

## 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<sup>®</sup> 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)
- DO NOT SUBSTITUTE FOR OR WITH OTHER PACLITAXEL FORMULATIONS.**

### RECENT MAJOR CHANGES

- |   |         |
|---|---------|
| • Indications and Usage. (1.2)                      | 10/2012 |
| • Dosage and Administration. (2.2)                  | 10/2012 |
| • Warnings and Precautions, Hypersensitivity. (5.3) | 09/2012 |

### 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)

### 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; carboplatin AUC 6 mg•min/mL is given intravenously on Day 1 of each 21 day cycle immediately after ABRAXANE administration. (2.2)
- No adjustment is necessary for patients with mild hepatic impairment. Withhold ABRAXANE if AST > 10 x ULN or bilirubin > 5 x ULN. Reduce starting dose in patients with moderate to severe hepatic impairment. (2.3)
- Dose Reductions: Dose reductions or discontinuation may be needed based on severe hematologic or neurologic toxicities. (2.4)

- Use caution when handling cytotoxic drugs. Closely monitor the infusion site for extravasation and infiltration. No premedication is required prior to administration. (2.5)

### DOSAGE FORMS AND STRENGTHS

- Single use vial containing 100 mg of paclitaxel. (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)
- Severe hypersensitivity reactions with fatal outcome have been reported. Do not re-challenge with this drug. (5.3)
- Exposure and toxicity of paclitaxel can be increased in patients with hepatic impairment; therefore administer with caution. (5.4)
- ABRAXANE contains albumin derived from human blood, which has a theoretical risk of viral transmission. (5.5)
- Fetal harm may occur when administered to a pregnant woman. Advise women of childbearing potential to avoid becoming pregnant while receiving ABRAXANE. (5.6)
- Advise men not to father a child while on ABRAXANE. (5.7)

### 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 when used in combination with carboplatin are anemia, neutropenia, thrombocytopenia, alopecia, peripheral neuropathy, nausea, and fatigue. (6.2)

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 (Patient Information).

Revised: XX/XX

FULL PRESCRIBING INFORMATION: CONTENTS\*

**WARNING: NEUTROPENIA**

**1 INDICATIONS AND USAGE**

- 1.1 Metastatic Breast Cancer
- 1.2 Non-Small Cell Lung Cancer

**2 DOSAGE AND ADMINISTRATION**

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

**3 DOSAGE FORMS AND STRENGTHS**

**4 CONTRAINDICATIONS**

**5 WARNINGS AND PRECAUTIONS**

- 5.1 Hematologic Effects
- 5.2 Nervous System
- 5.3 Hypersensitivity
- 5.4 Hepatic Impairment
- 5.5 Albumin (Human)
- 5.6 Use in Pregnancy
- 5.7 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 Post-Marketing Experience with ABRAXANE and other Paclitaxel Formulations

- 6.4 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

**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<sup>®</sup> 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)*].
- 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.

## 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. The recommended dose of carboplatin is AUC = 6 mg•min/mL on Day 1 only of each 21-day cycle, beginning immediately after the completion of ABRAXANE administration.

### 2.3 Dosage in Patients with Hepatic Impairment

No dose adjustment is necessary for patients with mild hepatic impairment. Patients with moderate and severe hepatic impairment treated with ABRAXANE may be at increased risk of toxicities known to paclitaxel. Withhold ABRAXANE if AST >10 x ULN or bilirubin > 5 x ULN. Recommendations for dosage adjustment for the first course of therapy are shown in Table 1.

For metastatic breast cancer, the dose of ABRAXANE can be increased from 130 mg/m<sup>2</sup> up to 200 mg/m<sup>2</sup> in patients with severe hepatic impairment in subsequent cycles based on individual tolerance.

For non-small cell lung cancer, reduce the dose of ABRAXANE to 50 mg/m<sup>2</sup> in patients with severe hepatic impairment. In subsequent cycles, the dose of ABRAXANE may be increased to 75 mg/m<sup>2</sup> as tolerated.

Monitor patients closely [see *Warnings and Precautions (5.4), Use in Specific Populations (8.6), and Clinical Pharmacology (12.3)*].

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

	SGOT (AST) Levels			Bilirubin Levels		ABRAXANE Dose <sup>a</sup>	
						MBC	NSCLC
Mild	< 10 x ULN			> ULN to ≤ 1.25 x ULN		260 mg/m <sup>2</sup>	100 mg/m <sup>2</sup>
Moderate	< 10 x ULN	AND		1.26 to 2 x ULN		200 mg/m <sup>2</sup>	75 mg/m <sup>2</sup>
Severe	< 10 x ULN			2.01 to 5 x ULN		130 mg/m <sup>2b</sup>	50 mg/m <sup>2c</sup>
	> 10 x ULN	OR		> 5 x ULN		not eligible	not eligible

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 200 mg/m<sup>2</sup> in subsequent courses should be considered based on individual tolerance.

<sup>c</sup> Increase dose to 75 mg/m<sup>2</sup> in subsequent courses, as tolerated.

## 2.4 Dose Reduction/Discontinuation Recommendations

### Metastatic Breast Cancer

Patients who experience severe neutropenia (neutrophil  $<500$  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 $>38^{\circ}\text{C}$ ) 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	

## 2.5 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.

Given the possibility of extravasation, it is advisable to closely monitor the infusion site for possible infiltration during drug administration. Limiting the infusion of ABRAXANE to 30 minutes, as directed, reduces the likelihood of infusion-related reactions [see *Adverse Reactions (6.3)*].

Premedication to prevent hypersensitivity reactions is generally not needed prior to the administration of ABRAXANE. Premedication may be needed in patients who have had prior hypersensitivity reactions to ABRAXANE. Patients who experience a severe hypersensitivity reaction to ABRAXANE should not be re-challenged with this drug [see *Warnings and Precautions (5.3)*].

## 2.6 Preparation for Intravenous Administration

ABRAXANE is supplied as a sterile lyophilized powder for reconstitution before use. **AVOID ERRORS, READ ENTIRE PREPARATION INSTRUCTIONS PRIOR TO RECONSTITUTION.**

1. Aseptically, reconstitute each vial by injecting 20 mL of 0.9% Sodium Chloride Injection, USP.
2. Slowly inject the 20 mL of 0.9% Sodium Chloride Injection, USP, over a minimum of 1 minute, using the sterile syringe to direct the solution flow onto the **INSIDE WALL OF THE VIAL.**



3. **DO NOT INJECT** the 0.9% Sodium Chloride Injection, USP, directly onto the lyophilized cake as this will result in foaming.
4. Once the injection is complete, allow the vial to sit for a minimum of 5 minutes to ensure proper wetting of the lyophilized cake/powder.
5. Gently swirl and/or invert the vial slowly for at least 2 minutes until complete dissolution of any cake/powder occurs. Avoid generation of foam.
6. If foaming or clumping occurs, stand solution for at least 15 minutes until foam subsides.

Each mL of the reconstituted formulation will contain 5 mg/mL paclitaxel.

Calculate the exact total dosing volume of 5 mg/mL suspension required for the patient:  $\text{Dosing volume (mL)} = \frac{\text{Total dose (mg)}}{5 \text{ (mg/mL)}}$

The reconstituted suspension should be milky and homogenous without visible particulates. If particulates or settling are visible, the vial should be **gently** inverted again to ensure complete resuspension prior to use. Discard the reconstituted suspension if precipitates are observed. Discard any unused portion.

Inject the appropriate amount of reconstituted ABRAXANE into an empty, sterile intravenous bag [plasticized polyvinyl chloride (PVC) containers, PVC or non-PVC type intravenous bag]. The use of specialized DEHP-free solution containers or administration sets is not necessary to prepare or administer ABRAXANE infusions. The use of an in-line filter is not recommended.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

## 2.7 Stability

Unopened vials of ABRAXANE are stable until the date indicated on the package when stored between 20°C to 25°C (68°F to 77°F) in the original package. Neither freezing nor refrigeration adversely affects the stability of the product.

### *Stability of Reconstituted Suspension in the Vial*

Reconstituted ABRAXANE in the vial should be used immediately, but may be refrigerated at 2°C to 8°C (36°F to 46°F) for a maximum of 8 hours if necessary. If not used immediately, each vial of reconstituted suspension should be replaced in the original carton to protect it from bright light. Discard any unused portion.

### *Stability of Reconstituted Suspension in the Infusion Bag*

The suspension for infusion when prepared as recommended in an infusion bag should be used immediately but may be stored at ambient temperature (approximately 25°C) and lighting conditions for up to 4 hours. Discard any unused portion.

## 3 DOSAGE FORMS AND STRENGTHS

Single use vials containing 100 mg of paclitaxel.

## 4 CONTRAINDICATIONS

- ABRAXANE should not be used in patients who have baseline neutrophil counts of  $< 1,500 \text{ cells/mm}^3$ .
- Patients who experience a severe hypersensitivity reaction to ABRAXANE should not be rechallenged with the drug.

# 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.