PACLITAXEL

Indications/Uses

Listed in Dosage.

Dosage/Direction for Use

Adult : IV Advanced ovarian carcinoma As conventional 6 mg/mL solution: Primary treatment in combination with cisplatin: 175 mg/m2 infused over 3 hours, every 3 weeks. Alternatively, 135 mg/m2 infused over 24 hours, repeated at 3-week intervals. Secondary treatment as monotherapy: 175 mg/m2 infused over 3 hours once every 3 weeks. Adjuvant therapy in node-positive breast cancer As 6 mg/mL conventional solution following anthracycline-containing regimen: 175 mg/m2 infused over 3 hours once every 3 weeks for 4 cycles. Locally advanced breast carcinoma; Metastatic breast carcinoma As 6 mg/mL conventional solution: 1st line treatment in combination with doxorubicin: 220 mg/m2. 2nd line treatment as monotherapy: 175 mg/m2. All doses are given via infusion over 3 hours once every 3 weeks. Metastatic breast carcinoma As albumin bound nanoparticles: 260 mg/m2 over 30 minutes every 3 weeks. HER2 overexpressing advanced or metastatic breast cancer As 6 mg/mL conventional solution in combination with trastuzumab: 175 mg/m2 infused over 3 hours once every 3 weeks. Advanced non-small cell lung cancer As 6 mg/mL conventional solution in combination with cisplatin: 175 mg/m2 infused over 3 hours or 135 mg/m2 over 24 hours, repeated at 3-week intervals. Locally advanced or metastatic non-small cell lung carcinoma As albumin bound paclitaxel nanoparticles in combination with carboplatin: 135 mg/m2 infused over 30 minutes, on days 1, 8, and 15 of a 21-day cycle. Metastatic adenocarcinoma of pancreas As albumin bound paclitaxel nanoparticles in combination of gemcitabine: 125 mg/m2 over 30 minutes on days 1, 8 and 15 of a 28-day cycle. AIDS-related Kaposi's sarcoma As 6 mg/mL conventional solution: 100 mg/m2 infused over 3 hours every 2 weeks. Dose reduction, dosing interruption, or discontinuation may be required according to individual safety and tolerability (refer to detailed product guideline).

Dosage Details

Intravenous

Metastatic breast cancer

Adult: As albumin bound paclitaxel nanoparticles: 260 mg/m2 over 30 minutes every 3 weeks. Dose reduction, dosing interruption, or discontinuation may be required according to individual safety and tolerability (refer to detailed product guideline).

Intravenous

Breast cancer

Adult: As 6 mg/mL conventional solution: Adjuvant therapy in patient with node-positive cases following anthracycline-containing regimen: 175 mg/m2 infused over 3 hours once every 3 weeks for 4 cycles. 1st line treatment in combination with doxorubicin: 220 mg/m2 via infusion over 3 hours once every 3 weeks. 2nd line treatment as monotherapy: 175 mg/m2 via infusion over 3 hours once every 3 weeks. Dose reduction, dosing interruption, or discontinuation may be required according to individual safety and tolerability (refer to detailed product guideline).

Intravenous

HER2-overexpressing advanced or metastatic breast cancer

Adult: As 6 mg/mL conventional solution in combination with trastuzumab: 175 mg/m2 infused over 3 hours once every 3 weeks. Dose reduction, dosing interruption, or discontinuation may be required according to individual safety and tolerability (refer to detailed product guideline).

Intravenous

Advanced ovarian carcinoma

Adult: As conventional 6 mg/mL solution: Primary treatment in combination with cisplatin: 175 mg/m2 infused over 3 hours every 3 weeks. Alternatively, 135 mg/m2 infused over 24 hours, repeated at 3-week intervals. Secondary treatment as monotherapy: 175 mg/m2 infused over 3 hours once every 3 weeks. Dose reduction, dosing interruption, or discontinuation may be required according to individual safety and tolerability (refer to detailed product guideline).

Intravenous

Locally advanced or metastatic non-small cell lung carcinoma

Adult: As albumin bound paclitaxel nanoparticles in combination with carboplatin: 135 mg/m2 infused over 30 minutes, on days 1, 8, and 15 of a 21-day cycle. Dose reduction, dosing interruption, or discontinuation may be required according to individual safety and tolerability (refer to detailed product guideline).

Intravenous

Advanced non-small cell lung cancer

Adult: As 6 mg/mL conventional solution in combination with cisplatin: 175 mg/m2 infused over 3 hours or 135 mg/m2 over 24 hours, repeated at 3-week intervals. Dose reduction, dosing interruption, or discontinuation may be required according to individual safety and tolerability (refer to detailed product guideline).

Intravenous

Metastatic adenocarcinoma of pancreas

Adult: As albumin bound paclitaxel nanoparticles in combination of gemcitabine: 125 mg/m2 over 30 minutes on days 1, 8 and 15 of a 28-day cycle. Dose reduction, dosing interruption, or discontinuation may be required according to individual safety and tolerability (refer to detailed product guideline).

Intravenous

AIDS-related Kaposi's sarcoma

Adult: As 6 mg/mL conventional solution: 100 mg/m2 infused over 3 hours every 2 weeks. Dose reduction, dosing interruption, or discontinuation may be required according to individual safety and tolerability (refer to detailed product guideline).

Hepatic Impairment

Advanced ovarian carcinoma; Breast cancer; HER2 overexpressing advanced or metastatic breast cancer; AIDS-related Kaposi's sarcoma:

Severe: Contraindicated.

Metastatic breast carcinoma; Locally advanced or metastatic non-small cell lung carcinoma; Metastatic adenocarcinoma of pancreas:

Moderate to severe: Reduce dose by 20%.

Reconstitution

Dilute vials labelled as containing 6 mg/mL solution with NaCl 0.9% or dextrose 5% inj to final concentration of 0.3-1.2 mg/mL. Reconstitute albumin-bound nanoparticles lyophilised powder labelled as containing 100 or 250 mg slowly with 20 mL or 50 mL NaCl 0.9% solution respectively, over a minimum of 1 minute. Inject diluents onto the inside wall of the vial to prevent foaming. Allow the vial to stand for 5 minutes then gently swirl or invert for at least 2 minutes until complete resuspension occurs.

Contraindications

Solid tumours in patients with baseline neutrophil counts <1500 cells/mm3. Kaposi sarcoma in patients with baseline neutrophil <1000 cells/mm3 and serious uncontrolled infection. Severe hepatic impairment (as conventional solution). Lactation.

Special Precautions

Patient with pre-existing neuropathies, conduction abnormalities. Hepatic impairment. Elderly. Pregnancy. Premedication with corticosteroid, antihistamine and histamine H2-receptor antagonist may be required to reduce risk of hypersensitivity reaction.

Adverse Reactions

Significant: Bone marrow suppression (e.g. neutropenia); hypotension, hypertension, bradycardia; extravasation, injection site reactions; sensory/peripheral neuropathy. sepsis, nausea, vomiting, diarrhoea. Rarely, conduction abnormalities, CHF, left ventricular dysfunction.

Blood and lymphatic system disorders: Anaemia, leukopenia, thrombocytopenia, febrile neutropenia.

Cardiac disorders: Tachycardia, arrhythmia, supraventricular tachycardia, chest pain, bradycardia, dyspnoea.

Eye disorders: Increased lacrimation, blurred vision.

Gastrointestinal disorders: Constipation, stomatitis, abdominal pain and distension.

General disorders and admin site conditions: Fatigue, asthenia, pyrexia, malaise, ataxia.

Infections and infestations: Candidiasis, conjunctivitis.

Injury, poisoning and procedural complications: Injection site reactions (including pain, erythema, localised oedema, induration).

Investigations: Increased AST, gamma-glutamyltransferase, blood alkaline phosphatase, serum creatinine; ECG abnormality.

Metabolism and nutrition disorders: Anorexia, dehydration, oedema.

Musculoskeletal and connective tissue disorders: Arthralgia, myalgia, back pain.

Nervous system disorders: Paraesthesia, headache, dizziness, vertigo.

Renal and urinary disorders: UTI.

Respiratory, thoracic and mediastinal disorders: Upper respiratory tract infection, cough, pulmonary embolism.

Skin and subcutaneous tissue disorders: Alopecia, rash, pruritus, erythema, nail discolouration, skin hyperpigmentation, nail changes.

Vascular disorders: Flushing, hypertension, hypotension, venous thrombosis.

Potentially Fatal: Anaphylaxis and severe hypersensitivity reactions, pneumonitis.

Pregnancy Category (US FDA)

IV/Parenteral: D

Patient Counseling Information

This drug may cause mild tiredness and dizziness, if affected, do not drive or operate machinery.

MonitoringParameters

Monitor CBC with differential and platelet count; LFT, kidney function; vital signs (frequently during the 1st hour of infusion); cardiac function; infusion site during infusion.

Drug Interactions

Increased plasma concentration and toxicity with CYP2C8 and CYP3A4 inhibitors (e.g. ketoconazole, erythromycin, fluoxetine, clopidogrel, cimetidine, ritonavir). Decreased plasma concentration and efficacy with CYP2C8 and CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, efavirenz).

Action

Description: Paclitaxel is an antineoplastic taxane derivative, originally derived from Pacific yew tree, Taxus brevifolia, and currently obtained semisynthetically from the needles of European yew, Taxus baccata. It promotes microtubule formation by enhancing the action of tubulin dimers, stabilising existing microtubules, and inhibiting their disassembly, interfering with the late G2 mitotic phase and inhibiting cell replication. It also suppresses cell proliferation and regulate immune response.

Pharmacokinetics:

Distribution: Widely distributed into tissues and body fluids. Volume of distribution: 227-688 L/m2 (24-hour infusion). Plasma protein binding: 89-98%.

Metabolism: Metabolised in the liver by CYP2C8 and CYP3A4 enzymes to 6α-hydroxypaclitaxel metabolite.

Excretion: Via faeces (approx 71%; approx 5% as unchanged drug); urine (approx 14%).

Chemical Structure

Click on icon to see table/diagram/image

Storage

Store below 25°C. Protect from light. This is a cytotoxic drug. Follow applicable procedures for receiving, handling, administration, and disposal.

MIMS Class

Cytotoxic Chemotherapy

ATC Classification

L01CD01 - paclitaxel ; Belongs to the class of plant alkaloids and other natural products, taxanes. Used in the treatment of cancer.