

**DRUG NAME: Paclitaxel, nanoparticle, albumin-bound (nab)****SYNONYM(S):** protein-bound paclitaxel<sup>1</sup>**COMMON TRADE NAME(S):** ABRAXANE®**CLASSIFICATION:** antimicrotubule agent*Special pediatric considerations are noted when applicable, otherwise adult provisions apply.***MECHANISM OF ACTION:**

Paclitaxel, the active ingredient of nanoparticle, albumin-bound (nab) paclitaxel, is an antimicrotubule agent that promotes the assembly and stabilization of microtubules, thus inhibiting normal dynamic reorganization of the microtubule network. Paclitaxel induces abnormal bundles of microtubules throughout the cell cycle and multiple asters of microtubules during mitosis. It is thought that albumin-bound paclitaxel (nab-paclitaxel) facilitates the transport of paclitaxel across the endothelial cell via an albumin-receptor mediated pathway. Nab-paclitaxel is cell cycle phase-nonspecific.<sup>2</sup>

**PHARMACOKINETICS:**

Distribution	extensive extravascular distribution and tissue binding	
	cross blood brain barrier?	no information found
	volume of distribution	632 L/m <sup>2</sup>
	plasma protein binding	89-98%
Metabolism	extensive; primarily via CYP 2C8, minor metabolites via CYP 3A4	
	active metabolite(s)	6 $\alpha$ -hydroxypaclitaxel (major), 3'- <i>p</i> -hydroxypaclitaxel (minor), and 6 $\alpha$ ,3'- <i>p</i> -dihydroxypaclitaxel (minor)
	inactive metabolite(s)	no information found
Excretion	extensive non-renal clearance	
	urine	4% (unchanged drug); <1% (6 $\alpha$ -hydroxypaclitaxel and 3'- <i>p</i> -hydroxypaclitaxel)
	feces	20%
	terminal half life	27 h
	clearance	15 L/h/m <sup>2</sup>

Adapted from standard reference<sup>2</sup> unless specified otherwise.**USES:****Primary uses:**

\* Breast cancer

\*Health Canada approved indication

**Other uses:**Lung cancer, non-small cell<sup>3</sup>**SPECIAL PRECAUTIONS:****Caution:**

- nab-paclitaxel is **NOT interchangeable** with other paclitaxel formulations and should not be substituted<sup>2</sup>
- nab-paclitaxel has not been studied in patients previously exhibiting hypersensitivity to paclitaxel or human albumin<sup>2</sup>
- routine premedication to prevent hypersensitivity reactions is not required before administration<sup>2</sup>
- nab-paclitaxel contains albumin which, although no cases have been identified, carries a remote risk for transmission of viral diseases<sup>2</sup>

**Carcinogenicity:** no information found<sup>2</sup>

**Mutagenicity:** not mutagenic in Ames test and mammalian *in vitro* mutation test. Paclitaxel is clastogenic in mammalian *in vitro* and *in vivo* chromosome tests.<sup>2</sup>

**Fertility:** In animal studies with paclitaxel, testicular atrophy/degeneration in males, as well as significantly reduced fertility, decreased pregnancy rates and increased loss of embryos in untreated female mates have been observed. Skeletal and soft tissue fetal anomalies were also observed. Men are advised not to father a child while receiving treatment with nab-paclitaxel.<sup>2</sup>

**Pregnancy:** FDA Pregnancy Category D.<sup>3</sup> In animal studies, paclitaxel has demonstrated embryo- and fetotoxicity, including fetal anomalies and intrauterine mortality. No studies have been conducted in women.<sup>2</sup> 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).

**Breastfeeding** is not recommended due to the potential secretion into breast milk. Concentrations in milk were detectable in animal studies.<sup>2</sup>

**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, and/or determined to be clinically important<sup>4,5</sup>.

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in <b>bold, italics</b>	
blood and lymphatic system/ febrile neutropenia	<b>anemia</b> (20-33%, severe 1%) <sup>2,6</sup> ; sometimes requiring blood transfusion
	bleeding (2%)
	febrile neutropenia (2%)
	<b>leucopenia</b> (72%)
	<b>neutropenia</b> (80%, severe 9%); dose-limiting; see paragraph following <b>Side Effects</b> table
	thrombocytopenia (2%, severe <1%); may require dose reduction
cardiac	<b>bradycardia</b> (<1%); usually asymptomatic, intervention not required
	<b>cardiovascular events</b> (3%), including cardiac arrest, chest pain, edema, hypertension, pulmonary emboli, supraventricular tachycardia, and thrombosis
	<b>hypotension</b> (5%); usually asymptomatic, intervention not required
eye (see paragraph following <b>Side Effects</b> table)	blurred vision (1%) <sup>3</sup>
	keratitis (1%) <sup>3</sup>
gastrointestinal	<i>emetogenic potential: low</i> <sup>7</sup>
	anorexia (>10%)
	constipation (>10%)
	<b>diarrhea</b> (27%, severe <1%) <sup>6</sup>
	<b>mucositis</b> (7%, severe <1%) <sup>6</sup> ; occurs a few days post treatment, usually decreases or disappears within 1 week <sup>2</sup>

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in <b>bold, italics</b>	
	<b>nausea</b> (30%, severe 3%) <sup>6</sup>
	<b>vomiting</b> (18%, severe 4%) <sup>6</sup>
general disorders and administration site conditions	<b>extravasation hazard: irritant</b> <sup>2,8</sup>
	fever (14%)
	fluid retention/edema (10%) <sup>6</sup>
	injection site reactions (1%); usually mild; rarely has included phlebitis, cellulitis, induration, exfoliation, necrosis, and fibrosis
immune system	<b>hypersensitivity reactions</b> (4%); see paragraph following <b>Side Effects</b> table
infections and infestations	<b>infections</b> (24%, severe 3%); oral candidiasis, pneumonia, and respiratory tract infections most frequently reported
investigations	alkaline phosphatase increase (36%)
	AST increase (39%)
	bilirubin increase (7%)
	ECG abnormalities (60%, 35% in patients with normal baseline); usually asymptomatic; not dose-limiting, intervention not required
	gamma-glutamyltransferase increase (50%, severe 3-14%)
	serum creatinine increase (11%, severe <1%); dose reductions or delays not required
metabolism and nutrition	dehydration (1-10%)
musculoskeletal and connective tissue	<b>arthralgia/myalgia</b> (44%, severe 8%); occurs two to three days post treatment, usually transient
	<b>asthenia</b> (47%, severe 8%), including fatigue, weakness, lethargy, and malaise; may affect ability to drive and operate machines
nervous system	<b>sensory neuropathy</b> (71%, severe 10%); may require dose reduction; see paragraph following <b>Side Effects</b> table
respiratory, thoracic and mediastinal	cough (6-7%) <sup>6</sup>
	<b>dyspnea</b> (12%)
	pneumothorax <sup>6</sup> (<1%)
	pulmonary embolism <sup>1</sup>
skin and subcutaneous tissue	<b>alopecia</b> (90%)
	nail changes (1%); includes changes in pigmentation or discoloration of nail bed
	pruritus (6%)
	rash (9%)
vascular	flushing (2%)

Adapted from standard reference<sup>2</sup> unless specified otherwise.

**Bone marrow suppression**, primarily neutropenia, is a dose-dependent and dose-limiting toxicity. Neutropenia is usually rapidly reversible. Frequent blood count monitoring is recommended, and treatment should not be initiated if baseline neutrophil counts are less than  $1.5 \times 10^9/L$ . Dose reduction is recommended for severe neutropenia lasting one week or longer and further reduction is recommended for recurrence of the same.<sup>1,2</sup>

**Hypersensitivity reactions** are reported in 4%, with none reported as severe. On the day of dosing, grades 1 and 2 dyspnea are reported in 1%, and flushing, hypotension, chest pain, and arrhythmia are reported in less than 1%

each. Nab-paclitaxel has not been studied in patients previously exhibiting hypersensitivity to paclitaxel or human albumin.<sup>2,6</sup>

**Neurologic toxicity** is dose-dependent and is influenced by prior and/or concomitant therapy with neurotoxic agents. In clinical trials, the frequency of sensory neuropathy increased with cumulative dose, and sometimes required discontinuation of treatment. It is suggested that grade 3 sensory neuropathy requires treatment interruption until resolution, followed by dose reduction for subsequent courses. Severe sensory symptoms typically improved a median of 22 days after treatment interruption. Cases of autonomic neuropathy resulting in paralytic ileus have been reported. Ischemic stroke, metabolic encephalopathy, confusion, dizziness/lightheadedness, and mood alteration/depression are neurologic events reported in less than 1%.<sup>2</sup>

**Ocular/visual disturbances** have been reported in 13%, with 1% of cases reported as severe. The severe cases (keratitis and blurred vision) were reported in patients receiving doses higher than recommended, and were usually reversible. Rarely, persistent optic nerve damage has been reported.<sup>2</sup>

### INTERACTIONS:

Drug interaction studies have not been conducted. However, nab-paclitaxel is a substrate of CYP 2C8 and 3A4 and caution should be exercised during concurrent therapy with known inhibitors or inducers of these enzymes. The clinical significance of these interactions is unknown.<sup>2,6</sup>

### SUPPLY AND STORAGE:

**Injection:** Abraxis BioScience Canada, Inc. supplies nanoparticle, albumin-bound (nab) paclitaxel in single use vials of sterile lyophilized powder containing 100 mg of paclitaxel and 900 mg of human albumin. Store at room temperature. Protect from light.<sup>2</sup>

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

### SOLUTION PREPARATION AND COMPATIBILITY:

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

**Additional information:** Gently swirl or slowly invert vial after reconstitution to avoid foaming. If foaming or clumping occurs, stand solution for a minimum 15 minutes until foaming subsides. Reconstituted product should be milky and homogeneous without visible particulates. Some settling may occur upon standing and vial should be gently inverted to ensure complete resuspension prior to use. Product must be discarded if precipitates are observed. Neither freezing nor refrigeration adversely affects stability of the product.<sup>2</sup>

**Compatibility:** consult detailed reference

### PARENTERAL ADMINISTRATION:

BCCA administration guideline noted in **bold, italics**

Subcutaneous	no information found
Intramuscular	no information found
Direct intravenous	no information found
Intermittent infusion <sup>2,9</sup>	<ul style="list-style-type: none"> <li>• <b>over 30 minutes*</b></li> <li>• do NOT filter</li> <li>• Non-PVC bags and tubing are NOT required.</li> </ul>

BCCA administration guideline noted in ***bold, italics***

Continuous infusion	no information found
Intraperitoneal	no information found
Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical	no information found

\* Limiting infusion time to 30 minutes reduces the likelihood of infusion-related reactions.<sup>2</sup>

**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:**

BCCA usual dose noted in ***bold, italics***

*Intravenous:* Cycle Length:  
**3 weeks:**<sup>2,9</sup> ***260 mg/m<sup>2</sup> IV for one dose on day 1***  
 4 weeks:<sup>3</sup> 100-150 mg/m<sup>2</sup> IV for one dose on days 1, 8 and 15

*Concurrent radiation:* no information found

*Dosage in myelosuppression:* modify according to protocol by which patient is being treated; if no guidelines available, refer to Appendix 6 "Dosage Modification for Myelosuppression"

*Dosage in renal failure:* no information found

*Dosage in hepatic failure:* suggested dose modification for every-3-week regimen<sup>1,3</sup>

	<b>AST</b>	<b>Serum bilirubin</b>	<b>Dose</b>
mild	< 10xULN	≤ 1.25xULN	260 mg/m <sup>2</sup> (100%)
moderate	< 10xULN	1.26-2xULN	reduce to 200 mg/m <sup>2</sup> *
severe	< 10xULN	2.01-5xULN	reduce to 130 mg/m <sup>2</sup> **
	> 10xULN	> 5xULN	not recommended

\* For subsequent cycles: dosing based on patient tolerability.

\*\* For subsequent cycles: may consider dose escalation to 200 mg/m<sup>2</sup> based on patient tolerability.

*Dosage in dialysis:* no information found

**Children:** no information found

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