

## 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), for intravenous use  
Initial U.S. Approval: 2005

### WARNING: SEVERE MYELOSUPPRESSION

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)
- Monitor for neutropenia, which may be severe and result in infection or sepsis. (5.1, 5.3)
- Perform frequent complete blood cell counts on all patients receiving ABRAXANE. (5.1, 5.3)

### RECENT MAJOR CHANGES

Dosage and Administration (2.1, 2.7)	8/2020
Contraindications (4)	8/2020
Warnings and Precautions (5.1, 5.2)	8/2020

### 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

- Do not substitute ABRAXANE for other paclitaxel products. (2.1)
- Extravasation: Closely monitor the infusion site for extravasation and infiltration. (2.1)
- Metastatic Breast Cancer (MBC): Recommended dosage of ABRAXANE is 260 mg/m<sup>2</sup> intravenously over 30 minutes every 3 weeks. (2.2)
- Non-Small Cell Lung Cancer (NSCLC): 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. (2.4)
- Use in Patients with Hepatic Impairment: ABRAXANE is not recommended for use in patients with AST > 10 x ULN; or bilirubin > 5 x ULN or with metastatic adenocarcinoma of the pancreas who have moderate to severe hepatic impairment. For MBC or NSCLC, reduce starting dose in patients with moderate to severe hepatic impairment. (2.5)

- Dose Reductions for Adverse Reactions: Dose reductions or discontinuation may be needed based on severe hematologic, neurologic, cutaneous, or gastrointestinal toxicities. (2.6)

### DOSAGE FORMS AND STRENGTHS

For injectable suspension: white to yellow, sterile, lyophilized powder containing 100 mg of paclitaxel formulated as albumin-bound particles in single-dose vial for reconstitution. (3)

### CONTRAINDICATIONS

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

### WARNINGS AND PRECAUTIONS

- 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 rechallenge with this drug. (4, 5.5)
- Exposure and toxicity of paclitaxel can be increased in patients with hepatic impairment, consider dose reduction and closely monitor patients with hepatic impairment. (2.5, 5.6)
- ABRAXANE contains albumin derived from human blood, which has a theoretical risk of viral transmission. (5.7)
- ABRAXANE can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception. (5.8, 8.1, 8.3)

### 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. (6.1)
- 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. (6.1)

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)

### USE IN SPECIFIC POPULATIONS

- Lactation: Advise not to breastfeed. (8.2)

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

Revised: 8/2020

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## FULL PRESCRIBING INFORMATION

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

#### WARNING: SEVERE MYELOSUPPRESSION

- Do not administer ABRAXANE therapy to patients who have baseline neutrophil counts of less than 1,500 cells/mm<sup>3</sup>. [see *Contraindications (4)*].
- Monitor for neutropenia, which may be severe and result in infection or sepsis, it is recommended that frequent [see *Warnings and Precautions (5.1, 5.3)*].
- Perform frequent complete blood cell counts on all patients receiving ABRAXANE [see *Contraindications (4), Warnings and Precautions (5.1, 5.3)*].

## 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 Important Administration Instructions

DO NOT SUBSTITUTE FOR OR WITH OTHER PACLITAXEL FORMULATIONS. **ABRAXANE** has different dosage and administration instructions from other paclitaxel products.

Closely monitor the infusion site for extravasation or drug infiltration during administration. Limiting the infusion of ABRAXANE to 30 minutes may reduce the risk of infusion-related reactions [see *Adverse Reactions (6.2)*].

Consider premedication in patients who have had prior hypersensitivity reactions to ABRAXANE. Do not re-challenge patients who experience a severe hypersensitivity reaction to ABRAXANE [see *Contraindications (4) and Warnings and Precautions (5.5)*].

### 2.2 Recommended Dosage for 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.

### 2.3 Recommended Dosage for 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)*].

### 2.4 Recommended Dosage for 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)*].

### 2.5 Dosage Modifications for Hepatic Impairment

For patients with moderate or severe hepatic impairment, reduce the starting dose of ABRAXANE as shown in Table 1.

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

	AST Levels		Bilirubin Levels	ABRAXANE Dose <sup>a</sup>		
				MBC	NSCLC <sup>c</sup>	Adenocarcinoma of Pancreas <sup>c</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

AST = Aspartate Aminotransferase; MBC = Metastatic Breast Cancer; NSCLC = Non-Small Cell Lung Cancer; ULN = Upper limit of normal.

<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.

**2.6 Dosage Modifications for Adverse Reactions**

**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 (6.1)].
- 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 (6.1)].

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

Adverse 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 reactions in patients with adenocarcinoma of the pancreas are provided in Table 5.

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

Adverse 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	

#### 2.7 Preparation for Intravenous Administration

ABRAXANE is a cytotoxic drug. Follow applicable special handling and disposal procedures.<sup>1</sup> 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.

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