IMPORTANT SAFETY INFORMATION

WARNING - NEUTROPENIA
• Do not administer ABRAXANE therapy to patients who have baseline neutrophil counts of less than 1500 cells/mm³. 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.
• 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

CONTRAINDICATIONS
Neutrophil Counts
• ABRAXANE should not be used in patients who have baseline neutrophil counts of <1500 cells/mm³.

Hypersensitivity
• Patients who experience a severe hypersensitivity reaction to ABRAXANE should not be rechallenged with the drug.

WARNINGS AND PRECAUTIONS
Hematologic Effects
• Bone marrow suppression (primarily neutropenia) is dose-dependent and a dose-limiting toxicity of ABRAXANE. In a clinical study, Grade 3–4 neutropenia occurred in 38% of patients with pancreatic cancer.
• Monitor for myelotoxicity by performing complete blood cell counts frequently, including prior to dosing on Days 1, 8, and 15 for pancreatic cancer.

Do not administer ABRAXANE to patients with baseline absolute neutrophil counts (ANC) of less than 1500 cells/mm³.
• In patients with adenocarcinoma of the pancreas, withhold ABRAXANE and gemcitabine if the ANC is less than 500 cells/mm³ or platelets are less than 50,000 cells/mm³ and delay initiation of the next cycle if the ANC is less than 1500 cells/mm³ or platelet count is less than 100,000 cells/mm³ on Day 1 of the cycle. Resume treatment with appropriate dose reduction if recommended.

Nervous System
• Sensory neuropathy is dose- and schedule-dependent.
• The occurrence of Grade 1 or 2 sensory neuropathy does not generally require dose modification.
• If ≥ Grade 3 sensory neuropathy develops, withhold ABRAXANE treatment until resolution to ≤ Grade 1 followed by a dose reduction for all subsequent courses of ABRAXANE.

Sepsis
• Sepsis occurred in 5% of patients with or without neutropenia who received ABRAXANE in combination with gemcitabine.
• Biliary obstruction or presence of biliary stent were risk factors for severe or fatal sepsis.
• If a patient becomes febrile (regardless of ANC), initiate treatment with broad-spectrum antibiotics.
• For febrile neutropenia, interrupt ABRAXANE and gemcitabine until fever resolves and ANC ≥1500 cells/mm³, then resume treatment at reduced dose levels.

Please refer to the NCCN Guidelines® for pancreatic cancer for a complete list of recommended treatment options.
• Of these most common adverse reactions, those with a ≥2% higher incidence of Grade 3-4 toxicity in the ABRAXANE/gemcitabine group compared to the gemcitabine group, respectively, are neutropenia (38%, 27%), fatigue (18%, 9%), peripheral neuropathy (17%, 1%), nausea (6%, 3%), diarrhea (6%, 1%), pyrexia (3%, 1%), vomiting (6%, 4%), decreased appetite (5%, 2%), and dehydration (7%, 2%)

• The most common serious adverse reactions of ABRAXANE (with a ≥1% higher incidence) are pyrexia (6%), dehydration (5%), pneumonia (4%), and vomiting (4%)

• The most common adverse reactions resulting in permanent discontinuation of ABRAXANE were peripheral neuropathy (8%), fatigue (4%), and thrombocytopenia (2%) in 74% of patients in the ABRAXANE/gemcitabine group vs 70% of patients in the gemcitabine group

• Of these most common adverse reactions, those with a ≥5% higher incidence for all-grade toxicity in the ABRAXANE/gemcitabine group compared to the gemcitabine group, respectively, are asthenia (9%, 5%), mucositis (10%, 4%), dysgeusia (16%, 8%), headache (14%, 5%), hypertension (12%, 7%), cough (17%, 7%), epistaxis (15%, 3%), urinary tract infection (11%, 5%), pain in extremity (11%, 6%), arthralgia (11%, 3%), myalgia (10%, 4%), and depression (12%, 6%)

• Other selected adverse reactions with a ≥5% higher incidence for all-grade toxicity in the ABRAXANE/gemcitabine group compared to the gemcitabine group, respectively, are anemia (10%, 5%), peripheral neuropathy (15%), nausea (5%, 1%), and diarrhea (5%)

• Other selected adverse reactions with a ≥5% higher incidence for grade 3-4 toxicity in the ABRAXANE/gemcitabine group compared to the gemcitabine group, respectively, are anemia (10%, 5%), peripheral neuropathy (15%), nausea (5%, 1%), and diarrhea (5%)

• There have been reports of extravasation of ABRAXANE. Given the possibility of extravasation, it is advisable to monitor closely the ABRAXANE infusion site for possible infiltration during drug administration

DRUG INTERACTIONS
• Caution should be exercised when administering ABRAXANE concomitantly with medicines known to inhibit or induce either CYP2C8 or CYP3A4

USE IN SPECIFIC POPULATIONS
Nursing Mothers
• It is not known whether paclitaxel is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother

Pediatric
• The safety and effectiveness of ABRAXANE in pediatric patients have not been evaluated

Geriatric
• Diarrhea, decreased appetite, dehydration, and epistaxis were more frequent in patients 65 years or older compared with patients younger than 65 years old who received ABRAXANE and gemcitabine in adenocarcinoma of the pancreas

Renal Impairment
• There are insufficient data to permit dosage recommendations in patients with severe renal impairment or end stage renal disease (estimated creatinine clearance <30 mL/min)

DOSAGE AND ADMINISTRATION
• Do not administer ABRAXANE to patients with metastatic adenocarcinoma of the pancreas who have moderate to severe hepatic impairment
• Do not administer ABRAXANE to any patient with total bilirubin greater than 5 x ULN or AST greater than 10 x ULN
• Dose reductions or discontinuation may be needed based on severe hematologic, neurologic, cutaneous, or gastrointestinal toxicity
• Monitor patients closely

Postmarketing Experience

ABRAXANE® and Other Paclitaxel Formulations
• Severe and sometimes fatal hypersensitivity reactions have been reported with ABRAXANE. The use of ABRAXANE in patients previously exhibiting hypersensitivity to paclitaxel injection or human albumin has not been studied
• There have been reports of congestive heart failure, left ventricular dysfunction, and atrioventricular block with ABRAXANE primarily among individuals with underlying cardiac history or prior exposure to cardiotoxic drugs
• There have been reports of extravasation of ABRAXANE. Given the possibility of extravasation, it is advisable to monitor closely the ABRAXANE infusion site for possible infiltration during drug administration

REFERENCES