PACLITAXEL (pak-li-tax-el)

PACLITAXEL PROTEIN-BOUND PARTICLES (ALBUMIN-BOUND)

Therapeutic:
anitneoplastics
Pharmacologic:
taxoids

Classification

Pregnancy Category D

Indications

Paclitaxel:
- Advanced ovarian cancer (with cisplatin).
- Non-small cell lung cancer when potentially curative surgery and/or radiation therapy is not an option.
- Metastatic breast cancer unresponsive to other therapy.
- Node-positive breast cancer when administered sequentially to standard combination chemotherapy that includes doxorubicin.
- Treatment of AIDS-related Kaposi’s sarcoma.

Paclitaxel (albumin-bound):
- Metastatic breast cancer after treatment failure or relapse where therapy included an anthracycline.
- Locally advanced or metastatic non-small cell lung cancer, in combination with carboplatin, when potentially curative surgery or radiation therapy is not an option.
- Metastatic pancreatic adenocarcinoma (with gemcitabine).

Action

Interferes with the normal cellular microtubule function that is required for interphase and mitosis. Therapeutic Effects: Death of rapidly replicating cells, particularly malignant ones.

Pharmacokinetics

Absorption: IV administration results in complete bioavailability.

Distribution: Crosses the placenta.

Protein Binding: 89–98%.

Metabolism and Excretion: Highlly metabolized by the liver (primarily by CYP2C8 and CYP3A4), 10% excreted unchanged in urine.

Half-life: Paclitaxel—15–52 hr; Paclitaxel protein-bound particles (albumin-bound)—27 hr.

Contraindications/Precautions

Contraindicated in:
- Hypersensitivity to paclitaxel or to castor oil (non-protein-bound vehicle contains polyoxyethylated castor oil);
- Known alcohol intolerance;
- OB, Lactation: Pregnancy or lactation; ANC <1500/mm³ in patients with ovarian, lung, or breast cancer; ANC <1000/mm³ in patients with AIDS-related Kaposi’s sarcoma.

Use Cautiously in:
- Moderate or severe hepatic impairment;
- Geri: q risk of neuropathy, myelosuppression, and cardiovascular events;
- OB: Childbearing potential;
- Active infection;
- p bone marrow reserve;
- Pedi: Safety and effectiveness not established.

Adverse Reactions/Side Effects

CNS:
- Dizziness, headache, seizures.

CV:
- ECG changes, edema, hypotension, bradycardia.

GI:
- Diarrhea, elevated liver enzymes, mucositis, nausea, vomiting, pancreatitis.

Derm:
- Alopecia.

Hemat:
- Anemia, neutropenia, thrombocytopenia.

MS:
- Arthralgia, myalgia.

GU:
- Renal failure.

Neuro:
- Peripheral neuropathy.

Resp:
- Pulmonary embolism, pulmonary fibrosis, cough, dyspnea, interstitial pneumonia.

Local:
- Injection site reactions.

Misc:
- Hypersensitivity reactions including anaphylaxis and Stevens-Johnson syndrome, sepsis, toxic epidermal necrolysis.

Interactions

Drug-Drug: CYP3A4 inhibitors including atazanavir, clarithromycin, indinavir, irinotecan, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, and telithromycin may q levels and risk of toxicity; concurrent use should be undertaken with caution. CYP3A4 inducers including carbamazepine, rifampin, and phenytoin may p levels and risk of treatment failure; concurrent use should be undertaken with caution. Gemfibrozil may q levels and risk of toxicity; concurrent use should be undertaken with caution. q levels and risk of treatment failure; concurrent use should be undertaken with caution. q levels and risk of treatment failure; concurrent use should be undertaken with caution.

CYP3A4 inducers including carbamazepine, rifampin, and phenytoin may q levels and toxicity of doxorubicin. May q levels and toxicity of doxorubicin. May q levels and toxicity of doxorubicin. Myasthenia gravis may q levels and risk of toxicity; concurrent use should be undertaken with caution. Myasthenia gravis may q levels and risk of toxicity; concurrent use should be undertaken with caution. May q levels and risk of toxicity; concurrent use should be undertaken with caution. Tumor necrosis factor-α may c anti-tumor necrosis factor-α antibody response to and q risk of adverse effects from live-virus vaccines.


Route/Dosage

Many other regimens are used.

Paclitaxel

Ovarian Cancer

IV (Adults): Previously untreated patients—175 mg/m² over 3 hr every 3 wk, or 135 mg/m² over 24 hr every 3 wk, followed by cisplatin. Previously treated patients—115 mg/m² or 175 mg/m² over 3 hr every 3 wk.

Breast Cancer

IV (Adults): Adjuvant treatment of node-positive breast cancer—175 mg/m² over 3 hr every 3 wk; compassionate use is recommended for patients with serious underlying conduction abnormalities or those concurrently taking doxorubicin. Non-Small Cell Lung Cancer

IV (Adults): 135 mg/m² over 24 hr every 3 wk; 100 mg/m² over 3 hr every 2 wk (dose adjustment may be necessary in patients with advanced HIV infection).

Paclitaxel Protein-Bound Particles (albumin-bound)

Breast Cancer

IV (Adults): 260 mg/m² over 30 min every 3 wk.

Hepatic Impairment

IV (Adults): Moderate hepatic impairment (AST levels ≥ 5 and bilirubin levels ≥ 5 ULN): 200 mg/m² over 30 min every 3 wk; severe hepatic impairment (AST levels ≥ 10 and bilirubin levels ≥ 10 ULN): 130 mg/m² over 30 min every 3 wk; dose may be qd to 200 mg/m² for subsequent courses based on individual tolerance; severe hepatic impairment (AST levels ≥ 10 and bilirubin levels ≥ 5 ULN): Avoid use.

Non-Small Cell Lung Cancer

IV (Adults): 175 mg/m² over 30 min on Days 1, 8, and 15 of each 21-day cycle.

Pancreatic Adenocarcinoma

IV (Adults): 125 mg/m² over 30–40 min on Days 1, 8, and 15 of each 21–day cycle.

NURSING IMPLICATIONS

Assessment

● Monitor vital signs frequently, especially during first hr of the infusion. Monitor cardiovascular status especially during first 3 hr of infusion. Hypotension and bradycardia are common but usually do not require treatment. Continuous ECG monitoring is recommended for patients with serious underlying conduction abnormalities or those concurrently taking doxorubicin.

● Monitor for bone marrow depression. Assess for bleeding (bleeding gums, bruising, petechiae, guaiac stools, urine, and emesis) and avoid IM injections and taking rectal temperatures if platelet count is low. Apply pressure to venipuncture sites for 10 min. Assess for signs of infection during neutropenia. Infection may occur. Monitor for thrombosis and hemorrhage. Granulocyte colony-stimulating factor (G-CSF) may be used if necessary.

● Assess for development of peripheral neuropathy. If severe symptoms occur, subsequent dose should be reduced by 20%.

● Monitor intake and output, appetite, and nutritional intake. Paclitaxel causes nausea and vomiting in 50% of patients. Prophylactic antiemetics may be used. Adjust diet as tolerated to help maintain fluid and electrolyte balance and nutritional status.

● Assess for rash periodically during therapy. May cause Stevens-Johnson syndrome and toxic epidermal necrolysis. Discontinue therapy if severe or if accompanied with fever, general malaise, fatigue, muscle or joint aches, blistering, oral lesions, conjunctivitis, hepatitis and/or eosinophilia.

Hepatic Impairment

IV (Adults): Moderate hepatic impairment (AST levels ≥ 10 and bilirubin levels ≥ 10–2 ULN): 75 mg/m² over 30 min on Days 1, 8, and 15 of each 21–day cycle. Severe hepatic impairment (AST levels ≥ 20–5 ULN and bilirubin levels ≥ 5–10 ULN): 50 mg/m² over 30 min on Days 1, 8, and 15 of each 21–day cycle; dose may be 5 to 75 mg/m² for subsequent courses based on individual tolerance; severe hepatic impairment (AST levels ≥ 10 and bilirubin levels ≥ 5–10 ULN): Avoid use.
Continued

Paclitaxel protein-bound particles (albumin-bound)

usually during the first 24 h of paclitaxel infusion. After the first or second dose, premedication is recommended for all patients and should include diphenhydramine 50 mg IV 20–60 min prior to paclitaxel and ranitidine 50 mg IV 20–60 min prior to paclitaxel. Most common manifestations are chills, flushing, tachycardia, rash, hypotension, and chest pain. If these occur, slow infusion and notify health care professional. Treatment may include bronchodilators, ephedrine, antihistamines, and corticosteroids. Asymptomatic and reactive hypotension occurs in the event of anaphylactic reactions. Other manifestations of hypersensitivity reactions include flushing and rash.

- No premedication for hypersensitivity is required for paclitaxel protein-bound particles (albumin-bound).

- Paclitaxel Protein-Bound Particles (albumin-bound). Monitor IV site and hemodynamic parameters prior to and periodically during therapy. The rate of leukopenia occurs in 11 days, with recovery by day 15–21. Notify health care professional if the leukocyte count is <1000/mm³ (500/mm³ in AIDS-related Kaposi’s sarcoma) and platelet count 100,000/mm³. Subsequent doses are usually held until leukocyte count is >1500/mm³ (1000/mm³ in AIDS-related Kaposi’s sarcoma) and platelet count ≥100,000/mm³.

- Paclitaxel Protein-Bound Particles (albumin-bound). Monitor IV site and hemodynamic parameters prior to and periodically during therapy. The rate of leukopenia occurs in 11 days, with recovery by day 15–21. Notify health care professional if the leukocyte count is <1500/mm³ (1000/mm³ in AIDS-related Kaposi’s sarcoma) or if the platelet count is <100,000/mm³. Subsequent doses are usually held until leukocyte count is >1500/mm³ (1000/mm³ in AIDS-related Kaposi’s sarcoma) and platelet count ≥100,000/mm³.

Potential Nursing Diagnoses

Risk for injury (Adverse Reactions)

Implementation

- Do not confuse Taxol (paclitaxel) with Taxotere (docetaxel). Do not confuse Taxol (paclitaxel) with Paxil (paroxetine).

- Therapy to detect hepatotoxicity.

- Treat neutropenic fever with broad-spectrum antibiotics. Keep these agents and resuscitative equipment close by in the event of an anaphylactic reaction. Other manifestations of hypersensitivity reactions include flushing and rash.


**Paclitaxel Protein-Bound Particles (albumin-bound)**

**IV Administration**

- **Intermittent Infusion:** Reconstitute by slowly adding 20 mL to each vial over at least 1 min for a concentration of 5 mg/mL. Direct solution to inside wall of vial to prevent foaming. Allow vial to sit for at least 5 min to ensure proper wetting of cake/powder. Gently swirl or invert vial for at least 2 min until powder is completely dissolved; avoid foaming. If foaming or clumping occurs, allow vial to stand for 15 min until foaming dissolves. Solution should be milky and homogenous without visible particles. If particles or settling are visible, gently invert vial to resuspend. Inject appropriate amount into sterile PVC IV bag. Do not use an in-line filter during administration. Do not administer solutions that are discolored or contain particulate matter. Reconstituted solution should be administered immediately but is stable for 8 hr if refrigerated. Discard unused portion.

- **Rate:** Administer over 30–40 min. Monitor infusion site closely for infiltration.

**Patient/Family Teaching**

- **Explain purpose of paclitaxel to patient.**
- **Advise patient to notify health care professional immediately of rash, difficulty breathing, or symptoms of hypersensitivity reaction occurs.**
- **Instruct patient to report health care professional promptly if fever, chills, cough, lobar pneumonia, signs of infection, lower back or side pain, painful or difficult urination, bleeding gums, bruising, petechiae, blood in stools, urine, or emesis, diarrhea, or orthostatic hypotension occurs. Caution patient to avoid crowds and persons with known infections. Instruct patient to use soft toothbrushes and electric razors and to avoid falls. Caution patient not to drink alcoholic beverages or to take medications containing aspirin or NSAIDs; may precipitate gastric bleeding.**
- **May cause dizziness. Caution patient to avoid driving or other activities requiring alertness until response to medication is known.**
- **Instruct patient to notify health care professional if abdominal pain, yellow skin, weakness, paresthesia, joint stiffening, or joint or muscle aches occur.**
- **Instruct patient to inspect oral mucosa for redness and ulceration. If mouth sores occur, advise patient to use sponge brush and rinse mouth with water after eating and drinking. Stomatitis usually resolves in 5–7 days.**
- **Discuss with patient the possibility of hair loss. Complete hair loss usually occurs between days 14 and 21 and is reversible after discontinuation of therapy. Explore coping strategies.**
- **Instruct patient not to receive any vaccinations without advice of health care professional.**
- **Advise patient to use a nonhemodialysis method of contraception and to avoid breast feeding, during therapy. Advise female patients not to father a child while receiving paclitaxel.**
- **Emphasize the need for periodic lab tests to monitor for side effects.**

**Evaluation/Desired Outcomes**

- **Decrease in size or spread of malignancy.**
- **Why was this drug prescribed for your patient?**

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