Paclitaxel NEAPOLIS

Paclitaxel 6 mg/ml

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist, or nurse. This applies to any side effect that is not mentioned in this leaflet. See section 4.

What is in this leaflet ?

1. WHAT IS PACLITAXEL NEAPOLIS 6 mg/ml, concentrate for solution for infusion AND IN WHICH CASE IS IT USED ?

pharmacotherapeutic Class : Antineoplastic agent (taxanes), cytotoxic agent ATC code : L01CD01

PACLITAXEL NEAPOLIS is an anticancer belonging to taxanes group. These agents inhibit the growth of cancer cells.

Paclitaxel is indicated in the treatment of :

Ovarian cancer

- As a first-line treatment (after initial surgery in combination with a treatment based on platinum salts : cisplatin)
- After a standard treatment with platinum salts has been tried but has not worked.

Breast cancer

- As a first-line treatment for an advanced disease or for a disease that has spread to other parts of the body (metastatic disease). Paclitaxel is combined with either an anthracycline (eg doxorubicin) or trastuzumab (in patients for whom treatment with anthracycline is not suitable and whose cancer cells have a surface protein called HER 2, see the package leaflet for trastuzumab),
- As additional treatment after initial surgery followed by treatment with anthracycline and cyclophosphamide (AC),
- As a second-line treatment in patients who have not responded to standard anthracycline treatments, or for whom this type of treatment cannot be used

Advanced non-small cell lung cancer

- In combination with cisplatin, when surgery and / or radiotherapy is not appropriate.

AIDS-related Kaposi's sarcoma

- When another treatment (example : liposomal anthracyclines) was tried but did not work.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE PACLITAXEL NEAPOLIS 6 mg/ml, concentrate for solution for infusion ?

Never take PACLITAXEL NEAPOLIS :

- If you are allergic (hypersensitive) to paclitaxel or to one of the other components contained in this medicine, listed in section 6, especially castor oil,
- If you breastfeed,
- If the number of your white blood cells (neutrophils) is too low. This count will be carried out by medical staff,
- If you have a severe or uncontrolled infection and paclitaxel is used to treat Kaposi's sarcoma.

If any of the above describes you, talk to your doctor before starting treatment with PACLITAXEL NEAPOLIS

Paclitaxel is not recommended in children (under 18 years).

Warnings and precautions

Talk to your doctor before using PACLITAXEL NEAPOLIS.

To minimize allergic reactions, you will be given other medicines before receiving PACLITAXEL NEAPOLIS.

- If you have severe allergic reactions (e.g. difficulty breathing, shortness of breath, tightness in the chest, drop in blood pressure, dizziness, headache, skin reactions such as extensive rash or swelling).
- If you have a fever, intense chills, sore throat or mouth ulcer (signs of myelosuppression).
- If you have tingling or weakness in your arms and legs (signs of peripheral neuropathy) ; lower doses of paclitaxel may be necessary.

If you have severe liver problems ; in this case, the use of paclitaxel is not recommended.

- If you have heart conduction problems.
- If you develop severe or persistent diarrhea, with fever and stomach pain, during or shortly after treatment with paclitaxel. Your colon may be inflamed (pseudomembranous colitis).
- If you previously had radiation to your chest (as this may increase the risk of lung inflammation)
- If you have redness or irritation of the mouth (sign of phlegm) and are being treated for Kaposi's sarcoma. You may need a lower dose. Paclitaxel should always be given into the veins. Administering paclitaxel into the arteries can cause inflammation of the arteries, and you may experience pain, swelling, redness, and warming.

Other medicines and PACLITAXEL NEAPOLIS

Tell your doctor if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

Indeed, PACLITAXEL NEAPOLIS or the other medicine may not be as effective as expected, or you may be more prone to an adverse reaction. Interaction means that different medicines may affect each other. Ask your doctor when taking paclitaxel along with one of the following products :

- Medicines to treat infections (i.e. antibiotics such as : erythromycin, rifampicin etc ; ask your doctor, nurse or pharmacist to confirm that you are taking an antibiotic) and including medicines for the treatment of fungal infections (e.g. ketoconazole)
- Medicines that serve to stabilize mood and also known as anti-depressants (for example fluoxetine)
- Medicines used to treat seizures (epilepsy) (e.g. carbamazepine, phenytoin)
- Medicines used to lower blood lipid levels (eg gemfibrozil)
- Medicines for heartburn or stomach ulcers (e.g. cimetidine)
- Medicines used to treat HIV and AIDS (e.g. ritonavir, saquinavir, indinavir, nelfinavir, efavirenz, nevirapine)
- A medicine called clopidogrel to prevent clots from forming.
- Vaccines : if you have been recently vaccinated, or if you plan to receive a vaccination, tell your doctor. The use of paclitaxel in combination with certain vaccines can lead to serious complications.
- Cisplatin (used to treat cancer) : paclitaxel should be given before cisplatin. Your kidney function should be checked more frequently.
- Doxorubicin (for the treatment of cancer) : paclitaxel should be given 24 hours after doxorubicin to avoid having a high level of doxorubicin in your body.

Pregnancy, breastfeeding and fertility

If you are pregnant or think you are pregnant, talk to your doctor before receiving paclitaxel treatment. If there is a chance you could get pregnant, use a safe and effective method of contraception during treatment. Paclitaxel should not be given during pregnancy unless absolutely necessary. Female and male patients of reproductive age, and / or their partners should use contraception for at least 6 months after treatment with paclitaxel.

Male patients should seek advice regarding cryopreservation of their semen before paclitaxel treatment, as there is a possibility of infertility.

Tell your doctor if you are breastfeeding. Stop breastfeeding if you are taking paclitaxel. Do not start breastfeeding until your doctor has given you permission to do so.

Driving and using machines

This medicine contains alcohol. Thus, it is not recommended to drive immediately after a treatment course. In any case, you should not drive if you feel dizzy or are not sure of yourself.

PACLITAXEL NEAPOLIS 6 mg / ml, concentrate for solution for infusion contains purified polyoxyethylene castor oil and ethanol.

This medicine contains ethanol (alcohol). This amount can be dangerous in patients with alcoholism. It should also be taken into account in pregnant or breastfeeding women, children and in high-risk patients as well as in those with liver problems or epilepsy.

PACLITAXEL NEAPOLIS may affect the effects of other medicines due to its high alcohol content.

This product also contains polyoxyethylene castor oil, which can cause severe hypersensitivity (allergic) reactions. If you are allergic to castor oil, tell your doctor before receiving PACLITAXEL NEAPOLIS

3. HOW TO TAKE PACLITAXEL NEAPOLIS 6 mg/ml, concentrate for solution for infusion ?

- To minimize allergic reactions, you will be given other medicines before you are given paclitaxel. These medicines given before receiving paclitaxel can be tablets, intravenous infusions or tablets and intravenous infusions.
- You will receive paclitaxel drip into one of your veins (by intravenous infusion) through a filter. Paclitaxel will be given to you by a healthcare professional. He or she will prepare the solution for infusion before it is given to you. The dose you receive will also depend on the results of your blood tests. Depending on the type and severity of the cancer, you will receive Paclitaxel alone or in combination with other anticancer agents.
- Paclitaxel must always be given in one of your veins for a period of 3 or 24 hours. It is usually given to you every 2 to 3 weeks unless your doctor decides otherwise. Your doctor will tell you how many paclitaxel courses you will need to receive. If you have any further questions on the use of this product, ask your doctor for more information.

If you have received more PACLITAXEL NEAPOLIS 6 mg / ml concentrate for solution for infusion than you should

There is no known antidote for overdose of paclitaxel. You will receive treatment for your symptoms.

4. POSSIBLE SIDE EFFECTS ?

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor immediately if you notice any signs of an allergic reaction. These may relate to one or more of the following effects :

- Hot flushes,
- Skin reactions,
- Itching
- Chest tightness,
- Shortness of breath or difficulty breathing,
- Swelling.

They can all be signs of severe side effects.

Inform your doctor immediately :

- If you have fever, intense chills, sore throat, or mouth ulcers (signs of myelosuppression).
- If you have tingling or weakness in your arms and legs (signs of peripheral neuropathy).
- If you develop severe or persistent diarrhea, with fever and stomach pain.

Very common (may affect more than 1 in 10 persons) :

- Minor allergic reactions such as flushing, redness, itching.
- Infections : mainly upper respiratory tract infection, urinary tract infection.
- Breathiness.
- Sore throat, mouth ulcers, redness or irritation of the mouth, diarrhea, feeling sick or sick (nausea, vomiting).
- Hair loss (the majority of cases of hair loss occurred less than a month after starting paclitaxel. When it occurs, this hair loss is pronounced (greater than 50%) in the majority of patients).
- Muscle pain, cramps, joint pain.
- Fever, intense chills, headache, dizziness, tiredness, pallor, bleeding, bruising more easily than normal.
- Tingling, stinging or pain in the legs or arms (peripheral neuropathy signs).
- Blood tests may show : reduced levels of platelets, white blood cells, red blood cells, low blood pressure.

common (may affect up to 1 in 10 persons) :

- Transient and slight modification of the nails and modifications of the skin, reactions at the injection site (localized swelling, pain, erythema).
- Analysis can reveal : decreased heart rate, significant elevation of liver enzymes (alkaline phosphatase, AST, SGOT).

Uncommon (may affect up to 1 in 100 persons) :

- Shock due to infection (known as septic shock)
- Palpitations, heart dysfunction (atrioventricular block), high heart rate, heart attack, respiratory distress.
- Fatigue, sweating, discomfort (syncope), severe allergic reactions, inflammation of a vein caused by a blood clot (thrombophlebitis), swelling of the face, lips, mouth, tongue or throat.
- Backache, chest pain, pain around the hands and feet, chills, abdominal (stomach) pain.
- Blood tests can reveal : severe elevation of bilirubin (jaundice), high blood pressure and blood clot.

Rare (may affect up to 1 in 1000 persons) :

- Decreased number of white blood cells with fever and increased risk of infection (febrile neutropenia).
- Nerve disorder with feeling of muscle weakness in the arms and legs (motor neuropathy).
- Shortness of breath, sudden blockage of a pulmonary artery (pulmonary embolism), swelling and scarring of the lungs (pulmonary fibrosis), inflammation of the lungs (interstitial pneumonia), accumulation of fluid between the tissues of the lungs and the chest cavity (pleural effusion).
- Bowel obstruction, bowel perforation, inflammation of the colon (ischemic colitis), inflammation of the pancreas (pancreatitis).
- Extensive rash (itching), redness of the skin (erythema).
- Generalized infection (sepsis), peritonitis.
- Fever, dehydration, asthenia, edema, malaise.
- Severe and sometimes fatal hypersensitivity reactions (anaphylactic reactions).
- Blood tests may reveal : increased creatinine in the blood, a sign of impaired kidney function.
- Heart failure.

Very rare (may effect up to 1 in 10 000 persons) :

- Fast and irregular heartbeat (atrial fibrillation, supraventricular tachycardia).
- Sudden disruption of blood cell formation (acute myeloid leukemia, myelodysplastic syndrome).
- Optic nerve and / or visual disturbances (scintillating scotoma)).
- Hearing loss or hearing reduction (ototoxicity), ringing in the ears (tinnitus), dizziness.
- cough.
- Blood clot in a vessel in the abdomen and intestine (mesenteric thrombosis), inflammation of the colon with sometimes persistent severe diarrhea (pseudomembranous colitis, neutropenic colitis), swelling of the abdomen (edema, ascites), esophagus inflammation (esophagitis), constipation.
- Severe hypersensitivity reactions with fever, redness of the skin, joint pain and / or inflammation of the eyes (Stevens-Johnson syndrome), local scaling (epidermal necrolysis), redness with irregular (exudative) spots (erythema multiforme), inflammation of skin with blisters and flaking (exfoliative dermatitis), hives, falling nails (patients under treatment must protect their hands and feet from the sun).
- Loss of appetite (anorexia).
- Severe and sometimes fatal hypersensitivity reactions with shock (anaphylactic shock).
- Disruption of liver functions (hepatic necrosis, hepatic encephalopathy (for both effects, cases of fatal outcome have been reported).
- Confusional state.
- Convulsions, severe stomach pain with bloating, intestinal cramps and vomiting (paralytic ileus) and dizziness when getting up, especially when sitting or lying down (orthostatic hypotension), brain disease causing headache and fever, progressing towards hallucinations, confusion, partial or total paralysis of the body, behavioral disorders, speech and eye movements, stiff neck and sensitivity to light (encephalopathy), convulsions, dizziness, instability when walking (ataxia), headache.

Unknown frequency (cannot be estimated from the available data) :

- Disseminated intravascular coagulation, or "DIC", has been postponed. This condition is linked to a serious illness that increases the tendency for bleeding, or blood clotting, or both.
- Hardening / thickening of the skin (scleroderma).
- Metabolic complications after anti-cancer treatment (tumor lysis syndrome).
- Eye disorders, such as thickened and swollen macula (macular edema), blinking light (photopsy) and spots, grains, speckles and "cobwebs" floating in your field of vision (glassy floats).
- Inflammation of the veins (phlebitis).
- Autoimmune disease with multiple symptoms such as red, scintillating spots on the skin, joint pain or fatigue (systemic lupus erythematosus).

Reporting side effects

If you get any side effects, talk to your doctor or nurse. This also applies to any side effect that is not mentioned in this leaflet. You can also report side effects directly via the national reporting system.

5. HOW TO STORE PACLITAXEL NEAPOLIS 6 mg/ml, concentrate for solution for infusion ?

Keep this medicine out of the sight and the reach of children.

Do not use this medicine after the expiry date which is stated on the box after EXP. The expiration date refers to the last day of this month.

Store at a temperature not exceeding 25 ° C.

Store in the original package to protect from light.

After dilution : the solution is stable for 30 hours at 25 ° C in 5% dextrose and 0.9% sodium chloride.

Do not use if the solution remains cloudy or if it forms an insoluble precipitate.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist to dispose of the medicines you no longer use. These measures will help protect the environment.

6. CONTENT OF THE PACKAGING AND OTHER INFORMATION

What PACLITAXEL NEAPOLIS 6 mg/ml, concentrate for solution for infusion contains

- the active substance is : Paclitaxel.
- the other components are : Anhydrous ethanol, polyoxyethylene castor oil (35) and anhydrous citric acid.

Excipients with known effect : Anhydrous ethanol, polyoxyethylene castor oil (35)

What PACLITAXEL NEAPOLIS 6 mg/ml, concentrate for solution for infusion looks like and content of the outer packaging

PACLITAXEL NEAPOLIS is a concentrate for solution for infusion available in 5 ml, 16.7 ml and 25 ml vials.

Supply and prescription Condition : Table A/ list 1

M.A. N :

PACLITAXEL NEAPOLIS 6mg/ml (30mg), box of 1 vial of 5mL : 939 310 1H

PACLITAXEL NEAPOLIS 6mg/ml (100mg), box of 1 vial of 16.7mL :

PACLITAXEL NEAPOLIS 6mg/ml (150mg), box of 1 vial of 25mL : 939 310 2H

Marketing autorisation holder and manufacturer :

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Paclitaxel NEAPOLIS

Paclitaxel 6 mg/ml

Information reserved for healthcare professionals

The following information is exclusively intended for healthcare professionals :

Instructions for use

ANTINEOPLASTIC AGENT

Handling of PACLITAXEL NEAPOLIS

Like all antineoplastics, PACLITAXEL NEAPOLIS should be handled with caution. The product must be diluted under conditions guaranteeing asepsis, by experienced personnel, in a place designated for this purpose. Precautions should be taken to avoid contact with the skin and mucous membranes. Following topical exposure, tingling, burning and erythema have been observed. Dyspnea, chest pain, burning throat and nausea have been reported with inhalation.

Protective instructions for the preparation of the solution for infusion of PACLITAXEL NEAPOLIS.

1. Use a face mask and wear gloves and coveralls. In the absence of a face mask, use mouth protection and protective glasses.
2. Open containers, as well as vials for injection, vials for infusion, as well as cannulas, syringes, catheters, tubes once used and residues of cytotoxic products should be considered as hazardous waste and be disposed of in accordance with local regulations on the handling of HAZARDOUS WASTE.
3. In the event of accidental release, comply with the following instructions :

- Wear protective clothing.
- Collect the broken glass and place it in the containers intended for HAZARDOUS WASTE.
- Wash contaminated surfaces with copious amounts of cold water, then wipe thoroughly and dispose of the material used for this purpose from HAZARDOUS WASTE.

4. If the paclitaxel solution comes into contact with the skin, wash the contaminated area thoroughly with running water, then wash with soap and water. In case of contact with the mucous membranes, wash the affected area thoroughly with water. If you feel unwell, contact a doctor.
5. If the paclitaxel solution comes into contact with the eyes, wash thoroughly and thoroughly with cold water. Immediately consult an ophthalmologist.

Preparing the solution for infusion

Do not use so-called "closed" dose collection devices, such as the Chemo-Dispensing Pin device or similar, since they could damage the stopper and thus cause the loss of sterile integrity of the vial.

Before the infusion, the PACLITAXEL NEAPOLIS solution must be diluted, according to techniques guaranteeing asepsis, in one of the following injectable solutions : 0.9% sodium chloride, 5% glucose, 5% glucose mixture and chloride of 0.9% sodium, or in a mixture of 5% glucose and Ringer's solution, until a final concentration of 0.3 to 1.2 mg / ml is obtained.

The diluted solution is supersaturated with paclitaxel (some rare reports have reported the formation of a precipitate related to the 24 hour duration of the infusion). Consequently, excessive agitation or vibration should be avoided.

During preparation, the solutions may have a certain turbidity attributed to the excipient of the product. This turbidity is not eliminated during filtration. To reduce the risk of precipitation, paclitaxel solution for infusion should be used as soon as possible after dilution.

Infusion technique

Paclitaxel solution for infusion should only be administered by intravenous infusion.

The paclitaxel solution must be infused using a tube fitted with a micropore filter membrane with a diameter ≤ 0.22 µm (no significant loss of activity was observed in simulated infusion studies in using IV tubing fitted with a filter).

The necessary infusion should be rinsed thoroughly before use. During the infusion, the appearance of the solution should be checked regularly and the infusion should be stopped if a precipitate occurs.

Stability and storage conditions

Unopened injection vials of PACLITAXEL NEAPOLIS must be stored at a temperature of 25 ° C, in their original packaging and protected from light. Any other storage period or condition is the sole responsibility of the user.

If unopened vials are stored in the refrigerator or frozen, a precipitate may appear. It dissolves at room temperature with little or no stirring. The quality of the product is not affected in any way. If the solution remains cloudy or if an insoluble precipitate forms, the vial concerned must be discarded.

After dilution, the solutions should be used immediately after opening the vial. Any other storage period or condition is the sole responsibility of the user. Diluted solutions should not be kept refrigerated. After dilution, the solution is intended for single use.

Incompatibilities

In order to minimize the patient's exposure to DEHP (di-2-ethylhexyl phthalate), which can be released by bags or PVC plasticized infusion sets, or by other devices, it is advisable to store paclitaxel solutions diluted in non-PVC vials (glass or polypropylene) or plastic bags (polypropylene or polyolefin) and administer them using polyethylene coated infusion systems. Connecting a plasticized filter (e.g. IVEX-2) to PVC at the inlet or outlet of the infusion sets did not cause a noticeable release of DEHP.

Waste disposal

Any material used for preparation, administration or having been in contact with paclitaxel must be disposed of in accordance with local regulations in force concerning the use of cytotoxic products.

THIS IS A MEDICINE

- A medicine is a product but not like the others.
- A medicine is a product that affects your health and its consumption without compliance to the prescription exposes you to danger.
- Strictly follow your doctor's prescription and directions for use, follow the advice of your pharmacist.
- Your doctor and pharmacist are familiar with the medicine, its indications and contraindications.
- Do not stop treatment on your own initiative during the prescribed period.
- Do not take it again, do not increase the doses without consulting your doctor.

KEEP THE MEDICINES OUT OF THE REACH OF CHILDREN

NEAPOLIS PHARMA

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