

Dosage and Method of Administration:

All patients must be premedicated with corticosteroids, antihistamines, and H₂ antagonists prior to paclitaxel infusion.

Ovarian carcinoma

First-line chemotherapy of ovarian carcinoma: although other dosage regimens are under investigation, a combination regimen of paclitaxel infusion and cisplatin is recommended. According to duration of infusion, two doses of paclitaxel infusion are recommended: paclitaxel infusion 175 mg/m² administered intravenously over 3 hours, followed by cisplatin at a dose of 75 mg/m² every three weeks or paclitaxel infusion 135 mg/m', in a 24-hour infusion, followed by cisplatin 75 mg/m', with a three week interval between courses.

Second-line chemotherapy of ovarian carcinoma: the recommended dose of paclitaxel infusion is 175 mg/m' administered over a period of three hours, with a three week interval between courses.

Breast carcinoma

Adjuvant chemotherapy in breast carcinoma: the recommended dose of paclitaxel infusion is 175 mg/m' administered over a period of three hours every three weeks for four courses, following AC therapy.

First-line chemotherapy of breast carcinoma: when used in combination with doxorubicin (50 mg/m'), paclitaxel infusion should be administered 24 hours after doxorubicin. The recommended dose of paclitaxel infusion is 220 mg/m' administered intravenously over a period of three hours, with a three-week interval between courses.

When used in combination with trastuzumab, the recommended dose of paclitaxel infusion is 175 mg/m' administered intravenously over a period of 3 hours, with a 3-week interval between courses. Paclitaxel infusion may be started the day following the first dose of trastuzumab or immediately after the subsequent doses of trastuzumab if the preceding

Second-line chemotherapy of breast carcinoma: the recommended dose of paclitaxel infusion is 175 mg/m' administered over a period of three hours, with a three-week interval between courses.

Advanced non-small cell lung carcinoma

Treatment of advanced NSCLC: the recommended dose of paclitaxel infusion is 175 mg/m' administered over a period of three hours, followed by cisplatin 80 mg/m', with a three week interval between courses.

AIDS-related Kaposi s sarcoma

Treatment of AIDS-related KS: the recommended dose of paclitaxel infusion is 100 mg/m' administered as a three-hour intravenous infusion every two weeks. Subsequent doses of paclitaxel infusion should be administered according to individual patient tolerance.

Paclitaxel infusion should not be readministered until the neutrophil count is \geq 1,500/mm' (\geq 1,000/mm' for KS patients) and the platelet count is \geq 100,000/mm' (\geq 75,000/mm' for KS patients). Patients who experience severe neutropenia (neutrophil count < 500/mm' for \geq 7 days) or severe peripheral neuropathy should receive a dose reduction of 20% for subsequent courses (25% for KS patients).

Patients with hepatic impairment: Inadequate data are available to recommend dosage alterations in patients with mild to moderate hepatic impairments (see 4.4 and 5.2). Patients with severe hepatic impairment should not be treated with paclitaxel.

Paediatric use: Paclitaxel is not recommended for use in children below 18 years due to lack of data on safety and efficacy.

Storage and Disposal

Do not store unopened vials above 25°C and keep in the outer carton to protect from light.

Disposal: All items used for preparation, administration or otherwise coming into contact with paclitaxel injection should undergo disposal according to local guidelines for the handling of cytotoxic compounds.

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4. POSSIBLE SIDE EFFECTS

Like all medicines, paclitaxel can cause side effects, although not everybody gets them. The following side effects may occur after treatment with paclitaxel infusion.

The most common side effects are hair loss and decreased blood cell count. Your hair grows back and your blood cell count returns to normal after you have finished your paclitaxel treatment. If any of the following happens, tell your doctor immediately:

- Any abnormal bruising, bleeding, or signs of infection such as a sore throat and high temperature.
- Severe allergic reaction - you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth, or throat (which may cause difficulty in swallowing or breathing), and you may feel you are going to faint.
- Breathlessness and dry cough due to damage to the lung.
- Reaction at the injection site e.g. local swelling, pain, redness.

Very common (affects more than 1 out of 10 people):

- An effect on the bone marrow, which can cause decreased numbers of some blood cells. This may cause anaemia. It can also lead to infections, mainly urinary tract and upper respiratory tract infections (with reported cases of fatal outcome).
- Decreased number of blood platelets and bleeding.
- Milder allergic (hypersensitivity) reactions, such as flushing and rash.
- Nerve problems affecting the hands and/or feet (peripheral neuropathy), which can cause tingling feelings in the skin, numbness and/or pain.
- Low blood pressure.
- Feeling sick (nausea), being sick (vomiting) and diarrhoea.
- Hair loss.
- Muscle or joint pain.
- Inflammation of areas such as the lining of the mouth.

Common (affects more than 1 out of 100 people):

- Slow heart beat (pulse).
- Mild changes in nail and skin which soon disappear.
- Painful swelling and inflammation where the injection is given which may cause tissue hardening [occasionally cellulitis, thickening and scarring of the skin (skin fibrosis), death of skin cells (skin necrosis)].
- Changes in blood tests that check how the liver is working.

Uncommon (affects less than 1 out of 100 people):

- A state of shock resulting from blood poisoning.
- Serious allergic (hypersensitivity) reactions with e.g. decreased or increased blood pressure, swelling of the face, difficulty in breathing, skin rash, chills, back pain, chest pain, fast heart beat, abdominal pain, pain in arms and legs, sweating.
- Serious heart problems like heart muscle degeneration (cardiomyopathy), serious changes to your heart s rhythm even with fainting. Heart attack.
- Increased blood pressure.
- Blood clot (thrombosis), inflammation of a vein in connection with blood clots.
- Yellowing of the skin (jaundice).

Rare (affects less than 1 out of 1,000 people):

- Pneumonia.
- Reduced number of a type of white blood cell with fever (febrile neutropenia).
- Serious allergic (anaphylactic) reaction.
- Effects on the nerves, which can cause muscle weakness in the arms and legs.
- Difficulty in breathing, fluid on the lungs, inflammation of the lungs and other lung problems (lung fibrosis, pulmonary embolism), markedly impaired pulmonary function (respiratory failure).
- Itching, rash and reddened skin.
- Weakness, high temperature (fever), dehydration, oedema, feeling ill.
- Blood poisoning.
- Blockage of the intestines, penetration of the wall of the small intestine or large bowel, inflammation of the lining of the belly (peritoneum), inflammation of the intestine caused by inadequate blood supply, inflammation of the pancreas.
- Increased level of the substance creatinine in the blood.

Very rare (occurs with less than 1 out of 10,000 of the people):

- Acute leukaemia (a type of blood cancer), myelodysplastic syndrome (a diverse collection of blood cell disorders).
- Life threatening allergic reaction (anaphylactic shock).
- Loss of appetite, shock due to decreased blood pressure, cough.
- Effects on the nervous system which can cause paralysis of the intestines (gut) and a decrease in blood pressure when standing up or sitting up from a lying down position, fits (epileptic seizures), cramps, confusion, dizziness, alteration in brain function or structure, headache, loss of the ability to coordinate muscular movement.
- Problems with eyesight and visual disturbances, usually in patients given larger doses.
- Reduction or loss of hearing, ringing in the ears (tinnitus), vertigo.
- Abnormal heart rhythm (atrial fibrillation, supraventricular tachycardia).
- A blood clot in the mesenteric artery, pseudomembranous colitis (an infection of the colon caused by specific bacteria), inflammation of the oesophagus, constipation. Collection of fluid in the abdomen (belly).
- Severe inflammation of the large bowel presenting with fever, watery or bloody diarrhoea, and cramping abdominal pain (neutropenic colitis).
- Death of the liver cells (necrosis of the liver), confusion and other effects (hepatic encephalopathy) caused by changes in the way the liver works (both with reported cases of fatal outcome).
- Hives (urticaria), scaling and shedding of the skin usually accompanied by redness.
- Severe inflammatory eruption of the skin and mucous membranes [severity ranging from erythema multiforme to Stevens-Johnson syndrome to the most serious toxic epidermal necrolysis (TEN)].
- Disintegration of nails. Hands and feet should be protected against sunshine during the treatment time

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report any side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom

Yellow Card Scheme - Website: www.mhra.gov.uk/yellowcard

Ireland

HPRA Pharmacovigilance, IRL - Dublin 2
Tel: +353 1 6764971, Fax: +353 1 6762517
Website:www.hpra.ie, e-mail: medsafety@hpra.ie

5. STORING PACLITAXEL

Keep out of the sight and reach of children.

Keep the vial in the outer carton to protect from light.

Do not use this medicinal product after the expiry date which is stated after "EXP". The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What paclitaxel contains:

The active substance is paclitaxel. 1ml of concentrate for solution for infusion contains 6mg paclitaxel.

The other ingredients are citric acid (anhydrous), macrogolglycerol ricinoleate, nitrogen and ethanol 96%.

What paclitaxel looks like and contents of the pack:
Paclitaxel is a clear, colourless to pale yellow, slightly viscous solution and is packed into glass vials.
Pack sizes:
1 x 5ml vial containing: 30mg paclitaxel in 5ml of solution
1 x 20ml vial containing: 100mg paclitaxel in 16.7ml of solution
1 x 50ml vial containing: 300mg paclitaxel in 16.7ml of solution
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer:
Peckforton Pharmaceuticals Ltd., Cewe Hall, Crewe, CW1 6UL, United Kingdom

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