Drug Monograph

A - Drug Name

nab-PACLitaxel

SYNONYM(S): nanoparticle albumin-bound paclitaxel; paclitaxel protein bound

COMMON TRADE NAME(S): Abraxane®

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B - Mechanism of Action and Pharmacokinetics

Nanoparticle albumin-bound (nab) paclitaxel is a form of paclitaxel which works as an antimicrotubule agent. Paclitaxel, the active ingredient in nab-paclitaxel promotes the assembly of microtubules from tubulin dimers and stabilizes microtubules by preventing depolymerization. This interferes with the normal dynamic reorganization of the microtubule network required for interphase and mitotic functions. It is hypothesized that nanoparticle albumin-bound paclitaxel facilitates the transport of paclitaxel across the endothelial cell via an albumin-receptor mediated pathway.

Absorption	Following intravenous administration of nab-paclitaxel, paclitaxel plasma concentrations declined in a biphasic manner, the initial rapid decline representing distribution to the peripheral compartment and the slower second phase representing drug elimination.
Distribution	Extensive extravascular distribution and/or tissue binding. Drug exposure is dose-proportional over 80 to 300 mg/m^2. PPB 94%
Metabolism	Hepatic metabolism (CYP2C8 forming major metabolite; minor metabolites via CYP3A4) account for the majority of elimination.

	Active metabolites	yes
	Inactive metabolites	yes
Elimination	Half-life	13-27 hours
	Feces	Approximately 20%
	Urine	4% as unchanged drug, <1% as metabolites

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C - Indications and Status

Health Canada Approvals:

- Breast cancer
- Pancreatic cancer

Refer to the product monograph for a full list and details of approved indications.

Other Uses:

- Bladder/Urothelial cancer
- Melanoma

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D - Adverse Effects

Emetogenic Potential: Low

Extravasation Potential: Irritant

The following adverse effects were reported in monotherapy trials for metastatic breast cancer. The incidence of many may be higher when used in combination with gemcitabine. Severe adverse events from other studies or post-marketing, may also be included.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	Arterial thromboembolism (<1%)	E
	Atrioventricular block (rare)	I E
	Bradycardia (<1%)	E
	Cardiotoxicity (<10%) (prior cardiac history or cardiotoxins)	D
	ECG changes (35%)	E
	Hypotension (5%)	I
	Venous thromboembolism (rare)	E
Dermatological	Alopecia (90%)	E
	Nail disorder (1%)	E
	Other - Scleroderma-like skin changes (rare)	E
	Photosensitivity (rare)	E
	Rash, pruritus (9%) (may be severe)	E
Gastrointestinal	Anorexia (very common)	E
	Constipation (very common)	E
	Dehydration (<10%)	E
	Diarrhea (27%) (may be severe)	E
	Esophagitis (rare)	E
	GI obstruction (<1%)	E
	GI perforation (<1%)	E
	Mucositis (7%)	E
	Nausea, vomiting (30%)	I
General	Edema (10%)	E
	Fatigue (47%) (8% severe)	E
Hematological	Hemolytic uremic syndrome (rare)	E
	Myelosuppression ± infection, bleeding (80%) (9% severe)	E
	Thrombotic thrombocytopenic purpura (TTP; rare)	E
Hepatobiliary	↑ LFTs (39%) (rarely severe)	E
	Pancreatitis (<1%)	E
Hypersensitivity	Hypersensitivity (4%) (rarely severe)	I
Injection site	Injection site reaction (1%) (including extravasation and radiation recall; rarely may be severe)	I E
Metabolic / Endocrine	Tumour lysis syndrome (rare)	E

Musculoskeletal	Musculoskeletal pain (44%) (8% severe)	E
Nervous System	Autonomic neuropathy (rare)	E D
	Cognitive disturbance (rare)	E
	Cranial neuropathy (rare)	E
	Dizziness (rare)	E
	Mood changes (rare)	E
	Sensory neuropathy (71%) (10% severe)	E D
Ophthalmic	Conjunctivitis (rare)	E
	Eye disorders (13%) (1% severe including keratitis and blurred vision)	E
	Optic neuritis (rare)	E
	Other - Cystoid macular edema (rare)	E
	Watering eyes (rare)	E
Renal	Creatinine increased (11%)	E
	Renal failure (<10%) (acute)	E
Respiratory	Cough, dyspnea (12%)	E
	Other - Lung Fibrosis (rare)	E D
	Pneumonitis (rare)	E D
	Pneumothorax (rare)	E D

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.
"*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
D = *delayed* (weeks to months) L = *late* (months to years)

The most common side effects for nab-paclitaxel include alopecia, myelosuppression ± infection, bleeding, sensory neuropathy, fatigue, musculoskeletal pain, ↑ LFTs, ECG changes, nausea, vomiting, diarrhea and eye disorders.

Myelosuppression, primarily neutropenia, is a dose-dependent and dose-limiting toxicity. Neutropenia is usually rapidly reversible and may be more frequent in patients receiving a combination with gemcitabine for pancreatic cancer. Significant risk factors included complications of underlying pancreatic cancer, such as biliary obstruction or presence of a biliary stent. Febrile patients, even if not neutropenic, should receive broad spectrum antibiotics.

Hypotension during the 30-minute infusion occurred in 5% of patients; however, this was generally asymptomatic and required neither specific therapy nor treatment discontinuation.

ECG abnormalities were common; they did not usually result in symptoms, were not dose-limiting and required no intervention. AV block requiring pacing has been reported; patients should be monitored and managed appropriately.

Hypersensitivity reactions were observed in 4% of patients; severe occurrences have been reported rarely during post-marketing. Premedication is not generally necessary prior to nab-paclitaxel, although may be needed in patients with prior mild to moderate hypersensitivity reactions. Discontinue nab-paclitaxel permanently if patient experiences a severe hypersensitivity reaction (do not re-challenge).

Sensory neuropathy is dose-related and cumulative, may be dose-limiting or even require discontinuation of therapy (3% in breast cancer trial). Frequency and severity is also influenced by prior and/or concomitant therapy with neurotoxic agents. Median time to first occurrence of grade 3 peripheral neuropathy was 140 days and median time to improvement to grade 1 or less was 29 days.

Cystoid macular edema (CME) resulting in reduced visual acuity has been reported rarely. Most reports of CME have resolved following therapy discontinuation.

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E - Dosing

Refer to protocol by which patient is being treated.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Do not substitute for or with other paclitaxel formulations.

Nab-paclitaxel should only be administered if neutrophils ≥ 1.5 x 10^9/L and platelets ≥ 100 x 10^9/L on day 1 of each treatment cycle.

In the pivotal trial for Metastatic Pancreatic Cancer where patients received nab-paclitaxel and gemcitabine:

- Patients were provided with a supply of antibiotic prophylaxis (ciprofloxacin or amoxicillin/clavulanate), to be used at first occurrence of fever ≥ 38.5C. The use of long-term antibiotic prophylaxis for recurrences in patients who had experienced a first febrile episode will be at the discretion of the treating physician.
- G-CSF may be given according to institutional guidelines (also refer to dose modifications).

Adults:

Metastatic breast cancer:

Intravenous: 260 mg/m² every 3 weeks (21 day cycle)

Alternative schedules (e.g. 100mg/m^2 to 150mg/m^2 IV days 1, 8, 15; every 4 weeks) have been used in clinical trials, but these have not been approved by Health Canada.

Metastatic pancreatic cancer:

Intravenous: 125 mg/m² Days 1, 8, 15 of 28 day cycle (in combination with gemcitabine)

For information pertaining to gemcitabine dosing refer to GEMCNPAC(W).

Dosage with Toxicity:

Metastatic Breast Cancer

Do not retreat until recovery from toxicity and neutrophils ≥ 1.5 x 109/L and platelets ≥ 100 x 10^9/L.

Table 1:

Worst Toxicity / Counts (x10^9/L) in previous cycle	**Nab-paclitaxel Dose (mg/m^2) Every 3 Weeks**		
	First occurrence	Second occurrence	Third Occurrence
ANC < 0.5 ≥ 7 days or Febrile neutropenia or Grade 4 platelets or bleeding	*220 mg/m^2	*180 mg/m^2	Discontinue
Grade 3 or 4 sensory neuropathy or other grade 3 related organ toxicity	*220 mg/m^2 OR consider discontinuing for Grade 4 neurotoxicity	*180 mg/m^2 OR consider discontinuing for Grade 4 neurotoxicity	Discontinue
Other grade 4 related organ toxicity; severe hypersensitivity, or any cystoid macular edema	Discontinue		

Pneumonitis	Hold and investigate; discontinue if confirmed	n/a
*Do not retreat until ANC ≥ 1.5 x 10^9/L, platelets ≥ 100 x 10^9/L and other toxicity ≤ grade 2.		

Metastatic Pancreatic Cancer

Table 2: Dose levels

Dose Level	Nab-paclitaxel Dose (mg/m^2)
Full dose	125
-1	100
-2	75
Further reduction required	Discontinue

Start Day 1 when ANC ≥ 1.5 x 10^9/L, platelets ≥ 100 x 10^9/L and other toxicities ≤ grade 2 or as stated below. Do not escalate reduced doses (with the exception of Day 15; see Table 4).

Table 3: Dose modifications at the start of cycle or during cycle

Worst Toxicity	Nab-paclitaxel Dose
Grade 3 or 4 febrile neutropenia	Hold until afebrile and ANC ≥ 1.5 x 10^9/L, then ↓1 dose level*
Grade 2 or 3 cutaneous toxicity	↓1 dose level; discontinue if persists
Grade 3 or 4 sensory neuropathy	Hold until ≤ grade 1*; restart at 1 dose level ↓ OR consider discontinuing for grade 4
Other grade 3 toxicity, including mucositis, diarrhea (except nausea/vomiting/alopecia)	Hold until ≤ grade 1*; restart at 1 dose level ↓
Other grade 4 toxicity or severe hypersensitivity, or any cystoid macular edema	Discontinue
Pneumonitis	Hold and investigate; discontinue if confirmed.

*In the clinical trial (Hoff et al), if treatment was delayed for ≥ 21 days (including neutropenia despite uninterrupted G-CSF treatment), treatment was discontinued.

Table 4: Hematologic dose modifications within cycle

Omitted doses during the cycle will not be made up. Note day 15 dose modifications depend on day 8 dosing.

Day 8 counts x 10^9/L	**Day 8** Nab-paclitaxel Dose	**Day 15** counts x 10^9/L	**Day 15** Nab-paclitaxel Doses
ANC ≥ 1 and platelets ≥ 75	Day 1 dose	**If Day 8 dose unchanged from Day 1:**	
		ANC ≥ 1 and platelets ≥ 75	Day 1 dose
		ANC 0.5-0.99 or platelets 50-74	Day 1 dose, add G-CSF[1, 2]
		ANC < 0.5 or platelets < 50	Omit**,** add G-CSF[2]
ANC 0.5- 0.99 or platelets 50-74	↓ 1 Dose Level	**If Day 8 dose was REDUCED:**	
		ANC ≥ 1 and platelets ≥ 75	Day 1 dose, add G-CSF[1, 2]
		ANC 0.5-0.99 or platelets 50-74	Day 8 dose, add G-CSF[1, 2]
		ANC < 0.5 or platelets < 50	Omit**,** add G-CSF[2]
ANC < 0.5 or platelets < 50	Omit for Day 8	**If Day 8 dose was OMITTED:**	
		ANC ≥ 1 and platelets ≥ 75	Day 1 dose , add G-CSF[1, 2]
		ANC 0.5-0.99 or platelets 50-74	↓ 1 Dose Level, add G-CSF[1, 2]
		ANC < 0.5 or platelets < 50	Omit**,** add G-CSF[2]

[1]If G-CSF is not available, suggest reducing an additional dose level. G-CSF was optional for isolated thrombocytopenia.

[2]G-CSF was optional in clinical trials for isolated thrombocytopenia.

Dosage with Hepatic Impairment:

Patients with hepatic impairment may be at increased risk of myelosuppression and should be closely monitored.

Nab-paclitaxel is not recommended in patients with metastatic pancreatic cancer who have moderate to severe hepatic impairment.

Bilirubin		AST	Nab-paclitaxel* (% previous dose - suggested)
>1 to ≤ 1.5 x ULN	and	≤ 10 x ULN	100%
>1.5 to ≤ 5 x ULN	and	≤ 10 x ULN	↓ to 80% for metastatic breast cancer**; Discontinue for metastatic pancreatic cancer (has not been studied).
> 5 x ULN	or	> 10 x ULN	Discontinue (has not been studied).

*Based on clinical judgment. Patients with elevated baseline bilirubin were excluded from clinical trials. Less conservative adjustments can be considered if hepatic changes are secondary to metastases rather than hepatic cirrhosis or hepatitis.

**Reduced dose may be escalated to 100% if treatment is tolerated for at least 2 cycles at the reduced dose.

Dosage with Renal Impairment:

Creatinine Clearance (mL/min)	Nab-paclitaxel* (% previous dose - suggested)
≥ 30 to < 90	100%
< 30	Discontinue (has not been studied).

*Based on clinical judgment. Patients with elevated baseline creatinine were excluded from clinical trials.

Dosage in the elderly:

No dose adjustment is required. Patients aged 65 years or older may have higher incidence of neutropenia in cycle 1. Patients aged 65 and older who received nab-paclitaxel monotherapy for metastatic breast cancer had a higher incidence of epistaxis, diarrhea, dehydration, fatigue and peripheral edema.

Patients 75 years and older who received nab-paclitaxel in combination with gemcitabine for pancreatic cancer had a higher incidence of serious adverse reactions and no demonstrated survival benefit.

Children:

Safety and effectiveness in children have not been determined.

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F - Administration Guidelines

- Refer to the product monograph for full instructions on reconstitution.
- The reconstituted suspension should be milky and homogenous without visible particulates.
- Avoid shaking drug suspension in order to minimize foaming.
- No further dilution is required after reconstitution. Transfer reconstituted drug to an empty, sterile IV PVC or non-PVC infusion bag.
- Infuse intravenously over 30 minutes (breast cancer) or over 30 to 40 minutes (pancreatic cancer). Slower infusion rates may increase the likelihood of infusion-related reactions.
- When administered as part of a combination chemotherapy regimen with gemcitabine, nab-paclitaxel should be given first, followed immediately by gemcitabine.
- DEHP-free containers or administration sets may be used but are not required.
- Do not admix with other drugs.
- Use of syringes and IV bags containing silicone oil as lubricant may cause formation of proteinaceous strands. If strands are observed by visual inspection of IV bag, administer reconstituted suspension through filter of at least 15 µm pore size. If this is not possible, discard the product.
- Store unopened vial at 20-25ºC in its original carton; protect from light.

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G - Special Precautions

Contraindications:

- Patients who have a hypersensitivity to this drug or any of its components (such as albumin) in the formulation or container
- Patients with baseline ANC of < 1.5 x 10^9/L on day 1 of each treatment cycle

Other Warnings/Precautions:

- Do not administer nab-paclitaxel to patients with platelets < 100 x 10^9/L.
- The use of nab-paclitaxel in patients exhibiting hypersensitivity to paclitaxel or human albumin has not been studied.
- Patients with elevated baseline bilirubin or elevated baseline creatinine were excluded from clinical trials.
- The use of albumin-containing solutions is associated with a remote risk of viral transmission, including CJD.
- Radiation recall and pneumonitis have been reported in patients with concurrent radiotherapy.
- Nab-paclitaxel is not recommended for use in patients with a history of interstitial lung disease, multiple allergies, progressive dyspnea or unproductive cough (cases of serious pneumonitis were reported in those treated with combination nab-paclitaxel and gemcitabine).
- Caution is recommended prior to driving or operating machinery if fatigue, weakness or dizziness are present.

Other Drug Properties:

- Carcinogenicity: Unknown

Pregnancy and Lactation:

- Clastogenicity: Yes
- Fetotoxicity: Yes
- Mutagenicity: No
- Teratogenicity: Probable
- Embryotoxicity: Yes
  Nab-paclitaxel is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners during treatment, and for at least **6 months** after the last dose.
- Excretion into breast milk: Documented in animals
  Breastfeeding is not recommended during treatment and for **2 weeks** after the last dose.
- Fertility effects: Probable

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H - Interactions

No drug interaction studies have been conducted with nab-paclitaxel, but are likely to be similar to those reported for paclitaxel, which is metabolized by CYP2C8 and CYP3A4 (refer to the paclitaxel drug monograph). Pharmacokinetic interactions between nab-paclitaxel and gemcitabine have not been evaluated in vivo. The drugs have different metabolic pathways.

AGENT	EFFECT	MECHANISM	MANAGEMENT
Radiation	Radiation pneumonitis	↑ pulmonary effects	Avoid/Caution
CYP2C8 substrates (e.g. paclitaxel, repaglinide, rosiglitazone)	May ↑/↓ effects of substrates or paclitaxel	Altered metabolism of CYP2C8 substrates or paclitaxel	Caution
CYP2C8 Inducers (e.g. rifampin)	May ↓ paclitaxel levels and effects	↑ metabolism of paclitaxel	Caution
CYP 2C8 inhibitors (i.e. gemfibrozil, montelukast)	May ↑ paclitaxel levels and effects	↓ metabolism of paclitaxel	Caution
CYP 3A4 substrates (i.e., verapamil, etoposide, dexamethasone, vincristine)	May ↑/↓ effects of substrates or paclitaxel	Altered metabolism of CYP3A4 substrates or paclitaxel	Caution
CYP3A4 inducers (i.e. phenytoin, rifampin, dexamethasone, carbamazepine, phenobarbital, St. John's Wort, etc)	May ↓ paclitaxel levels and effects	↑ metabolism of paclitaxel	Caution
CYP3A4 inhibitors (i.e. ketoconazole, clarithromycin, ritonavir, fruit or juice from grapefruit, Seville oranges or starfruit)	May ↑ paclitaxel levels and effects	↓ metabolism of paclitaxel	Caution

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

Monitor Type	Monitor Frequency
Liver function tests	Baseline, before each cycle and as clinically indicated
CBC	Baseline and before each dose
Renal function tests	Baseline and as clinically indicated
ECG monitoring especially in patients who have cardiac risk factors	Baseline and as clinically indicated
Clinical toxicity assessment of fatigue, neuropathy, infection and bleeding, hypersensitivity, musculoskeletal, GI, ophthalmic, thromboembolism, local reactions and pneumonitis	At each visit

Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Supplementary Public Funding

New Drug Funding Program (NDFP Website)

- Nab-Paclitaxel - Metastatic Breast Cancer
- Gemcitabine and Nab-Paclitaxel - Advanced Pancreatic Cancer
- Nab-Paclitaxel - Hypersensitivity Reactions to Taxanes

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K - References

Drug Development and Drug Interactions: Table of Substrates, Inhibitors and Inducers. U.S. Food and Drug Administration. Accessed May 29, 2013. Available from: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionsLabeling/ucm093664.htm

Gradishar WJ, Krasnojon D, Cheporov S, et al. Phase II trial of nab-paclitaxel compared with docetaxel as first-line chemotherapy in patients with metastatic breast cancer: final analysis of overall survival. Clin Breast Cancer 2012;12(5):313-21.

Gradishar WJ, Krasnojon D, Cheporov S, et al. Significantly longer progression-free survival with nab-paclitaxel compared with docetaxel as first-line therapy for metastatic breast cancer. J Clin Oncol 2009; 27: 3611-9.

Gradishar WJ, Tjulandin S, Davidson N, et al. Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil–based paclitaxel in women with breast cancer. J Clin Oncol 2005; 23: 7794-803.

P450 Drug Interaction Table. Indiana University School of Medicine, January 12, 2009. Available from: http://medicine.iupui.edu/clinpharm/ddis/table.aspx

Prescribing information: Abraxane® (paclitaxel protein-bound). Abraxis BioScience (US), September 2009 and August 2020.

Product Monograph: Abraxane® (nab-paclitaxel). Celgene Inc., May 2018 and Aug 2023.

Robinson DM, Keating GM. Albumin-bound paclitaxel in metastatic breast cancer. Drugs 2006; 66(7): 941-8.

Von Hoff DD, Ervin T, Arena FP, et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. N Engl J Med 2013;369(18):1691-703.

December 2024 Added NDFP form

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L - Disclaimer

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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