

DRUG NAME: Paclitaxel**SYNONYM(S):** benzenepropanoic acid¹**COMMON TRADE NAME(S):** TAXOL®, ONXOL®**CLASSIFICATION:** antimicrotubule agent*Special pediatric considerations are noted when applicable, otherwise adult provisions apply.***MECHANISM OF ACTION:**

Paclitaxel is a taxane. Paclitaxel binds to tubulin, the protein component of microtubules, simultaneously promoting their assembly and disassembly to form stable, nonfunctional microtubules.^{1,2} Although some reports indicate a cross-reactivity rate of 90% between docetaxel and paclitaxel, others suggest it does not occur consistently.^{2,3} Stabilization of microtubules blocks cells in the M phase of the cell cycle, inhibiting cell division and causing cell death.² Paclitaxel acts as a radiosensitizing agent by blocking cells in the G₂ phase.⁴ Paclitaxel is an immunosuppressant.^{5,6}

PHARMACOKINETICS:

Oral Absorption	no information found	
Distribution	biphasic: initial distribution to peripheral compartment, then slow efflux from the peripheral compartment; widely distributed into body fluids and tissues ^{1,7} ; small changes in dose may lead to large changes in peak plasma concentrations and total drug exposure due to saturable, nonlinear pharmacokinetics ²	
	cross blood brain barrier? ^{2,8}	no
	volume of distribution ^{1,2,5,6}	67 L/m ² for 1-6 h infusion; varies with dose and infusion time; 198-688 L/m ² for 24 h infusion
	plasma protein binding ^{1,2,5}	88-98%
Metabolism	extensively metabolized in liver via CYP 2C8 (primarily) and CYP 3A4; activity of metabolites is unknown ^{1,2,7}	
	metabolite(s) ^{2,4,9}	<ul style="list-style-type: none"> • 67% as 6α-hydroxypaclitaxel via CYP 2C8; • 37% as 3-p-hydroxypaclitaxel and 6α,3-p-dihydroxypaclitaxel via CYP 3A4
Excretion	primarily via bile ^{1,2,5,7,8}	
	urine	14% (1-13% as unchanged drug)
	feces	71% (5% as unchanged drug)
	terminal half life ^{1,2,6,7}	10 h; varies with dose and infusion time
	clearance ^{1,2,7}	12 L/h/m ² ; varies with dose and infusion time
Children ²	clearance: 19 to 260 L/m ²	

Adapted from standard reference⁷ unless specified otherwise.**USES:****Primary uses:**

- *Breast cancer
- *Lung cancer, non-small cell
- *Ovarian cancer
- *Kaposi's Sarcoma

Other uses:

- Lung cancer, small cell²
- Esophageal cancer²
- Bladder cancer²
- Head and Neck cancer²
- Cervical cancer²
- Endometrial cancer²

*Health Canada approved indication

SPECIAL PRECAUTIONS:**Caution:**

- **Preexisting liver impairment** may impair elimination of paclitaxel^{1,7}; dose reduction is suggested^{2,9}; see **Dosage Guidelines**.

Special populations:

- **Elderly patients** may have more myelosuppression, neuropathy and cardiovascular toxicities²
- Patients with **AIDS-related Kaposi's sarcoma** may have more hematologic toxicities, infections and febrile neutropenia.⁷

Carcinogenicity: no information found

Mutagenicity: Not mutagenic in Ames test and mammalian *in vitro* mutation test. Paclitaxel is clastogenic in human lymphocytes *in vitro* but not in other mammalian *in vivo* chromosome tests.^{1,2,7}

Fertility: In animal studies, reduced fertility has been observed, with decreased pregnancy rates and increased embryo loss in females and testicular atrophy/degeneration in males.^{1,2}

Pregnancy: FDA Pregnancy Category D.^{5,10} There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective). Paclitaxel has shown to be embryotoxic and fetotoxic in animal studies; soft tissue and skeletal malformations have been reported.^{1,2,7}

Breastfeeding is not recommended due to the potential secretion into breast milk.^{1,2,7}

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials.¹¹⁻¹⁴

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in bold, italics	
blood and lymphatic system/ febrile neutropenia	<i>anemia</i> (62-78%, severe 6-16%) ^{1,7}
	<i>febrile neutropenia</i> (2%) ⁶
	<i>leukopenia</i> (86-90%, severe 4-17%) ^{1,7}
	<i>neutropenia</i> (87-90%, severe 27-52%) ^{1,2,7} ; nadir 10-12 days, recovery 15-21 days; may require dose reduction
	thrombocytopenia (6-20%, severe 1-7%) ^{1,2,7} ; nadir 8-9 days ²
cardiac	bradycardia (3-4%); first 3 h of infusion ^{1,7} ; see paragraph following Side Effects table
	<i>cardiovascular events</i> (severe 1-2%) ^{1,7} ; see paragraph following Side Effects table
ear and labyrinth	hearing loss, tinnitus, vertigo, ototoxicity (<1%)
eye	optic nerve and/or visual disturbances, photopsia, visual floaters (<1%); generally reversible, may be dose-related
gastrointestinal	<i>emetogenic potential: low-moderate</i> ¹⁵
	abdominal pain; with intraperitoneal administration ⁶
	anorexia (25%) ¹
	constipation (18%) ¹

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in bold, italics	
	diarrhea (25-79%)
	intestinal obstruction (4%) ¹
	mucositis (20-31%); more common with 24 h infusion ^{1,7}
	nausea and vomiting (44-52%)
	taste changes ²
general disorders and administration site conditions	extravasation hazard: irritant , ^{16,17} treat as vesicant ¹⁸ ; see paragraph following Side Effects table
	edema (17-21%, severe 1%); localized under skin at no specific site
	fever (12%) ⁷
	injection site reactions (4-13%) ^{1,7}
immune system	hypersensitivity reactions (5-42%, severe 1-2%) ^{1,7,19} ; see paragraph following Side Effects table
infections and infestations	infections (18-30%, severe 1%); primarily urinary tract and upper respiratory tract ^{1,7}
injury, poisoning, and procedural complications	radiation recall dermatitis ²
investigations	ECG abnormalities (8-14%, severe <1%) ^{1,2,7} ; see paragraph following Side Effects table
	alkaline phosphatase, elevated (18-22%, severe 1%) ^{1,7}
	AST, elevated (18-19%, severe 1%) ^{1,7}
	bilirubin, elevated (4-7%, severe 1%) ^{1,7}
musculoskeletal and connective tissue	arthralgia/myalgia (54-60%, severe 8-12%) ^{1,7} ; see paragraph following Side Effects table
nervous system	autonomic neuropathy, resulting in paralytic ileus and orthostatic hypotension (<1%)
	motor neuropathy, with resultant minor distal weakness (<1%)
	peripheral neuropathy (52-64% severe 2-4%) ^{1,7} ; see paragraph following Side Effects table
respiratory, thoracic and mediastinal	dyspnea (2%) ^{5,6}
	radiation recall pneumonitis ²
skin and subcutaneous tissue	alopecia (87-93%) ^{1,7} ; usually complete, generally occurs 14-21 days after administration of paclitaxel; onset sudden, often occurring in a single day ²
	nail discolouration (2%) ⁷
	rash (12-14%) ^{1,7}
vascular	hypotension (11-24%); during first 3 h of infusion ^{1,7}
	phlebitis ^{1,7}

Adapted from standard reference⁷ unless specified otherwise.

Arthralgia/myalgia may be severe in some patients; however, there is no consistent correlation between cumulative dose and infusion duration of paclitaxel and frequency or severity of the arthralgia/myalgia. Symptoms are usually transient, occurring within 2 or 3 days after paclitaxel administration, and resolving within days.^{2,7} If arthralgia/myalgia is not relieved by adequate doses of ibuprofen, or short-term, low-dose dexamethasone or

prednisone^{20,21}, gabapentin may be tried.²⁰⁻²² Dose reducing paclitaxel may lessen the severity of arthralgias/myalgias; however, there is no data on efficacy of reduced doses in a curative setting. Dose reduction should be considered only if symptom severity precludes continuing paclitaxel.^{11,12,23}

Cardiovascular effects present as bradycardia, hypotension and ECG changes. Bradycardia and hypotension typically occur during the first 3 hours of infusion; however, they are usually asymptomatic and do not require treatment. Paclitaxel administration may require interruption or discontinuation in some cases. Frequency of hypotension and bradycardia is not influenced by dose, schedule or prior anthracycline therapy. Common ECG changes are non-specific repolarization abnormalities, sinus bradycardia, sinus tachycardia, and premature beats. Among patients with normal ECG at baseline, prior therapy with anthracyclines did not influence the frequency of ECG abnormalities. Severe cardiovascular effects are rarely reported, including cases of atrial fibrillation, supraventricular tachycardia, myocardial infarction, congestive heart failure, and thromboembolic events. When reported, these patients had underlying disease or previous radiotherapy or chemotherapy which was thought to have contributed to the event.^{2,7}

Paclitaxel **extravasation** may rarely cause local tissue necrosis, leading to the suggestion that paclitaxel may have vesicant properties. In some reports, patients have experienced recall reactions from previous paclitaxel extravasations. No correlation has been made between concentration or volume of paclitaxel extravasated and the risk of tissue necrosis. Extravasation injuries due to paclitaxel may be either immediate or delayed and thus patients may require an extended follow-up; patient complaints of pain, burning, or stinging at the injection site occurring several days after the infusion should be investigated. Specific treatment recommendations for paclitaxel extravasation are still unclear as experience is anecdotal.^{7,16,17} For management of extravasation reactions, see BC Cancer Policy Number III-20 **[Prevention and Management of Extravasation of Chemotherapy](#)**.

Hypersensitivity reactions typically occur within the first 10 minutes of the first two cycles.^{2,24} Reactions are caused by either a histamine release in response to polyoxyl 35 castor oil (Cremophor® EL), or a non-IgE mediated reaction to the taxane moiety. Frequent, minor hypersensitivity reactions include: flushing (28%), rash (12%), hypotension (4%), dyspnea (2%), tachycardia (2%), and hypertension (1%). Chills, abdominal pain, and back pain are more rare.^{2,7} Severe hypersensitivity reactions include: dyspnea requiring bronchodilators, hypotension requiring treatment, flushing, chest pain, tachycardia, angioedema, and generalized urticaria. Severe reactions rarely occur after the third cycle of treatment.^{2,7} The incidence and severity of hypersensitivity reactions are reduced with premedication although rare, fatal reactions may occur despite premedication.⁷ A single IV dexamethasone dose with an antihistamine and an H₂-antagonist reduces the incidence of hypersensitivity reactions from 40% to 2-3%.^{7,25} The frequency and severity of hypersensitivity reactions are not affected by the dose or duration of infusion of paclitaxel.^{7,26} For management of hypersensitivity reactions, see **[BC Cancer Protocol Summary for Management of Hypersensitivity Reactions to Chemotherapeutic Agents](#)**.

Rechallenge after a severe hypersensitivity reaction:

The occurrence of hypersensitivity reactions does not preclude rechallenge with paclitaxel. In the event of a hypersensitivity reaction, the patient may be rechallenged the same day after additional premedication, slowing the rate of infusion, and close monitoring.^{23,25} Subsequent cycles may benefit from a regimen of oral dexamethasone given 12 and 6 hours before paclitaxel, plus antihistamines and H₂-antagonists given 30 minutes to 1 hour before paclitaxel.^{24,26,27} Consider substituting paclitaxel with docetaxel or implementing a desensitization protocol if a patient develops a reaction following a rechallenge.²⁴ For management of hypersensitivity reactions, see **[BC Cancer Protocol Summary for Management of Hypersensitivity Reactions to Chemotherapeutic Agents](#)**.

Peripheral sensory neuropathy presents with numbness and tingling in a stocking-and-glove distribution, perioral numbness, and hyperesthesia. Onset of symptoms can be within days following infusion. Frequency of symptoms increases with repeated exposure and cumulative dose.^{2,7} Pre-existing neuropathies from prior therapies are not a contraindication for treatment with paclitaxel; however, the incidence of neuropathy appears to be increased in this patient population. A dose reduction of 20% is recommended for all subsequent cycles of paclitaxel for patients who experience severe peripheral neuropathy. Sensory neuropathy usually improves or resolves within months of paclitaxel discontinuation.⁷

INTERACTIONS:

AGENT	EFFECT	MECHANISM	MANAGEMENT
cisplatin ^{2,7,28}	may increase neutropenia when paclitaxel is given <i>after</i> cisplatin	paclitaxel clearance is decreased by 25-33% when given <i>after</i> cisplatin	preferred method is to give paclitaxel first when administering as sequential infusions
dexamethasone ^{1,7}	does not affect protein binding of paclitaxel		
diphenhydramine ¹	does not affect protein binding of paclitaxel		
disulfiram ²⁹	development of acute alcohol intolerance reactions	inhibition of aldehyde dehydrogenase by disulfiram, leading to development of toxic metabolites of ethanol (found in the solution)	avoid disulfiram concurrently with paclitaxel administration
doxorubicin ^{2,7,28}	may increase cardiac toxicity from doxorubicin when given concurrently with paclitaxel	doxorubicin clearance is decreased leading to increased plasma levels of doxorubicin and doxorubicinol	monitor for increased cardiotoxicity
metronidazole and derivatives ²⁹	development of acute alcohol intolerance reactions; the risk for most patients appears slight	inhibition of aldehyde dehydrogenase by metronidazole, leading to development of toxic metabolites of ethanol (found in solution)	avoid metronidazole and its derivatives concurrently with paclitaxel administration
vaccines, live ²⁹	enhanced viral replication may increase the risk of disseminated disease	decreased immune response allows live vaccine to produce infection	avoid live vaccines during treatment
warfarin ²⁹	may increase anticoagulant effect of warfarin when given concurrently with paclitaxel	paclitaxel may displace warfarin from plasma protein binding sites when given concurrently	monitor INR and adjust warfarin dosing accordingly; consider use of LMWH with chemotherapy ³⁰

Paclitaxel is a **substrate** of CYP 3A4 and CYP 2C8 isoenzymes. Strong inhibitors of CYP 3A4 or 2C8 may decrease paclitaxel metabolism resulting in increased plasma levels and toxicity. Avoid concurrent use if possible; if unavoidable, consider reducing the paclitaxel dose.^{2,7,28} Strong inducers of CYP 3A4 or 2C8 may increase paclitaxel metabolism, potentially resulting in a reduced therapeutic effect of paclitaxel.^{1,2,7}

SUPPLY AND STORAGE:***Injection:***

Accord Healthcare Inc. supplies paclitaxel as 30 mg, 100 mg, and 300 mg vials in a concentration of 6 mg/mL. Store at room temperature. Product may precipitate if refrigerated; precipitate redissolves at room temperature. Non-medicinal ingredients per mL of solution: 527 mg Cremophor® EL (polyethoxylated castor oil) and 39.1%(w/v) ethanol.³¹

Biolyse Pharma supplies paclitaxel as 30 mg and 100 mg single dose vials and a 300 mg multi-dose vial in a concentration of 6 mg/mL. Refrigerate. Do not freeze. Potency is not affected when transported or stored for up to 2 months at room temperature. Non-medicinal ingredients per mL of solution: 527 mg Cremophor® EL (polyethoxylated castor oil) and 49.7%(v/v) alcohol.¹

Pfizer Canada Inc. (Hospira Healthcare) supplies paclitaxel as 30 mg, 100 mg, 150 mg, and 300 mg multi-use vials in a concentration of 6 mg/mL. Store at room temperature. Protect from light. If refrigerated, product may precipitate; precipitate redissolves at room temperature. Non-medicinal ingredients per mL of solution: 527 mg Cremophor® EL (polyethoxylated castor oil) and 46.5%(v/v) alcohol.^{32,33}

For basic information on the current brand used at BC Cancer, see [Chemotherapy Preparation and Stability Chart](#) in Appendix.

SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at BC Cancer, see [Chemotherapy Preparation and Stability Chart](#) in Appendix.

Additional information:

- concentrated solution must be diluted prior to IV infusion^{1,7}
- to prevent extraction of plasticizer DEHP from container, prepare solutions in non-DEHP containers and administer using non-DEHP administration sets.^{1,7}

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BC Cancer administration guideline noted in **bold, italics**

Subcutaneous	no information found
Intramuscular	no information found
Direct intravenous	not recommended; dilution required prior to administration ^{1,7}
<i>Intermittent infusion</i>	<i>over 1-3 h^{5,34-36}</i> ; use non-DEHP administration sets <i>and inline filters no greater than 0.22 microns^{31,33,37}</i>
Continuous infusion	has been given ^{1,7}
<i>Intraperitoneal</i>	<i>infuse into abdominal cavity as rapidly as possible by gravity</i> (use non-DEHP equipment) ^{2,38,39}
	<i>hyperthermic intraperitoneal chemotherapy (HIPEC):</i> pump solution into abdominal cavity and circulate as per protocol using hyperthermia pump; solutions and dwell time vary by protocol ^{40,41}
Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical	no information found

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response, and concomitant therapy. Guidelines for dosing also include consideration of absolute neutrophil count (ANC). Dosage may be reduced, delayed or discontinued in patients with bone marrow depression due to cytotoxic/radiation therapy or with other toxicities.

Adults:

BC Cancer usual dose noted in **bold, italics**

	Cycle Length:	
Intravenous:	3 weeks ^{42,43} :	80 mg/m² IV for one dose on days 1, 8 and 15 (total dose per cycle 240 mg/m ²)
	3 weeks ⁴⁴⁻⁶⁰ :	175 mg/m² (range 135-175 mg/m ²) IV for one dose on day 1 (total dose per cycle 135-175 mg/m ²)
	3 weeks ⁶¹⁻⁶⁴ :	200 mg/m² IV for one dose on day 1 (total dose per cycle 200 mg/m ²)
	4 weeks ^{34,35,42,65-67} :	80 mg/m² IV for one dose on days 1, 8, 15 and 21 (total dose per cycle 320 mg/m ²)
	4 weeks ⁶⁸ :	110 mg/m² IV for one dose on days 1, 8 and 15 (total dose per cycle 330 mg/m ²)

Premedication regimen^{2,7,19,25,26,65,69}:

30 minutes before paclitaxel: dexamethasone 20 mg IV plus diphenhydramine 50 mg IV plus ranitidine 50 mg IV

alternate regimen:

12 h and 6 h before paclitaxel: dexamethasone 20 mg PO plus
30 minutes before paclitaxel: diphenhydramine 50 mg IV plus ranitidine 50 mg IV

Concurrent radiation:

has been given⁷

Dosage in myelosuppression:

modify according to protocol by which patient is being treated; if no guidelines available, refer to Appendix "Dosage Modification for Myelosuppression"

Dosage in renal failure^{1,6}:

no dosage adjustment required for creatinine clearance less than 50 mL/min

Dosage in hepatic failure^{2,6}:

Suggested guidelines for first course; subsequent courses should be based on individual tolerance

ALT or AST		bilirubin	dose
<10 X ULN	and	≤1.25 X ULN	175 mg/m ²
<10 X ULN	and	1.26-2 X ULN	135 mg/m ²
<10 X ULN	and	2.01-5 X ULN	90 mg/m ²
≥10 X ULN	or	>5 X ULN	not recommended

Dosage in dialysis:

hemodialysis: no significant removal²; may give standard dose before or after hemodialysis⁷⁰⁻⁷²

chronic ambulatory peritoneal dialysis (CAPD): no significant removal; may give standard dose before or after CAPD⁷¹⁻⁷³

Children:

	Cycle Length:	
Intravenous:	3 weeks ^{8,74} :	135-250 mg/m ² IV for one dose on day 1
	3 weeks ^{75,76} :	200-350 mg/m ² IV for one dose on day 1

REFERENCES:

1. Biolyse. PACLITAXEL FOR INJECTION® product monograph. St. Catherines, Ontario; 2 December 2005.
2. AHFS Drug Information® (database on the Internet). Paclitaxel. Lexi-Comp Inc., November 2011. Available at: <http://online.lexi.com>. Accessed 7 February 2012.
3. Dizon DS, Schwartz J, Rojan A, et al. Cross-sensitivity between paclitaxel and docetaxel in a women's cancers program. *Gynecologic Oncology* 2006;100:149-151.
4. Cresteil T, Monsarrat B, Dubois J, et al. Regioselective metabolism of taxoids by human cyp3A4 and 2C8: structure-activity relationship. *Drug Metabolism and Disposition* 2004;30(4):438-445.
5. Lexi-Drugs® (database on the Internet). Paclitaxel. Lexi-Comp Inc., January 2012. Available at: <http://online.lexi.com>. Accessed 7 February 2012.
6. Basow DS editor. Paclitaxel. Topic 9735 Version 26.0 ed. Waltham, Massachusetts: UpToDate®; accessed 28 February 2012.
7. Bristol-Myers Squibb Canada. TAXOL® product monograph. Montreal, Ontario; 22 February 2010.
8. Pizzo P, Poplack D. Principles and Practice of Pediatric Oncology. 6th ed. Philadelphia, Pennsylvania: Lippincott Williams & Wilkins; 2011. p. 292-294, 325.
9. Joerger M, Huitema ADR, Huizing MT, et al. Safety and pharmacology of paclitaxel in patients with impaired liver function: a population pharmacokinetic-pharmacodynamic study. *Br J Clin Pharmacol* 2007;64(5):622-633.
10. Briggs GG, Freeman RK, Yaffe SJ. *Drugs in Pregnancy and Lactation*. 8th ed. Philadelphia: Williams & Wilkins; 2008. p. 1389-1391.
11. Anna Tinker MD. Personal communication. BC Cancer Agency Gynecology Tumour Group; 29 March 2012.
12. Caroline Lohrlich MD. Personal communication. BC Cancer Agency Breast Tumour Group; 05 April 2012.
13. James Conklin Pharmacist. Personal communication. BC Cancer Agency Gynecology Tumour Group; 29 March 2012.
14. Kimberly Kuik Pharmacist. Personal communication. BC Cancer Agency Breast Tumour Group; 13 April 2012.
15. BC Cancer Agency. (SCNAUSEA) Guidelines for Prevention and Treatment of Chemotherapy-induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer Agency; 1 Mar 2012.
16. Stanford BL, Hardwicke F. A review of clinical experience with paclitaxel extravasations. *Support Care Cancer* 2003;11(5):270-277.
17. Anne-Catherine McDuff. Personal communication. Associate Medical Information and Drug Safety, Bristol-Myers Squibb Canada; 18 October 2005.
18. BC Cancer Agency Provincial Systemic Therapy Program. Provincial Systemic Therapy Program Policy III-20: Prevention and Management of Extravasation of Chemotherapy. Vancouver, British Columbia: BC Cancer Agency; 1 August 2014.
19. Kintzel PE. Prophylaxis for paclitaxel hypersensitivity reactions. *Ann Pharmacother* 2001;35(9):1114-1117.
20. Nguyen VH, Lawrence HJ. Use of gabapentin in the prevention of taxane-induced arthralgias and myalgias. *J Clin Oncol* 2004;22(9):1767-1769.
21. Garrison JA, McCune JS, Livingston RB, et al. Myalgias and arthralgias associated with paclitaxel. *Oncology* 2003;17(2):1-11.
22. Turker H, Unsal M, Onar MK. Gabapentin in taxane-induced arthralgia. *The Pain Clinic* 2006;18(3):271-276.
23. Karen Gelmon MD. Personal communication. Medical Oncologist, BC Cancer Agency, Vancouver Cancer Centre, Breast Tumour Group Head.; February 18, 2006.
24. Lee C, Gianos M, Klaustermeyer WB. Diagnosis and management of hypersensitivity reactions related to common cancer chemotherapy agents. *Ann Allergy Asthma Immunol* 2009(102):179-187.
25. Micha JP, Rettenmaier MA, Dillman R, et al. Single-dose dexamethasone paclitaxel premedication. *Gyne Oncol* 1998;69:122-124.
26. Kwon JS, Eliit L, Finn M, et al. A comparison of two prophylactic regimens for hypersensitivity reactions to paclitaxel. *Gyne Oncol* 2002;84:420-425.
27. Kloover JS, den Bakker MA, Gelderblom H, et al. Fatal outcome of a hypersensitivity reaction to paclitaxel: a critical review of premedication regimens. *Br J Cancer* 2004;90:304-305.
28. Bun SS, Ciccolini J, Bun H, et al. Drug interactions of paclitaxel metabolism in human liver microsomes. *J Chemother* 2003;15(3):266-274.
29. Facts and Comparisons® Drug Interactions (database on the Internet). Paclitaxel. Wolters Kluwer Health Inc. Facts and Comparisons® eAnswers, updated monthly. Available at: <http://online.factsandcomparisons.com>. Accessed 14 February 2012.
30. Ken Swenerton MD. Personal communication (paclitaxel indication). BC Cancer Agency Gynecological Tumour Group; March 2006.
31. Accord Healthcare Inc. Paclitaxel injection product monograph. Markham, Ontario; 13 August 2012.
32. Hospira Healthcare Corporation. PACLITAXEL FOR INJECTION® product monograph. Saint-Laurent, Quebec; 1 September 2009.
33. Pfizer Canada Inc. Paclitaxel injection product monograph. Kirkland, Quebec; 10 August 2017.
34. Loesch D, Robert N, Asmar L, et al. Phase II multicenter trial of a weekly paclitaxel and carboplatin regimen in patients with advanced breast cancer. *J Clin Oncol* 2002;20(18):3857-3864.
35. Wildiers H, Paridaens R. Taxanes in elderly breast cancer patients. *Cancer Treat Rev* 2004;30(4):333-42.
36. Wist EA, Sommer HH, Ostenstad B, et al. Weekly one-hour paclitaxel as first-line chemotherapy for metastatic breast cancer.[see comment]. *Acta Oncol* 2004;43(1):11-4.
37. Biolyse. PACLITAXEL FOR INJECTION® product monograph. St. Catherines, Ontario; 12 September 2013.
38. Armstrong DK, Bundy B, Wenzel L, et al. Intraperitoneal Cisplatin and Paclitaxel in Ovarian Cancer. *N Engl J Med* 2006;354(1):34-43.
39. Cannistra SA. Intraperitoneal chemotherapy comes of age.[comment]. *New England Journal of Medicine* 2006;354(1):77-9.

40. Yan TD, Deraco M, Baratti D, et al. Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Malignant Peritoneal Mesothelioma: Multi-Institutional Experience. *Journal of Clinical Oncology* 2009;27(36):6237-6242.
41. BC Cancer Agency Gastrointestinal Tumour Group. (GIPMHIPEC) BCCA Protocol Summary for Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for Patients with Peritoneal Mesothelioma Using DOXOrubicin, CISplatin, and PACLitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 December 2015.
42. BC Cancer Agency Breast Tumour Group. (BRAVT7) BCCA Protocol Summary for Palliative Therapy for Metastatic Breast Cancer using Weekly Paclitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 January 2012.
43. BC Cancer Agency Breast Tumour Group. (UBRAJACTW) BCCA Protocol Summary for Adjuvant Therapy for Early Breast Cancer Using Doxorubicin and Cyclophosphamide Followed by Weekly Paclitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 June 2011.
44. BC Cancer Agency Breast Tumour Group. (BRAJACT) BCCA Protocol Summary for Adjuvant Therapy for Breast Cancer using Doxorubicin and Cyclophosphamide followed by Paclitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 June 2011.
45. BC Cancer Agency Breast Tumour Group. (BRAJACTG) BCCA Protocol Summary for Adjuvant Therapy for Breast Cancer using Dose Dense Therapy: Doxorubicin and Cyclophosphamide followed by Paclitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 June 2011.
46. BC Cancer Agency Breast Tumour Group. (BRAJACTT) BCCA Protocol Summary for Adjuvant Therapy for Breast Cancer using Doxorubicin and Cyclophosphamide followed by Paclitaxel and Trastuzumab. Vancouver, British Columbia: BC Cancer Agency; 1 June 2011.
47. BC Cancer Agency Breast Tumour Group. (BRAJACTTG) BCCA Protocol Summary for Adjuvant Therapy for Breast Cancer Using Dose Dense Therapy: Doxorubicin and Cyclophosphamide Followed by Paclitaxel and Trastuzumab. Vancouver, British Columbia: BC Cancer Agency; 1 June 2011.
48. BC Cancer Agency Breast Tumour Group. (BRAVGEMT) BCCA Protocol Summary for Palliative Therapy for Metastatic Breast Cancer using Gemcitabine and Paclitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 May 2009.
49. BC Cancer Agency Breast Tumour Group. (BRAVTAX) BCCA Protocol Summary for Palliative Therapy for Metastatic Breast Cancer using Paclitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 January 2012.
50. BC Cancer Agency Breast Tumour Group. (BRAVTPC) BCCA Protocol Summary for Palliative Therapy for Metastatic Breast Cancer using Trastuzumab, PACLitaxel and CARBOplatin as First-Line Treatment for Advanced Breast Cancer. Vancouver, British Columbia: BC Cancer Agency; 1 June 2011.
51. BC Cancer Agency Breast Tumour Group. (BRAVTRAP) BCCA Protocol Summary for Palliative Therapy for Metastatic Breast Cancer using Trastuzumab and Paclitaxel as First-Line Treatment for Advanced Breast Cancer. Vancouver, British Columbia: BC Cancer Agency; 1 June 2011.
52. BC Cancer Agency Gynecology Tumour Group. (GOCXCAT) BCCA Protocol Summary for Primary Treatment of Advanced/Recurrent Non-Small Cell Cancer of the Cervix with CARBOplatin and PACLitaxel in Ambulatory Care Settings. Vancouver, British Columbia: BC Cancer Agency; 1 April 2011.
53. BC Cancer Agency Gynecology Tumour Group. (GOENDCAT) BCCA Protocol Summary for Treatment of Primary Advanced or Recurrent Endometrial Cancer using CARBOplatin and PACLitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 April 2011.
54. BC Cancer Agency Gynecology Tumour Group. (GOOVCATM) BCCA Protocol Summary for Primary Treatment of No Visible Residual (Moderate-High Risk) Invasive Epithelial Ovarian, Fallopian Tube and Primary Peritoneal Cancer Using CARBOplatin and PACLitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 April 2011.
55. BC Cancer Agency Gynecology Tumour Group. (GOOVCATR) BCCA Protocol Summary for Second Line Treatment of Invasive Epithelial Ovarian, Fallopian Tube or Peritoneal Cancer Relapsing after Primary Treatment Using PACLitaxel and CARBOplatin. Vancouver, British Columbia: BC Cancer Agency; 1 April 2011.
56. BC Cancer Agency Gynecology Tumour Group. (GOOVIPPC) BCCA Protocol Summary for Primary Treatment for Stage III less than or equal to 1 cm Visible Residual Invasive Epithelial Ovarian Cancer or Stage I Grade 3 or Stage II Grade 3 Papillary Serous Ovarian Cancer Using Intravenous and Intraperitoneal PACLitaxel and Intraperitoneal CARBOplatin. Vancouver, British Columbia: BC Cancer Agency; 1 March 2012.
57. BC Cancer Agency Gynecology Tumour Group. (GOOVCATX) BCCA Protocol Summary for Primary Treatment of Visible Residual (Extreme Risk) Invasive Epithelial Ovarian, Fallopian Tube or Peritoneal Cancer Using CARBOplatin and PACLitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 March 2012.
58. BC Cancer Agency Gynecology Tumour Group. (GOOVTAX3) BCCA Protocol Summary for Treatment of Relapsed/Progressing Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Carcinoma Using PACLitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 March 2012.
59. BC Cancer Agency Gynecology Tumour Group. (GOSMCCRT) BCCA Protocol Summary for Treatment of Small Cell or Neuroendocrine Carcinoma of Gynecologic System Origin using PACLitaxel, CISplatin, Etoposide and CARBOplatin with Radiation (GO 95 02). Vancouver, British Columbia: BC Cancer Agency; 1 June 2011.
60. BC Cancer Agency Genitourinary Tumour Group. (UGUTIP) BCCA Protocol Summary for Advanced Therapy for Relapsed Testicular Germ Cell Cancer Using PACLitaxel, Ifosfamide and CISplatin (TIP). Vancouver, British Columbia: BC Cancer Agency; 1 March 2012.
61. BC Cancer Agency Head and Neck Tumour Group. (UHNNAVPC) BCCA Protocol Summary for Treatment of Recurrent or Metastatic Nasopharyngeal Carcinoma with CARBOplatin and PACLitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 April 2011.
62. BC Cancer Agency Lung Tumour Group. (LUAJPC) BCCA Protocol Summary for Adjuvant CARBOplatin and PACLitaxel Following Resection of Stage I, II and IIIA Non-Small Cell Lung Cancer. Vancouver, British Columbia: BC Cancer Agency; 1 April 2011.
63. BC Cancer Agency Lung Tumour Group. (LUAVPC) BCCA Protocol Summary for First-Line Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) with CARBOplatin and PACLitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 August 2011.

64. BC Cancer Agency Primary Unknown Tumour Group. (PUCAT) BCCA Protocol Summary for Primary Treatment of Cancer of Unknown Primary Origin Using CARBOplatin and PACLitaxel. Vancouver, British Columbia: BC Cancer Agency; 1 April 2011.
65. Quock J, Dea G, Tanaka M, et al. Premedication strategy for weekly paclitaxel. *Cancer Investigation* 2002;20(5-6):666-72.
66. Perez EA, Vogel CL, Irwin DH, et al. Weekly paclitaxel in women age 65 and above with metastatic breast cancer. *Breast Cancer Res Treat* 2002;73(1):85-8.
67. Perez EA, Vogel CL, Irwin DH, et al. Multicenter phase II trial of weekly paclitaxel in women with metastatic breast cancer. *J Clin Oncol* 2001;19(22):4216-23.
68. BC Cancer Agency Genitourinary Tumour Group. (UGUTAXGEM) BCCA Protocol Summary for Palliative Therapy for Germ Cell Cancers Using Paclitaxel and Gemcitabine. Vancouver, British Columbia: BC Cancer Agency; 1 May 2009.
69. Markman M, Kennedy A, Webster K, et al. Simplified regimen for the prevention of paclitaxel-associated hypersensitivity reactions. *J Clin Oncol* 1997;15(12):3517.
70. Janus N, Thariat J, Boulanger H, et al. Proposal for dosage adjustment and timing of chemotherapy in hemodialyzed patients. *Ann Oncol* 2010;21:1395-1403.
71. Bailie GR, Mason NA. Paclitaxel. 2011 Dialysis of Drugs. Saline, Michigan, USA: Renal Pharmacy Consultants, LLC; 2011. p. 41.
72. Aronoff GR, Bennett WM, Berns JS, et al. Drug Prescribing in Renal Failure, Paclitaxel. Available at: <http://lib.mylibrary.com/Open.aspx?id=186806&loc=&srch=undefined&src=0>. Accessed March 1, 2012.
73. Heijns JB, van der Burg ME, van Gelder T, et al. Continuous ambulatory peritoneal dialysis: pharmacokinetics and clinical outcome of paclitaxel and carboplatin treatment. *Cancer Chemother.Pharmacol.* 2008;62(5):841-847.
74. Roberta Esau Pharmacist. Personal communication. BC Children's Hospital; 7 March 2012.
75. Hurwitz CA, Relling MV, Weitman SD, et al. Phase I trial of paclitaxel in children with refractory solid tumors: a Pediatric Oncology Group Study. *J Clin Oncol* 1993;11(12):2324-9.
76. Jeff Davis MD. Personal communication. BC Children's Hospital; 7 March 2012.