

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ABRAXANE safely and effectively. See full prescribing information for ABRAXANE.

**ABRAXANE® for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension)  
(albumin-bound)  
Initial U.S. Approval: 2005**

### WARNING: NEUTROPENIA

See full prescribing information for complete boxed warning.

- Do not administer ABRAXANE therapy to patients with baseline neutrophil counts of less than 1,500 cells/mm<sup>3</sup>. (4)
- It is recommended that frequent peripheral blood cell counts be performed to monitor the occurrence of bone marrow suppression. (4, 5.1, 6.1, 6.2, 6.3)

**DO NOT SUBSTITUTE FOR OR WITH OTHER PACLITAXEL FORMULATIONS.**

### RECENT MAJOR CHANGES

- |  |         |
|--|---------|
| • Dosage and Administration (2.4, 2.8)               | 12/2014 |
| • Dosage and Administration (2.7)                    | 07/2015 |
| • Warnings and Precautions, Hepatic Impairment (5.6) | 12/2014 |

### INDICATIONS AND USAGE

ABRAXANE is a microtubule inhibitor indicated for the treatment of:

- Metastatic breast cancer, after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated. (1.1)
- Locally advanced or metastatic non-small cell lung cancer (NSCLC), as first-line treatment in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy. (1.2)
- Metastatic adenocarcinoma of the pancreas as first-line treatment, in combination with gemcitabine. (1.3)

### DOSAGE AND ADMINISTRATION

- Metastatic Breast Cancer: Recommended dosage of ABRAXANE is 260 mg/m<sup>2</sup> intravenously over 30 minutes every 3 weeks. (2.1)
- Non-Small Cell Lung Cancer: Recommended dosage of ABRAXANE is 100 mg/m<sup>2</sup> intravenously over 30 minutes on Days 1, 8, and 15 of each 21-day cycle; administer carboplatin on Day 1 of each 21-day cycle immediately after ABRAXANE. (2.2)
- Adenocarcinoma of the Pancreas: Recommended dosage of ABRAXANE is 125 mg/m<sup>2</sup> intravenously over 30-40 minutes on Days 1, 8 and 15 of each 28-day cycle; administer gemcitabine on Days 1, 8 and 15 of each 28-day cycle immediately after ABRAXANE. (2.3)
- Do not administer ABRAXANE to any patient with AST > 10 x ULN or bilirubin > 5 x ULN. Do not administer ABRAXANE to patients with metastatic adenocarcinoma of the pancreas who have moderate to severe hepatic impairment. For diseases other than metastatic adenocarcinoma of the pancreas, reduce starting dose in patients with moderate to severe hepatic impairment. (2.4)
- Dose Reductions: Dose reductions or discontinuation may be needed based on severe hematologic, neurologic, cutaneous, or gastrointestinal toxicities. (2.5)
- Use caution when handling cytotoxic drugs. Closely monitor the infusion site for extravasation and infiltration. No premedication is required prior to administration. (2.6)

### DOSAGE FORMS AND STRENGTHS

- For injectable suspension: lyophilized powder containing 100 mg of paclitaxel formulated as albumin-bound particles in single-use vial for reconstitution. (3)

### CONTRAINDICATIONS

- Neutrophil counts of < 1,500 cells/mm<sup>3</sup>. (4)
- Severe hypersensitivity reaction to ABRAXANE. (4)

### WARNINGS AND PRECAUTIONS

- ABRAXANE causes myelosuppression. Monitor CBC and withhold and/or reduce the dose as needed. (5.1)
- Sensory neuropathy occurs frequently and may require dose reduction or treatment interruption. (5.2)
- Sepsis occurred in patients with or without neutropenia who received ABRAXANE in combination with gemcitabine; interrupt ABRAXANE and gemcitabine until sepsis resolves, and if neutropenia, until neutrophils are at least 1500 cells/mm<sup>3</sup>, then resume treatment at reduced dose levels. (5.3)
- Pneumonitis occurred with the use of ABRAXANE in combination with gemcitabine; permanently discontinue treatment with ABRAXANE and gemcitabine. (5.4)
- Severe hypersensitivity reactions with fatal outcome have been reported. Do not re-challenge with this drug. (5.5)
- Exposure and toxicity of paclitaxel can be increased in patients with hepatic impairment; therefore administer with caution. (5.6)
- ABRAXANE contains albumin derived from human blood, which has a theoretical risk of viral transmission. (5.7)
- Fetal harm may occur when administered to a pregnant woman. Advise women of childbearing potential to avoid becoming pregnant while receiving ABRAXANE. (5.8)
- Advise men not to father a child while on ABRAXANE. (5.9)

### ADVERSE REACTIONS

- The most common adverse reactions (≥ 20%) in metastatic breast cancer are alopecia, neutropenia, sensory neuropathy, abnormal ECG, fatigue/asthenia, myalgia/arthralgia, AST elevation, alkaline phosphatase elevation, anemia, nausea, infections, and diarrhea. (6.1)
- The most common adverse reactions (≥ 20%) in NSCLC are anemia, neutropenia, thrombocytopenia, alopecia, peripheral neuropathy, nausea, and fatigue. (6.2)
- The most common (≥ 20%) adverse reactions of ABRAXANE in adenocarcinoma of the pancreas are neutropenia, fatigue, peripheral neuropathy, nausea, alopecia, peripheral edema, diarrhea, pyrexia, vomiting, decreased appetite, rash, and dehydration. (6.3)

To report SUSPECTED ADVERSE REACTIONS, contact Celgene Corporation at 1-888-423-5436 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

- Use caution when concomitantly administering ABRAXANE with inhibitors or inducers of either CYP2C8 or CYP3A4. (7)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 07/2015

FULL PRESCRIBING INFORMATION: CONTENTS\*

**WARNING: NEUTROPENIA**

**1 INDICATIONS AND USAGE**

- 1.1 Metastatic Breast Cancer
- 1.2 Non-Small Cell Lung Cancer
- 1.3 Adenocarcinoma of the Pancreas

**2 DOSAGE AND ADMINISTRATION**

- 2.1 Metastatic Breast Cancer
- 2.2 Non-Small Cell Lung Cancer
- 2.3 Adenocarcinoma of the Pancreas
- 2.4 Dosage in Patients with Hepatic Impairment
- 2.5 Dose Reduction/Discontinuation Recommendations
- 2.6 Preparation and Administration Precautions
- 2.7 Preparation for Intravenous Administration
- 2.8 Stability

**3 DOSAGE FORMS AND STRENGTHS**

**4 CONTRAINDICATIONS**

**5 WARNINGS AND PRECAUTIONS**

- 5.1 Hematologic Effects
- 5.2 Nervous System
- 5.3 Sepsis
- 5.4 Pneumonitis
- 5.5 Hypersensitivity
- 5.6 Hepatic Impairment
- 5.7 Albumin (Human)
- 5.8 Use in Pregnancy
- 5.9 Use in Men

**6 ADVERSE REACTIONS**

- 6.1 Clinical Trials Experience in Metastatic Breast Cancer
- 6.2 Clinical Trials Experience in Non-Small Cell Lung Cancer
- 6.3 Clinical Trials Experience in Adenocarcinoma of the Pancreas

- 6.4 Postmarketing Experience with ABRIXANE and other Paclitaxel Formulations
- 6.5 Accidental Exposure

**7 DRUG INTERACTIONS**

**8 USE IN SPECIFIC POPULATIONS**

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Patients with Hepatic Impairment
- 8.7 Patients with Renal Impairment

**10 OVERDOSAGE**

**11 DESCRIPTION**

**12 CLINICAL PHARMACOLOGY**

- 12.1 Mechanism of Action
- 12.3 Pharmacokinetics

**13 NONCLINICAL TOXICOLOGY**

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

**14 CLINICAL STUDIES**

- 14.1 Metastatic Breast Cancer
- 14.2 Non-Small Cell Lung Cancer
- 14.3 Adenocarcinoma of the Pancreas

**15 REFERENCES**

**16 HOW SUPPLIED/STORAGE AND HANDLING**

- 16.1 How Supplied
- 16.2 Storage
- 16.3 Handling and Disposal

**17 PATIENT COUNSELING INFORMATION**

\* Sections or subsections omitted from the Full Prescribing Information are not listed.

## FULL PRESCRIBING INFORMATION

ABRAXANE® for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) (albumin-bound)

### WARNING: NEUTROPENIA

- Do not administer ABRAXANE therapy to patients who have baseline neutrophil counts of less than 1,500 cells/mm<sup>3</sup>. In order to monitor the occurrence of bone marrow suppression, primarily neutropenia, which may be severe and result in infection, it is recommended that frequent peripheral blood cell counts be performed on all patients receiving ABRAXANE [see *Contraindications (4), Warnings and Precautions (5.1) and Adverse Reactions (6.1, 6.2, 6.3)*].
- Note: An albumin form of paclitaxel may substantially affect a drug's functional properties relative to those of drug in solution. DO NOT SUBSTITUTE FOR OR WITH OTHER PACLITAXEL FORMULATIONS.

## 1 INDICATIONS AND USAGE

### 1.1 Metastatic Breast Cancer

ABRAXANE is indicated for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.

### 1.2 Non-Small Cell Lung Cancer

ABRAXANE is indicated for the first-line treatment of locally advanced or metastatic non-small cell lung cancer, in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy.

### 1.3 Adenocarcinoma of the Pancreas

ABRAXANE is indicated for the first-line treatment of patients with metastatic adenocarcinoma of the pancreas, in combination with gemcitabine.

## 2 DOSAGE AND ADMINISTRATION

### 2.1 Metastatic Breast Cancer

After failure of combination chemotherapy for metastatic breast cancer or relapse within 6 months of adjuvant chemotherapy, the recommended regimen for ABRAXANE is 260 mg/m<sup>2</sup> administered intravenously over 30 minutes every 3 weeks.

### 2.2 Non-Small Cell Lung Cancer

The recommended dose of ABRAXANE is 100 mg/m<sup>2</sup> administered as an intravenous infusion over 30 minutes on Days 1, 8, and 15 of each 21-day cycle. Administer carboplatin on Day 1 of each 21 day cycle immediately after ABRAXANE [see *Clinical Studies (14.2)*].

### 2.3 Adenocarcinoma of the Pancreas

The recommended dose of ABRAXANE is 125 mg/m<sup>2</sup> administered as an intravenous infusion over 30-40 minutes on Days 1, 8 and 15 of each 28-day cycle. Administer gemcitabine immediately after ABRAXANE on Days 1, 8 and 15 of each 28-day cycle [see *Clinical Studies (14.3)*].

### 2.4 Dosage in Patients with Hepatic Impairment

For patients with mild hepatic impairment (total bilirubin greater than ULN and less than or equal to 1.5 x ULN and aspartate aminotransferase [AST] less than or equal to 10 x ULN), no dose adjustments are required, regardless of indication.

Do not administer ABRAXANE to patients with metastatic adenocarcinoma of the pancreas who have moderate to severe hepatic impairment.

Do not administer ABRAXANE to patients with total bilirubin greater than 5 x ULN or AST greater than 10 x ULN regardless of indication as these patients have not been studied.

Recommendations for dosage adjustment for the first course of therapy are shown in Table 1.

**Table 1: Recommendations for Starting Dose in Patients with Hepatic Impairment**

	SGOT (AST) Levels		Bilirubin Levels	ABRAXANE Dose <sup>a</sup>		
				MBC	NSCLC <sup>c</sup>	Pancreatic <sup>c</sup> Adenocarcinoma
Mild	< 10 x ULN	AND	> ULN to ≤ 1.5 x ULN	260 mg/m <sup>2</sup>	100 mg/m <sup>2</sup>	125 mg/m <sup>2</sup>
Moderate	< 10 x ULN	AND	> 1.5 to ≤ 3 x ULN	200 mg/m <sup>2b</sup>	80 mg/m <sup>2b</sup>	not recommended
Severe	< 10 x ULN	AND	> 3 to ≤ 5 x ULN	200 mg/m <sup>2b</sup>	80 mg/m <sup>2b</sup>	not recommended
	> 10 x ULN	OR	> 5 x ULN	not recommended	not recommended	not recommended

MBC = Metastatic Breast Cancer; NSCLC = Non-Small Cell Lung Cancer.

<sup>a</sup> Dosage recommendations are for the first course of therapy. The need for further dose adjustments in subsequent courses should be based on individual tolerance.

<sup>b</sup> A dose increase to 260 mg/m<sup>2</sup> for patients with metastatic breast cancer or 100 mg/m<sup>2</sup> for patients with non-small cell lung cancer in subsequent courses should be considered if the patient tolerates the reduced dose for two cycles.

<sup>c</sup> Patients with bilirubin levels above the upper limit of normal were excluded from clinical trials for pancreatic or lung cancer.

**2.5 Dose Reduction/Discontinuation Recommendations**

*Metastatic Breast Cancer*

Patients who experience severe neutropenia (neutrophils less than 500 cells/mm<sup>3</sup> for a week or longer) or severe sensory neuropathy during ABRAXANE therapy should have dosage reduced to 220 mg/m<sup>2</sup> for subsequent courses of ABRAXANE. For recurrence of severe neutropenia or severe sensory neuropathy, additional dose reduction should be made to 180 mg/m<sup>2</sup>. For Grade 3 sensory neuropathy hold treatment until resolution to Grade 1 or 2, followed by a dose reduction for all subsequent courses of ABRAXANE [see *Contraindications (4), Warnings and Precautions (5.1, 5.2) and Adverse Reactions (6.1)*].

*Non-Small Cell Lung Cancer*

- Do not administer ABRAXANE on Day 1 of a cycle until absolute neutrophil count (ANC) is at least 1500 cells/mm<sup>3</sup> and platelet count is at least 100,000 cells/mm<sup>3</sup> [see *Contraindications (4), Warnings and Precautions (5.1) and Adverse Reactions (6.2)*].
- In patients who develop severe neutropenia or thrombocytopenia withhold treatment until counts recover to an absolute neutrophil count of at least 1500 cells/mm<sup>3</sup> and platelet count of at least 100,000 cells/mm<sup>3</sup> on Day 1 or to an absolute neutrophil count of at least 500 cells/mm<sup>3</sup> and platelet count of at least 50,000 cells/mm<sup>3</sup> on Days 8 or 15 of the cycle. Upon resumption of dosing, permanently reduce ABRAXANE and carboplatin doses as outlined in Table 2.
- Withhold ABRAXANE for Grade 3-4 peripheral neuropathy. Resume ABRAXANE and carboplatin at reduced doses (see Table 2) when peripheral neuropathy improves to Grade 1 or completely resolves [see *Warnings and Precautions (5.2) and Adverse Reactions (6.2)*].

**Table 2: Permanent Dose Reductions for Hematologic and Neurologic Adverse Drug Reactions in NSCLC**

Adverse Drug Reaction	Occurrence	Weekly ABRAXANE Dose (mg/m <sup>2</sup> )	Every 3-Week Carboplatin Dose (AUC mg·min/mL)
Neutropenic Fever (ANC less than 500/mm <sup>3</sup> with fever >38°C) OR Delay of next cycle by more than 7 days for ANC less than 1500/mm <sup>3</sup> OR ANC less than 500/mm <sup>3</sup> for more than 7 days	First	75	4.5
	Second	50	3
	Third	Discontinue Treatment	
Platelet count less than 50,000/mm <sup>3</sup>	First	75	4.5
	Second	Discontinue Treatment	
Severe sensory Neuropathy – Grade 3 or 4	First	75	4.5
	Second	50	3
	Third	Discontinue Treatment	

*Adenocarcinoma of the Pancreas*

Dose level reductions for patients with adenocarcinoma of the pancreas, as referenced in Tables 4 and 5, are provided in Table 3.

**Table 3: Dose Level Reductions for Patients with Adenocarcinoma of the Pancreas**

Dose Level	ABRAXANE (mg/m <sup>2</sup> )	Gemcitabine (mg/m <sup>2</sup> )
Full dose	125	1000
1 <sup>st</sup> dose reduction	100	800
2 <sup>nd</sup> dose reduction	75	600
If additional dose reduction required	Discontinue	Discontinue

Recommended dose modifications for neutropenia and thrombocytopenia for patients with adenocarcinoma of the pancreas are provided in Table 4.

**Table 4: Dose Recommendation and Modifications for Neutropenia and/or Thrombocytopenia at the Start of a Cycle or within a Cycle for Patients with Adenocarcinoma of the Pancreas**

Cycle Day	ANC (cells/mm <sup>3</sup> )		Platelet count (cells/mm <sup>3</sup> )	ABRAXANE / Gemcitabine
Day 1	< 1500	OR	< 100,000	Delay doses until recovery
Day 8	500 to < 1000	OR	50,000 to < 75,000	Reduce 1 dose level
	< 500	OR	< 50,000	Withhold doses
<b>Day 15: If Day 8 doses were reduced or given without modification:</b>				
	500 to < 1000	OR	50,000 to < 75,000	Reduce 1 dose level from Day 8
	< 500	OR	< 50,000	Withhold doses
<b>Day 15: If Day 8 doses were withheld:</b>				
	≥ 1000	OR	≥ 75,000	Reduce 1 dose level from Day 1
	500 to < 1000	OR	50,000 to < 75,000	Reduce 2 dose levels from Day 1
	< 500	OR	< 50,000	Withhold doses

ANC = Absolute Neutrophil Count

Recommended dose modifications for other adverse drug reactions in patients with adenocarcinoma of the pancreas are provided in Table 5.

**Table 5: Dose Modifications for Other Adverse Drug Reactions in Patients with Adenocarcinoma of the Pancreas**

Adverse Drug Reaction	ABRAXANE	Gemcitabine
<b>Febrile Neutropenia:</b> Grade 3 or 4	Withhold until fever resolves and ANC ≥ 1500; resume at next lower dose level	
<b>Peripheral Neuropathy:</b> Grade 3 or 4	Withhold until improves to ≤ Grade 1; resume at next lower dose level	No dose reduction
<b>Cutaneous Toxicity:</b> Grade 2 or 3	Reduce to next lower dose level; discontinue treatment if toxicity persists	
<b>Gastrointestinal Toxicity:</b> Grade 3 mucositis or diarrhea	Withhold until improves to ≤ Grade 1; resume at next lower dose level	

**2.6 Preparation and Administration Precautions**

ABRAXANE is a cytotoxic drug and, as with other potentially toxic paclitaxel compounds, caution should be exercised in handling ABRAXANE. The use of gloves is recommended. If ABRAXANE (lyophilized cake or reconstituted suspension) contacts the skin, wash the skin immediately and thoroughly with soap and water. Following topical exposure to paclitaxel, events may include tingling, burning and redness. If ABRAXANE contacts mucous membranes, the membranes should be flushed thoroughly with water.

# Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

## Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

## Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

## Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

## API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

## LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

## FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

## E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.