Paclitaxel (conventional): Drug information

(For additional information see "Paclitaxel (conventional): Patient drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

ALERT: US Boxed Warning

Experienced physician:

Administer under the supervision of a health care provider experienced in the use of cancer chemotherapeutic agents. Appropriate management of complications is possible only when adequate diagnostic and treatment facilities are readily available.

Hypersensitivity reactions:

Anaphylaxis and severe hypersensitivity reactions characterized by dyspnea and hypotension requiring treatment, angioedema, and generalized urticaria have occurred in 2% to 4% of patients in clinical trials. Fatal reactions have occurred in patients despite premedication. Pretreat all patients with corticosteroids, diphenhydramine, and histamine H_2 antagonists. Do not rechallenge patients who experience severe hypersensitivity reactions to paclitaxel.

Bone marrow suppression:

Do not give to patients with solid tumors who have baseline neutrophil counts of less than 1,500 cells/mm^3 or to patients with AIDS-related Kaposi sarcoma if the baseline neutrophil count is less than 1,000 cells/mm^3. To monitor the occurrence of bone marrow suppression, primarily neutropenia, which may be severe and result in infection, perform frequent peripheral blood cell counts on all patients.

Brand Names: Canada

Apo-Paclitaxel; Paclitaxel for Injection; Paclitaxel Injection USP

Pharmacologic Category

Antineoplastic Agent, Antimicrotubular; Antineoplastic Agent, Taxane Derivative

Dosing: Adult

Note: Premedication with dexamethasone (20 mg orally at 12 and 6 hours prior to the dose [reduce dexamethasone dose to 10 mg orally with advanced HIV disease]), diphenhydramine (50 mg IV 30 to 60 minutes prior to the dose), and cimetidine, famotidine, or ranitidine (IV 30 to 60 minutes prior to the dose) is recommended.

Breast cancer, adjuvant treatment: IV: 175 mg/m^2 over 3 hours every 3 weeks for 4 cycles (administer sequentially following an anthracycline-containing regimen)

Breast cancer, metastatic or relapsed: IV: 175 mg/m^2 over 3 hours every 3 weeks

Non-small cell lung cancer: IV: 135 mg/m^2 over 24 hours every 3 weeks (in combination with cisplatin)

Ovarian cancer, advanced:

Previously treated: IV: 135 or 175 mg/m^2 over 3 hours every 3 weeks

Previously untreated: IV: 175 mg/m^2 over 3 hours every 3 weeks (in combination with cisplatin) or 135 mg/m^2 over 24 hours administered every 3 weeks (in combination with cisplatin)

Intraperitoneal (off-label route): 60 mg/m^2 on day 8 of a 21-day treatment cycle for 6 cycles, in combination with IV paclitaxel (135 mg/m^2 over 24 hours on day 1) and intraperitoneal cisplatin (Armstrong, 2006). **Note:** Administration of intraperitoneal paclitaxel should include the standard paclitaxel premedication regimen.

Previously untreated (off-label combination): IV: 175 mg/m^2 over 3 hours every 3 weeks (in combination with carboplatin) for 6 cycles, or 60 mg/m^2 over 1 hour weekly (in combination with carboplatin) for 18 weeks (Pignata, 2014)

Kaposi sarcoma, AIDS related: IV: 135 mg/m^2 over 3 hours every 3 weeks **or** 100 mg/m^2 over 3 hours every 2 weeks (due to dose-related toxicity, the 100 mg/m^2 dose should be used for patients with a lower performance status). **Note:** Reduce the dexamethasone premedication dose to 10 mg.

Bladder cancer, advanced or metastatic (off-label use): IV: 150 mg/m^2 every 2 weeks (in combination with gemcitabine) (Sternberg, 2001) **or** 200 mg/m^2 over 1 hour every 3 weeks (in combination with gemcitabine) for 6 cycles (Meluch, 2001)

Cervical cancer, advanced (off-label use): IV: 135 or 175 mg/m^2 every 3 weeks (in combination with bevacizumab and cisplatin) until disease progression or unacceptable toxicity (Tewari, 2014) **or** 175 mg/m^2 every 3 weeks (in combination with bevacizumab and topotecan) until disease progression or unacceptable toxicity (Tewari, 2014) **or** 135 mg/m^2 over 24 hours every 3 weeks (in combination with cisplatin) for 6 cycles (Monk, 2009; Moore, 2004).

Esophageal/gastric cancer, preoperative chemoradiation (off-label use): IV: 50 mg/m^2 on days 1, 8, 15, 22, and 29 (in combination with carboplatin and radiation therapy) followed by surgery within 4 to 6 weeks (van Hagen, 2012)

Head and neck cancers, advanced (off-label use): IV: 175 mg/m^2 over 3 hours every 3 weeks (in combination with cisplatin) for at least 6 cycles (Gibson, 2005)

Penile cancer, metastatic (off-label use): IV: 175 mg/m^2 over 3 hours every 3 to 4 weeks (in combination with ifosfamide and cisplatin) for 4 cycles (Pagliaro, 2010)

Small cell lung cancer, relapsed/refractory (off-label use): IV: 175 mg/m^2 over 3 hours every 3 weeks (as a single agent) for up to 5 cycles (Smit, 1998) **or** 80 mg/m^2 over 1 hour weekly for 6 weeks of an 8-week treatment cycle (as a single agent) until disease progression or unacceptable toxicity (Yamamoto, 2006)

Soft tissue sarcoma (angiosarcoma), advanced/unresectable (off-label use): IV: 80 mg/m^2 over 1 hour on days 1, 8, and 15 of a 4-week treatment cycle (as a single agent) for up to 6 cycles (Penel, 2008) **or** 135 to 175 mg/m^2 over 3 hours every 3 weeks (as a single agent) (Schlemmer, 2008) **or** 75 to 100 mg/m^2 once weekly (as a single agent) (Schlemmer, 2008)

Testicular germ cell tumors, relapsed/refractory (off-label use): IV: 80 mg/m^2 over 1 hour on days 1

and 8 of a 3-week treatment cycle (in combination with gemcitabine and oxaliplatin) for 2 cycles beyond best response and up to a maximum of 8 cycles (Bokemeyer, 2008) **or** 250 mg/m^2 over 24 hours on day 1 of a 3-week treatment cycle (in combination with ifosfamide, mesna, cisplatin, and filgrastim) for 4 cycles (Kondagunta, 2005) **or** 100 mg/m^2 over 1 hour on days 1, 8, and 15 of a 4-week treatment cycle (in combination with gemcitabine) for up to 6 cycles (Einhorn, 2007)

Thymoma/thymic carcinoma, advanced (off-label use): IV: 225 mg/m^2 over 3 hours every 3 weeks (in combination with carboplatin) for up to 6 cycles (Lemma, 2011)

Unknown primary adenocarcinoma (off-label use): IV: 200 mg/m^2 over 3 hours every 3 weeks (in combination with carboplatin) for 6 to 8 cycles (Briasoulis, 2000) **or** 200 mg/m^2 over 1 hour every 3 weeks (in combination with carboplatin and etoposide) for 4 to 8 cycles (Greco, 2000)

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

There are no dosage adjustments provided in the manufacturer's labeling. The following have been recommended:

CrCl <50 mL/minute: Adults: No dosage adjustment is necessary (Aronoff 2007).

Hemodialysis: Paclitaxel may be used in cancer patients on hemodialysis and because paclitaxel is not dialyzable, it may be used either before or after hemodialysis (Janus 2010).

Dosing: Hepatic Impairment

Note: The manufacturer's labeling recommendations are based upon the patient's first course of therapy where the usual dose would be 135 mg/m^2 dose over 24 hours or the 175 mg/m^2 dose over 3 hours in patients with normal hepatic function. Dosage in subsequent courses should be based upon individual tolerance. Adjustments for other regimens are not available.

24-hour infusion:

Transaminases <2 times upper limit of normal (ULN) and bilirubin level ≤1.5 mg/dL: 135 mg/m^2

Transaminases 2 to <10 times ULN and bilirubin level ≤1.5 mg/dL: 100 mg/m^2

Transaminases <10 times ULN and bilirubin level 1.6 to 7.5 mg/dL: 50 mg/m^2

Transaminases ≥10 times ULN or bilirubin level >7.5 mg/dL: Avoid use

3-hour infusion:

Transaminases <10 times ULN and bilirubin level ≤1.25 times ULN: 175 mg/m^2

Transaminases <10 times ULN and bilirubin level 1.26 to 2 times ULN: 135 mg/m^2

Transaminases <10 times ULN and bilirubin level 2.01 to 5 times ULN: 90 mg/m^2

Transaminases ≥10 times ULN or bilirubin level >5 times ULN: Avoid use

Dosing: Obesity

ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer: Utilize patient's actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider resumption of full weight-based

dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs, 2012).

Dosing: Adjustment for Toxicity

Dosage modification for toxicity (solid tumors, including ovary, breast, and lung carcinoma): Courses of paclitaxel should not be repeated until the neutrophil count is ≥1,500/mm^3 and the platelet count is ≥100,000/mm^3; reduce dosage by 20% for patients experiencing severe peripheral neuropathy or severe neutropenia (neutrophil <500/mm^3 for a week or longer)

Dosage modification for immunosuppression in advanced HIV disease: Paclitaxel should not be given to patients with HIV if the baseline or subsequent neutrophil count is <1000 cells/mm^3. Additional modifications include: Reduce dosage of dexamethasone in premedication to 10 mg orally; reduce dosage by 20% in patients experiencing severe peripheral neuropathy or severe neutropenia (neutrophil <500/mm^3 for a week or longer); initiate concurrent hematopoietic growth factor (G-CSF) as clinically indicated

Dosage Forms

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Concentrate, Intravenous:

Generic: 100 mg/16.7 mL (16.7 mL); 30 mg/5 mL (5 mL); 150 mg/25 mL (25 mL); 300 mg/50 mL (50 mL)

Concentrate, Intravenous [preservative free]:

Generic: 100 mg/16.7 mL (16.7 mL); 30 mg/5 mL (5 mL); 300 mg/50 mL (50 mL)

Generic Equivalent Available (US)

Yes

Dosage Forms Considerations

Paclitaxel injection contains polyoxyl 35/olyoxyethylated castor oil (Cremophor EL)

Administration

IV: Infuse over 3 or 24 hours (depending on indication/protocol); some off-label protocols use a 1-hour infusion. Infuse through a 0.22-micron in-line filter and polyethylene-lined (non-PVC) administration set. When administered as a part of a combination chemotherapy regimen, sequence of administration may vary by regimen; refer to specific protocol for sequence recommendation.

Premedication with dexamethasone (20 mg orally or IV at 12 and 6 hours before the dose; reduce to 10 mg with advanced HIV disease), diphenhydramine (50 mg IV 30 to 60 minutes prior to the dose), and cimetidine 300 mg, famotidine 20 mg, or ranitidine 50 mg (IV 30 to 60 minutes prior to the dose) is recommended.

Irritant with vesicant-like properties; avoid extravasation. Ensure proper needle or catheter position prior to administration.

Extravasation management: If extravasation occurs, stop infusion immediately and disconnect (leave

cannula/needle in place); gently aspirate extravasated solution (do **NOT** flush the line); remove needle/cannula; initiate antidote (hyaluronidase); remove needle/cannula; elevate extremity. Information conflicts regarding the use of warm or cold compresses (Perez Fidalgo, 2012; Polovich, 2009).

Hyaluronidase: If needle/cannula still in place: Administer 1 to 6 mL (150 units/mL) into existing IV line; usual dose is 1 mL for each 1 mL of extravasated drug; if needle/cannula has been removed, inject subcutaneously in a clockwise manner around area of extravasation; may repeat several times over the next 3 to 4 hours (Ener, 2004).

Intraperitoneal (off-label route): Solution was prepared in warmed saline and infused as rapidly as possible through an implantable intraperitoneal catheter (Armstrong, 2006).

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends double gloving, a protective gown, ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator), and (if compatible) closed system transfer devices (CSTDs) for preparation. Double gloving, a gown, and (if dosage form allows) CSTDs are required during administration (NIOSH 2016).

Use

Breast cancer: Adjuvant treatment of node-positive breast cancer; treatment of metastatic breast cancer after failure of combination chemotherapy or relapse within 6 months of adjuvant chemotherapy (prior therapy should have included an anthracycline)

Kaposi sarcoma (AIDS-related): Second-line treatment of AIDS-related Kaposi sarcoma

Non-small cell lung cancer: First-line treatment of non-small cell lung cancer (in combination with cisplatin) in patients who are not candidates for potentially curative surgery and/or radiation therapy

Ovarian cancer: Subsequent therapy for treatment of advanced ovarian cancer; first-line therapy of ovarian cancer (in combination with cisplatin)

Use: Off-Label

Bladder cancer, advanced or metastatic; Cervical cancer, advanced; Esophageal/gastric cancer, preoperative chemoradiation; Head and neck cancers, advanced; Ovarian cancer, intraperitoneal (off-label route); Penile cancer, metastatic; Small cell lung cancer, relapsed/refractory; Soft tissue sarcoma (angiosarcoma), advanced/unresectable; Testicular germ cell tumors, relapsed/refractory; Thymoma/thymic carcinoma, advanced; Unknown primary adenocarcinoma; Endometrial carcinoma; Esophageal cancer (metastatic/unresectable); Gastric cancer (metastatic/unresectable); Melanoma; Thyroid cancer (anaplastic).

Medication Safety Issues

Sound-alike/look-alike issues:

PACLitaxel may be confused with cabazitaxel, DOCEtaxel, PARoxetine, Paxil

PACLitaxel (conventional) may be confused with PACLitaxel (protein-bound)

Taxol may be confused with Abraxane, Paxil, Taxotere

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Adverse Reactions

Percentages reported with single-agent therapy.

>10%:

Cardiovascular: Flushing (28%), ECG abnormality (14% to 23%), edema (21%), hypotension (4% to 12%)

Central nervous system: Peripheral neuropathy (42% to 70%; grades 3/4: ≤7%)

Dermatologic: Alopecia (87%), skin rash (12%)

Gastrointestinal: Nausea (≤52%), vomiting (≤52%), diarrhea (38%), mucositis (17% to 35%), stomatitis (15%; most common at doses >390 mg/m^2), abdominal pain (with intraperitoneal administration)

Hematologic & oncologic: Neutropenia (78% to 98%; grade 4: 14% to 75%; onset: 8 to 10 days; median nadir: 11 days; recovery: 15 to 21 days), leukopenia (90%; grade 4: 17%), anemia (47% to 90%; grades 3/4: 2% to 16%), thrombocytopenia (4% to 20%; grades 3/4: 1% to 7%), hemorrhage (14%)

Hepatic: Increased serum alkaline phosphatase (22%), increased serum AST (19%)

Hypersensitivity: Hypersensitivity reaction (31% to 45%; grades 3/4: ≤2%)

Infection: Infection (15% to 30%)

Local: Injection site reaction (erythema at injection site, skin discoloration at injection site, swelling at injection site, tenderness at injection site: 13%)

Neuromuscular & skeletal: Arthralgia (≤60%), myalgia (≤60%), weakness (17%)

Renal: Increased serum creatinine (observed in Kaposi sarcoma patients only: 18% to 34%, severe: 5% to 7%)

1% to 10%:

Cardiovascular: Bradycardia (3%), tachycardia (2%), hypertension (1%), cardiac arrhythmia (1%), syncope (1%), venous thrombosis (1%)

Dermatologic: Changes in nails (2%)

Hematologic & oncologic: Febrile neutropenia (2%)

Hepatic: Increased serum bilirubin (7%)

Respiratory: Dyspnea (2%)

<1%, postmarketing, and/or case reports: Anaphylaxis, ataxia, atrial fibrillation, atrioventricular block, back pain, brain disease (neurological), cardiac conduction disturbance, cardiac failure, cellulitis, chills, conjunctivitis, dehydration, desquamation, enterocolitis, exacerbation of scleroderma, fibrosis at injection site, hepatic encephalopathy, hepatic necrosis, increased lacrimation, induration at injection site, intestinal obstruction, intestinal perforation, interstitial pneumonitis, ischemic colitis, ischemic heart disease, maculopapular rash, malaise, myocardial infarction, neutropenic enterocolitis, ototoxicity (tinnitus and hearing loss), pancreatitis, paralytic ileus, phlebitis, pneumonitis, pruritus, pulmonary embolism, pulmonary fibrosis, radiation recall phenomenon, radiation pneumonitis, renal insufficiency, seizure, skin edema (diffuse), skin necrosis, skin sclerosis, Stevens-Johnson syndrome, supraventricular tachycardia, thickening of skin, toxic epidermal necrolysis, typhlitis (neutropenic), ventricular tachycardia (asymptomatic), visual disturbance (scintillating scotomata)

Contraindications Hypersensitivity to paclitaxel, polyoxyl 35/polyoxyethylated castor oil (Cremophor EL), or any component of the formulation; treatment of solid tumors in patients with baseline neutrophil counts <1,500/mm^3; treatment of Kaposi sarcoma in patients with baseline neutrophil counts <1,000/mm^3.

Warnings/Precautions

Concerns related to adverse effects:

• Bone marrow suppression: **[US Boxed Warning]: Bone marrow suppression (primarily neutropenia; may be severe or result in infection) may occur. Monitor blood counts frequently. Do not administer if baseline neutrophil count is <1,500/mm^3 (for solid tumors) or <1,000/mm^3 (for patients with AIDS-related Kaposi sarcoma).** Bone marrow suppression (usually neutropenia) is dose-dependent and is the dose-limiting toxicity; neutrophil nadir is usually at a median of 11 days. Subsequent cycles should not be administered until neutrophils are >1,500/mm^3 (for solid tumors) and 1,000/mm^3 (for Kaposi sarcoma); platelets should recover to 100,000/mm^3. Reduce future doses by 20% for severe neutropenia (<500/mm^3 for 7 days or more) and consider the use of supportive therapy, including growth factor treatment.

• Cardiovascular effects: Infusion-related hypotension, bradycardia, and/or hypertension may occur; frequent monitoring of vital signs is recommended, especially during the first hour of the infusion. Rare but severe conduction abnormalities have been reported; conduct continuous cardiac monitoring during subsequent infusions for these patients. In a scientific statement from the American Heart Association, conventional paclitaxel has been determined to be an agent that may either cause direct myocardial toxicity or exacerbate underlying myocardial dysfunction (magnitude: moderate) (AHA [Page 2016])

• Extravasation: Paclitaxel is an irritant with vesicant-like properties; ensure proper needle or catheter placement prior to and during infusion; avoid extravasation. Injection-site reactions are generally mild (skin discoloration, tenderness, erythema, or swelling) and occur more commonly with an extended infusion duration (eg, 24 hours); injection-site reactions may be delayed (7 to 10 days). More severe reactions (phlebitis, cellulitis, skin exfoliation, necrosis, fibrosis, and induration) have also been reported. Recall skin reactions may occur despite administering through a different IV site.

• Hypersensitivity reactions: **[US Boxed Warning]: Anaphylaxis and severe hypersensitivity reactions (dyspnea requiring bronchodilators, hypotension requiring treatment, angioedema, and/or generalized urticaria) have occurred in 2% to 4% of patients in clinical studies. Premedicate with corticosteroids, diphenhydramine, and H_2 antagonists prior to infusion. Some reactions have been fatal despite premedication. If severe hypersensitivity occurs, stop infusion and do not rechallenge.** Minor hypersensitivity reactions (flushing, skin reactions, dyspnea, hypotension, or tachycardia) do not require interruption of treatment.

• Peripheral neuropathy: Peripheral neuropathy may commonly occur; patients with preexisting neuropathies from prior chemotherapy or coexisting conditions (eg, diabetes mellitus) may be at a higher risk; reduce dose by 20% for severe neuropathy.

Disease-related concerns:

• Hepatic impairment: Use with extreme caution in patients with hepatic dysfunction (myelotoxicity may be worsened in patients with total bilirubin >2 times ULN); dose reductions are recommended.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Special populations:

• Elderly: Use with caution in the elderly; increased risk of toxicity (severe neutropenia, neuropathy, and cardiovascular events).

Other warnings/precautions:

• Excipients: Conventional paclitaxel formulations contain polyoxyl 35/polyoxyethylated castor oil (Cremophor EL), which is associated with hypersensitivity reactions. Formulations also contain dehydrated alcohol which may cause adverse CNS effects.

• Experienced physician: **[US Boxed Warning]: Should be administered under the supervision of an experienced cancer chemotherapy physician. Administer in a facility sufficient to appropriately diagnose and manage complications.**

• Intraperitoneal administration: Intraperitoneal administration of paclitaxel is associated with a higher incidence of chemotherapy- related toxicity (Armstrong 2006).

Metabolism/Transport Effects

Substrate of CYP2C8 (major), CYP3A4 (major), P-glycoprotein;
Note: Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Abiraterone Acetate: May increase the serum concentration of CYP2C8 Substrates. *Risk C: Monitor therapy*

Alfuzosin: May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

Amifostine: Blood Pressure Lowering Agents may enhance the hypotensive effect of Amifostine. Management: When amifostine is used at chemotherapy doses, blood pressure lowering medications should be withheld for 24 hours prior to amifostine administration. If blood pressure lowering therapy cannot be withheld, amifostine should not be administered. *Risk D: Consider therapy modification*

Antineoplastic Agents (Anthracycline, Systemic): Taxane Derivatives may enhance the adverse/toxic effect of Antineoplastic Agents (Anthracycline, Systemic). Taxane Derivatives may increase the serum concentration of Antineoplastic Agents (Anthracycline, Systemic). Taxane Derivatives may also increase the formation of toxic anthracycline metabolites in heart tissue. *Risk D: Consider therapy modification*

Antipsychotic Agents (Second Generation [Atypical]): Blood Pressure Lowering Agents may enhance the hypotensive effect of Antipsychotic Agents (Second Generation [Atypical]). *Risk C: Monitor therapy*

Aprepitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Atazanavir: May increase the serum concentration of PACLitaxel (Conventional). Management: Use of paclitaxel or other narrow therapeutic index CYP2C8 substrates with atazanavir without concurrent ritonavir is not recommended. If paclitaxel is used with ritonavir-boosted atazanavir, no significant interaction is expected. *Risk X: Avoid combination*

Barbiturates: May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

BCG (Intravesical): Immunosuppressants may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

BCG (Intravesical): Myelosuppressive Agents may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

Benperidol: May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

Bexarotene (Systemic): PACLitaxel (Conventional) may increase the serum concentration of Bexarotene (Systemic). Bexarotene (Systemic) may decrease the serum concentration of PACLitaxel (Conventional). *Risk C: Monitor therapy*

Blood Pressure Lowering Agents: May enhance the hypotensive effect of Hypotension-Associated Agents. *Risk C: Monitor therapy*

Bosentan: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Brimonidine (Topical): May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

CloZAPine: Myelosuppressive Agents may enhance the adverse/toxic effect of CloZAPine. Specifically, the risk for neutropenia may be increased. *Risk C: Monitor therapy*

Coccidioides immitis Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioides immitis Skin Test. *Risk C: Monitor therapy*

Conivaptan: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

CYP2C8 Inducers (Strong): May increase the metabolism of CYP2C8 Substrates. Management: Consider an alternative for one of the interacting drugs. Some combinations may be specifically

contraindicated. Consult appropriate manufacturer labeling. *Risk D: Consider therapy modification*

CYP2C8 Inhibitors (Moderate): May decrease the metabolism of CYP2C8 Substrates. *Risk C: Monitor therapy*

CYP2C8 Inhibitors (Strong): May decrease the metabolism of CYP2C8 Substrates. *Risk D: Consider therapy modification*

CYP3A4 Inducers (Moderate): May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inducers (Strong): May increase the metabolism of CYP3A4 Substrates. Management: Consider an alternative for one of the interacting drugs. Some combinations may be specifically contraindicated. Consult appropriate manufacturer labeling. *Risk D: Consider therapy modification*

CYP3A4 Inhibitors (Moderate): May decrease the metabolism of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inhibitors (Strong): May decrease the metabolism of CYP3A4 Substrates. *Risk D: Consider therapy modification*

Dabrafenib: May decrease the serum concentration of CYP3A4 Substrates. Management: Seek alternatives to the CYP3A4 substrate when possible. If concomitant therapy cannot be avoided, monitor clinical effects of the substrate closely (particularly therapeutic effects). *Risk D: Consider therapy modification*

Dabrafenib: May decrease the serum concentration of CYP2C8 Substrates. Management: Seek alternatives to the CYP2C8 substrate when possible. If concomitant therapy cannot be avoided, monitor clinical effects of the substrate closely (particularly therapeutic effects). *Risk D: Consider therapy modification*

Dasatinib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Deferasirox: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Deferasirox: May increase the serum concentration of CYP2C8 Substrates. *Risk C: Monitor therapy*

Deferiprone: Myelosuppressive Agents may enhance the neutropenic effect of Deferiprone. *Risk X: Avoid combination*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Diazoxide: May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

Dipyrone: May enhance the adverse/toxic effect of Myelosuppressive Agents. Specifically, the risk for agranulocytosis and pancytopenia may be increased *Risk X: Avoid combination*

DOXOrubicin (Conventional): Taxane Derivatives may decrease the metabolism of DOXOrubicin (Conventional). Management: Consider using docetaxel instead of paclitaxel as a way to avoid this potential interaction, and monitor closely for toxic effects of doxorubicin. Administer doxorubicin prior to paclitaxel when used concomitantly. *Risk D: Consider therapy modification*

DULoxetine: Blood Pressure Lowering Agents may enhance the hypotensive effect of DULoxetine. *Risk C: Monitor therapy*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Enzalutamide: May decrease the serum concentration of CYP3A4 Substrates. Management: Concurrent use of enzalutamide with CYP3A4 substrates that have a narrow therapeutic index should be avoided. Use of enzalutamide and any other CYP3A4 substrate should be performed with caution and close monitoring. *Risk D: Consider therapy modification*

Fingolimod: Immunosuppressants may enhance the immunosuppressive effect of Fingolimod. Management: Avoid the concomitant use of fingolimod and other immunosuppressants when possible. If combined, monitor patients closely for additive immunosuppressant effects (eg, infections). *Risk D: Consider therapy modification*

Fosaprepitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Fusidic Acid (Systemic): May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Herbs (Hypotensive Properties): May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

Hypotension-Associated Agents: Blood Pressure Lowering Agents may enhance the hypotensive effect of Hypotension-Associated Agents. *Risk C: Monitor therapy*

Idelalisib: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Lenograstim: Antineoplastic Agents may diminish the therapeutic effect of Lenograstim. *Risk D: Consider therapy modification*

Levodopa: Blood Pressure Lowering Agents may enhance the hypotensive effect of Levodopa. *Risk C: Monitor therapy*

Lormetazepam: May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

MiFEPRIStone: May increase the serum concentration of CYP2C8 Substrates. Management: Use CYP2C8 substrates at the lowest recommended dose, and monitor closely for adverse effects (including myopathy), during and in the 2 weeks following mifepristone treatment. *Risk D: Consider therapy modification*

MiFEPRIStone: May increase the serum concentration of CYP3A4 Substrates. Management: Minimize doses of CYP3A4 substrates, and monitor for increased concentrations/toxicity, during and 2 weeks following treatment with mifepristone. Avoid cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus. *Risk D: Consider therapy modification*

Mitotane: May decrease the serum concentration of CYP3A4 Substrates. Management: Doses of CYP3A4 substrates may need to be adjusted substantially when used in patients being treated with mitotane. *Risk D: Consider therapy modification*

Molsidomine: May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

Naftopidil: May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Netupitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Nicergoline: May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

Nicorandil: May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

Nitroprusside: Blood Pressure Lowering Agents may enhance the hypotensive effect of Nitroprusside. *Risk C: Monitor therapy*

Nivolumab: Immunosuppressants may diminish the therapeutic effect of Nivolumab. *Risk D: Consider therapy modification*

Obinutuzumab: May enhance the hypotensive effect of Blood Pressure Lowering Agents. Management: Consider temporarily withholding blood pressure lowering medications beginning 12 hours prior to obinutuzumab infusion and continuing until 1 hour after the end of the infusion. *Risk D: Consider therapy modification*

Ocrelizumab: May enhance the immunosuppressive effect of Immunosuppressants. *Risk C: Monitor therapy*

Palbociclib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Palifermin: May enhance the adverse/toxic effect of Antineoplastic Agents. Specifically, the duration and severity of oral mucositis may be increased. Management: Do not administer palifermin within 24 hours before, during infusion of, or within 24 hours after administration of myelotoxic chemotherapy. *Risk D: Consider therapy modification*

Pentoxifylline: May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

P-glycoprotein/ABCB1 Inhibitors: May increase the serum concentration of P-glycoprotein/ABCB1 Substrates. P-glycoprotein inhibitors may also enhance the distribution of p-glycoprotein substrates to specific cells/tissues/organs where p-glycoprotein is present in large amounts (e.g., brain, T-lymphocytes, testes, etc.). *Risk C: Monitor therapy*

Pholcodine: Blood Pressure Lowering Agents may enhance the hypotensive effect of Pholcodine. *Risk C: Monitor therapy*

Phosphodiesterase 5 Inhibitors: May enhance the hypotensive effect of Blood Pressure Lowering

Agents. *Risk C: Monitor therapy*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Platinum Derivatives: May enhance the myelosuppressive effect of Taxane Derivatives. Administer Taxane derivative before Platinum derivative when given as sequential infusions to limit toxicity. *Risk D: Consider therapy modification*

Promazine: May enhance the myelosuppressive effect of Myelosuppressive Agents. *Risk C: Monitor therapy*

Prostacyclin Analogues: May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

Quinagolide: May enhance the hypotensive effect of Blood Pressure Lowering Agents. *Risk C: Monitor therapy*

Ranolazine: May increase the serum concentration of P-glycoprotein/ABCB1 Substrates. *Risk C: Monitor therapy*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Sarilumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Siltuximab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Simeprevir: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

SORAfenib: May enhance the adverse/toxic effect of PACLitaxel (Conventional). Management: Concurrent sorafenib with carboplatin and paclitaxel in patients with squamous cell lung cancer is contraindicated. Use in other settings is not specifically contraindicated but should be approached with added caution. *Risk X: Avoid combination*

St John's Wort: May decrease the serum concentration of CYP3A4 Substrates. Management: Consider an alternative for one of the interacting drugs. Some combinations may be specifically contraindicated. Consult appropriate manufacturer labeling. *Risk D: Consider therapy modification*

Stiripentol: May increase the serum concentration of CYP3A4 Substrates. Management: Use of stiripentol with CYP3A4 substrates that are considered to have a narrow therapeutic index should be avoided due to the increased risk for adverse effects and toxicity. Any CYP3A4 substrate used with stiripentol requires closer monitoring. *Risk D: Consider therapy modification*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Tertomotide: Immunosuppressants may diminish the therapeutic effect of Tertomotide. *Risk C: Monitor therapy*

Tocilizumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Tofacitinib: Immunosuppressants may enhance the immunosuppressive effect of Tofacitinib.

Management: Concurrent use with antirheumatic doses of methotrexate or nonbiologic disease modifying antirheumatic drugs (DMARDs) is permitted, and this warning seems particularly focused on more potent immunosuppressants. *Risk X: Avoid combination*

Trastuzumab: May decrease the serum concentration of PACLitaxel (Conventional). PACLitaxel (Conventional) may increase the serum concentration of Trastuzumab. *Risk C: Monitor therapy*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). Management: Vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

Vinorelbine: PACLitaxel (Conventional) may enhance the neurotoxic effect of Vinorelbine. *Risk C: Monitor therapy*

Pregnancy Risk Factor

D (show table)

Pregnancy Implications

Adverse events (embryotoxicity, fetal toxicity, and maternal toxicity) have been observed in animal reproduction studies at doses less than the recommended human dose. An *ex vivo* human placenta perfusion model illustrated that paclitaxel crossed the placenta at term. Placental transfer was low and affected by the presence of albumin; higher albumin concentrations resulted in lower paclitaxel placental transfer (Berveiller, 2012). Some pharmacokinetic properties of paclitaxel may be altered in pregnant women (van Hasselt, 2014). Women of childbearing potential should be advised to avoid becoming pregnant. A pregnancy registry is available for all cancers diagnosed during pregnancy at Cooper Health (877-635-4499).

Breast-Feeding Considerations

Paclitaxel is excreted in breast milk (case report). The mother (3 months postpartum) was treated with paclitaxel 30 mg/m^2 (56.1 mg) and carboplatin once weekly for papillary thyroid cancer. Milk samples were obtained 4-316 hours after the infusion given at the sixth and final week of therapy. The average paclitaxel milk concentration over the testing interval was 0.78 mg/L. Although maternal serum concentrations were not noted in the report, the relative infant dose to a nursing infant was calculated to be ~17% of the maternal dose. Paclitaxel continued to be detected in breast milk when sampled at 172 hours after the dose and was below the limit of detection when sampled at 316 hours after the infusion (Griffin, 2012). Due to the potential for serious adverse reactions in a nursing infant, breast-feeding is not recommended.

Monitoring Parameters

CBC with differential and platelet count, liver and kidney function; monitor for hypersensitivity reactions, vital signs (frequently during the first hour of infusion), continuous cardiac monitoring (patients with conduction abnormalities); monitor infusion site during infusion.

Mechanism of Action

Paclitaxel promotes microtubule assembly by enhancing the action of tubulin dimers, stabilizing existing microtubules, and inhibiting their disassembly, interfering with the late G_2 mitotic phase, and inhibiting cell replication. In addition, the drug can distort mitotic spindles, resulting in the breakage of chromosomes. Paclitaxel may also suppress cell proliferation and modulate immune response.

Pharmacodynamics/Kinetics

V_{dss}: 24-hour infusion: 227 to 688 L/m^2; biphasic with initial rapid distribution to the peripheral compartment; later phase is a slow efflux of paclitaxel from the peripheral compartment; widely distributed into body fluids and tissues; affected by dose and duration of infusion

Protein binding: 89% to 98%

Metabolism: Hepatic via CYP2C8 and 3A4; forms metabolites (primarily 6α-hydroxypaclitaxel)

Half-life elimination:

Children: 4.6 to 17 hours (varies with dose and infusion duration)

Adults:

3-hour infusion: Mean (terminal): ~13 to 20 hours

24-hour infusion: Mean (terminal): ~16 to 53 hours

Excretion: Feces (~71%; ~5% as unchanged drug); urine (~14%)

Pricing: US

Concentrate (PACLitaxel Intravenous)

30 mg/5 mL (5 mL): $15.36

100 mg/16.7 mL (16.7 mL): $49.88

150 mg/25 mL (25 mL): $79.20

300 mg/50 mL (50 mL): $152.40

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

Aclipak (SG); Aclixel (MX); Acoexel (CR, DO, GT, HN, NI, PA, SV); Alzene (CO); Anzatax (AE, AU, CN, EG, HK, KR, LB, MY, NZ, PH, QA, SA, SG, TH, TW); Asotax (AR, CR, DO, GT, HN, MX, NI, PA, SV); Biotax (IL); Bristaxol (MX); Britaxol (CL); Canpaxel (VN); Celtax (JO); Clitaxel (VE); Cryoxet (CR, DO, GT, HN, MX, NI, PA, SV); Dalys (PE, PY, UY); Ebetaxel (AE, HK, ID, IL, LB, QA, SA, SG); Genaxol (TW); Genetaxyl (TH); Intaxel (ET, IN, JO, LK, TH, TW, VN, ZW); Meditaxel (PE); Neotaksel (UA); Ofoxel (CR, DO, GT, HN, NI, PA, SV); Paclitaxin (LK, TH); Paclitex (BD); Pacxel (KR); Padexol (KR); Panataxel (EC); Parexel (CO, PY); Paxel (KR, PH); Paxene (AT, BE, BG, CH, CZ, DE, DK, EE, FI, FR, GB, GR, HN, IE, IT, MT, NL, NO, PL, PT, RU, SE, SK, TR); Paxomed (ID); Paxus (ID); Praxel (CL, CR, DO, GT, HN, MX, NI, PA, SV, TH); Santotaxel (ID); Sindaxel (BG, HR, ID, MT, RO, TH); Taksaval (UA); Taxocris (UY); Taxol (AE, AR, AT, BE, BH, BR, CH, CN, CO, CZ, DE, DK, EE, EG, FI, FR, GR, HK, HN, IT, JO, KR, KW, LB, NL, NZ, PK, PL, RU, SE, SI, TH, TR, VN, ZA); Vexel (PH); Xelpac (BD, LK)

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