV of D5W or NS. Usual maximum dose 2.0-2.5mg IV per week IVPB - over 20-30 minutes in 0.9% NaCl or D5W In patients with serum bilirubin greater than 3mg/dl use 50% dose reduction. Consult specific protocol for dosage and dosage adjustment guidelines.
<b>KINETICS</b>	Vincristine is rapidly, extensively (>90%), and reversibly protein bound. Plasma half-life ranges from 19-155 hours. Vincristine is largely metabolized by the liver. Primary elimination is biliary excretion with only 10% urinary excretion.
<b>ADVERSE EFFECTS</b>	<ol style="list-style-type: none"> <li>1. NEUROTOXICITY - cumulative and dose dependent. Peripheral neuropathy including decrease or loss of deep tendon reflexes, numbness, weakness, myalgia, cramping, severe motor difficulties, bone pain, jaw pain(rare), constipation, paralytic ileus. These side effects may be reversible within 6 weeks following discontinuation of therapy, however some neuromuscular abnormalities may be irreversible.</li> <li>2. VESICANT - Pain and tissue necrosis upon extravasation.</li> <li>3. MYELOSUPPRESSION - mild anemia, leukopenia; 10 day nadir (usually not dose limiting). Preexisting thrombocytopenia may improve before marrow remission appears.</li> <li>4. GASTROINTESTINAL - Nausea/vomiting is rare except in the presence of paralytic ileus.</li> <li>5. OTHER - SIADH resulting in high urinary sodium excretion in the presence of hyponatremia; alopecia.</li> </ol>
<b>NURSING</b>	<ol style="list-style-type: none"> <li>1. Vesicant - Manufacturer recommends local injection of hyaluronidase and application of warm compress to disperse the drug. Upon extravasation consult extravasation policy and procedure.</li> <li>2. IV use only.</li> <li>3. Constipation - prophylactic stool softeners, bulk forming laxatives, or high-fiber diet.</li> </ol>

<b>Generic Name</b>	Vinorelbine
<b>Trade Name</b>	Navelbine (GlaxoSmithKline)
<b>Classification</b>	Vinca alkaloid, cell cycle specific
<b>Mechanism of Action</b>	Blocks formation of microtubules, leading to impaired formation of mitotic spindle
<b>Indication</b>	Non small cell lung cancer, advanced breast cancer, ovarian cancer, Hodgkin's disease
<b>Dosage Form</b>	Solution for Injection: 10 mg/1 ml and 50 mg/5 ml vials
<b>Storage and Stability</b>	Intact vials - refrigerate and protect from light. Vials stored at room temp are stable for 72 hours. Diluted solution at 0.5 mg/ml is stable for 3 days in NS and 7 days in D5W in PVC bags.
<b>Dose/Administration</b>	<p>Single agent - 30 mg/m<sup>2</sup> q week. Dose adjustments for granulocyte counts and total bilirubin levels are recommended. Refer to package insert for guidelines.</p> <p>In combination with cisplatin for Non small cell lung cancer. For Breast Cancer- vinorelbine has been studied in combination with mitomycin, doxorubin, mitoxantrone, 5-fluouracil, and ifosfamide.</p> <p>Vinorelbine can be administered as:</p> <p>IVP - dilute to 1.5-3 mg/ml in NS or D5W over 6-10 minutes</p> <p>IVPB - dilute to 0.5 - 2 mg/ml in NS, D5W, 1/2NS, LR over 15-30 minutes</p> <p>Consult specific protocol for dosage and dosage adjustment guidelines.</p>

**Kinetics**

Lipophilic and highly distributed into peripheral tissues (Vd = 27L)  
Elimination - triphasic, primarily hepatic (60%), fecal (20%), urinary (8-18%)  
Half-life - alpha = 2-6 mins, beta = 1.9 hrs, gamma = 40 hrs; tissue binding (80%), platelets binding (78%) and lymphocytes (5%)  
Oral administration - 24% bioavailability

**Adverse Effects**

1. Hematologic - leukopenia, non-cumulative, nadir 7-10 days with recovery in 14 days; thrombocytopenia only reported in pretreated ovarian cancer pts; anemia (2%)
2. Gastrointestinal - mild nausea/vomiting, constipation (29%- neuropathy), diarrhea and stomatitis (<20%)
3. Neurotoxicity - decreased deep tendon reflex (6-29%), constipation, paresthesias (2-10%), prior vinca therapy and radiation increases the risk of paresthesias
4. Alopecia (25%)
5. Vesicant – moderate
6. Hepatic - transient liver enzyme elevation without clinical symptoms
7. Cardiovascular - chest pain (5%) in pts with history of CV disease or tumor in the chest
8. Pulmonary - short of breath (3%), interstitial pulmonary changes reported, allergic reaction can be pre-medicated with dexamethasone 10-20 mg IVP
9. Miscellaneous - asthenia, jaw pain, myalgias, arthralgias, rash (<5%), SIADH (<1%), hemorrhagic cystitis.
10. Embryogenic but not teratogenic

**Nursing Implications**

1. Vesicant - treat with warm pack and use hyaluronidase 150 units ID around site
2. IVPB administration should be avoided in peripheral line administration, central venous access is preferred.

<b>Generic Name</b>	zoledronate
<b>Trade Name</b>	Zometa® (Novartis)
<b>NSC Number</b>	
<b>Classification</b>	Third generation biphosphonate
<b>Action</b>	It is a highly potent inhibitor (100 to 850 times more active than pamidronate) of osteoclastic bone resorption and also inhibits the formation and dissolution of calcium hydroxyapatite crystals <i>in vitro</i> .
<b>Indication</b>	Paget's disease, tumor-induced hypercalcemia osteoporosis, metastatic bone disease
<b>Dose/Form</b>	Zoledronate is formulated as 0.1, 1.0, and 4 mg dry powder in vials for IV injection. The vial is reconstituted with 5 ml sterile water for injection, USP.
<b>Storage/Stability</b>	<b>NOTE:</b> Glass containers should <b>NOT</b> be used for storing or preparing. Zoledronate should also <b>NOT</b> be mixed into calcium-containing IV infusions. It is also recommended by the manufacturer that this biphosphonate not be administered with other biphosphonates or other agents commonly used to treat hypercalcemia because of additive anti-resorptive effects. Since zoledronate does bind to bone, it is possible that it could interfere with radionuclide bone scanning. As with other biphosphonates, mild hypocalcemia may result post therapy.
<b>Dose/Administration</b>	<b>IV, over 15 minute infusion</b>
<b>Kinetics</b>	Absorption: Rapid and complete with over 60% retained in bone at 6 months Distribution: primarily to bone with high turnover rates Metabolism: minimal Excretion: renally for that portion not bond to bone (approx. 15%)
<b>Adverse Effects</b>	
<b>Common (20-90%)</b>	skeletal pain, nausea, fatigue, vomiting, headache, fever, diarrhea, viral infection, anemia, arthralgia, myalgia, paresthesias, site phlebitis
<b>Less Common (10-20%)</b>	back pain, idiopathic hypocalcemia, idiopathic hypophosphatemia, peripheral edema, upper respiratory tract infection, urinary tract infection, dyspnea, abdominal pain
<b>Infrequent (1-10%)</b>	thrombocytopenia, depression, arm pain, leg pain, somnolence, syncope, rash, rigors, anorexia
<b>Rare (&lt;1%)</b>	conjunctivitis, scleritis
<b>Nursing Implications</b>	Watch for common side effects