

Package leaflet: Information for the user

[product name] <100 mg> <powder for concentrate for solution for infusion>

[product name] <500 mg> <powder for concentrate for solution for infusion>

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

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What <Product Name> is and what it is used for
2. What you need to know before you use <Product Name>
3. How to use <Product Name>
4. Possible side effects
5. How to store <Product Name>
6. Contents of the pack and other information

1. What <Product Name> is and what it is used for

<Product Name> is a medicine used in the treatment of cancer.

This medicine is given in combination with cisplatin, another anti-cancer medicine, as treatment for malignant pleural mesothelioma, a form of cancer that affects the lining of the lung, to patients who have not received prior chemotherapy.

This medicine is also given in combination with cisplatin for the initial treatment of patients with advanced stage of lung cancer.

This medicine can be prescribed to you if you have lung cancer at an advanced stage if your disease has responded to treatment or it remains largely unchanged after initial chemotherapy.

This medicine is also a treatment for patients with advanced stage of lung cancer whose disease has progressed after other initial chemotherapy has been used.

2. What you need to know before you use <Product Name>

Do not use <Product Name>

- if you are allergic (hypersensitive) to pemetrexed or any of the other ingredients of this medicine (listed in section 6).
- if you are breast-feeding; you must discontinue breast-feeding during treatment with This medicine.
- if you have recently received or are about to receive a vaccine against yellow fever.

Warnings and precautions

Talk to your doctor or hospital pharmacist before receiving <Product Name>.

If you currently have or have previously had problems with your kidneys, talk to your doctor or hospital pharmacist as you may not be able to receive this medicine. Before each infusion you will have samples of your blood taken to evaluate if you have sufficient kidney and liver function and to check that you have enough blood cells to receive this medicine. Your doctor may decide to change the dose or delay treating you depending on your general condition and if your blood cell counts are too low. If you are also receiving cisplatin, your doctor will make sure that you are properly hydrated and receive appropriate treatment before and after receiving cisplatin to prevent vomiting.

If you have had or are going to have radiation therapy, please tell your doctor, as there may be an early or late radiation reaction with this medicine.

If you have been recently vaccinated, please tell your doctor, as this can possibly cause bad effects with this medicine.

If you have heart disease or a history of heart disease, please tell your doctor.

If you have an accumulation of fluid around your lungs, your doctor may decide to remove the fluid before giving you this medicine.

Children and adolescents

There is no relevant use of <Product Name> in the paediatric population

Other medicines and <Product Name>

Please tell your doctor if you are taking any medicine for pain or inflammation (swelling), such as medicines called “nonsteroidal anti-inflammatory drugs” (NSAIDs), including medicines purchased without a doctor’s prescription (such as ibuprofen). There are many sorts of NSAIDs with different durations of activity. Based on the planned date of your infusion of <Product Name> and/or on the status of your kidney function, your doctor needs to advise you on which medicines you can take and when you can take them. If you are unsure, ask your doctor or pharmacist if any of your medicines are NSAIDs.

Please tell your doctor or hospital pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy

If you are pregnant, think you may be pregnant or are planning to have a baby, **tell your doctor**. The use of <Product Name> should be avoided during pregnancy. Your doctor will discuss with you the potential risk of taking this medicine during pregnancy. Women must use effective contraception during treatment with this medicine.

Breast-feeding

If you are breast-feeding, tell your doctor.

Breast-feeding must be discontinued during <Product Name> treatment.

Fertility

Men are advised not to father a child during and up to 6 months following treatment with <Product Name> and should therefore use effective contraception during treatment with this medicine and for up to 6 months afterwards. If you would like to father a child during the treatment or in the 6 months following receipt of treatment, seek advice from your doctor or pharmacist. You may want to seek counselling on sperm storage before starting your therapy.

Driving and using machines

<Product Name> may make you feel tired. Be careful when driving a car or using machines.

<Product Name> contains sodium

[product name] <100 mg> <powder for concentrate for solution for infusion> contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially 'sodium-free'.

[product name] <500 mg> <powder for concentrate for solution for infusion> contains 54 mg sodium (main component of cooking/table salt) per vial. This is equivalent to 2.7% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use <Product Name>

The dose of <Product Name> is 500 milligrams for every square metre of your body's surface area. Your height and weight are measured to work out the surface area of your body. Your doctor will use this body surface area to work out the right dose for you. This dose may be adjusted, or treatment may be delayed depending on your blood cell counts and on your general condition. A hospital pharmacist, nurse or doctor will have mixed this medicine with 9 mg/ml (0.9 %) sodium chloride solution for injection before it is given to you.

You will always receive<Product Name>by infusion into one of your veins. The infusion will last approximately 10 minutes.

When using <Product Name> in combination with cisplatin:

The doctor or hospital pharmacist will work out the dose you need based on your height and weight. Cisplatin is also given by infusion into one of your veins, and is given approximately 30 minutes after the infusion of this medicine has finished. The infusion of cisplatin will last approximately 2 hours.

You should usually receive your infusion once every 3 weeks.

Additional medicines:

Corticosteroids: your doctor will prescribe you steroid tablets (equivalent to 4 milligram of dexamethasone twice a day) that you will need to take on the day before, on the day of, and the day after <Product Name> treatment. This medicine is given to you to reduce the frequency and severity of skin reactions that you may experience during your anticancer treatment.

Vitamin supplementation: your doctor will prescribe you oral folic acid (vitamin) or a multivitamin containing folic acid (350 to 1000 micrograms) that you must take once a day while you are taking this medicine. You must take at least 5 doses during the seven days before the first dose of this medicine. You must continue taking the folic acid for 21 days after the last dose of this medicine. You will also receive an injection of vitamin B₁₂ (1000 micrograms) in the week before administration of this medicine and then approximately every 9 weeks (corresponding to 3 courses of <Product Name> treatment). Vitamin B₁₂ and folic acid are given to you to reduce the possible toxic effects of the anticancer treatment.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

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

You must contact your doctor immediately if you notice any of the following:

- Fever or infection (common): if you have a temperature of 38°C or greater, sweating or other signs of infection (since you might have less white blood cells than normal which is very common). Infection (sepsis) may be severe and could lead to death
- If you start feeling chest pain (common) or having a fast heart rate (uncommon)
- If you have pain, redness, swelling or sores in your mouth (very common)
- Allergic reaction: if you develop skin rash (very common) / burning or prickling sensation (common), or fever (common). Rarely, skin reactions may be severe and could lead to death. Contact your doctor if you get a severe rash, or itching, or blistering (Stevens-Johnson Syndrome or Toxic epidermal necrolysis)
- If you experience tiredness, feeling faint, becoming easily breathless or if you look pale (since you might have less haemoglobin than normal which is very common)
- If you experience bleeding from the gums, nose or mouth or any bleeding that would not stop, reddish or pinkish urine, unexpected bruising (since you might have less platelets than normal which is very common)
- If you experience sudden breathlessness, intense chest pain or cough with bloody sputum (uncommon) (may indicate a blood clot in the blood vessels of the lungs)

Side effects with <Product Name> may include:

Very common (may affect more than 1 in 10 people)

- Low white blood cells
- Low haemoglobin level (anaemia)
- Low platelet count
- Diarrhoea
- Vomiting
- Pain, redness, swelling or sores in your mouth
- Nausea
- Loss of appetite
- Fatigue (tiredness)
- Skin rash
- Hair loss
- Constipation
- Loss of sensation
- Kidney: abnormal blood tests

Common (may affect up to 1 in 10 people)

- Allergic reaction: skin rash / burning or prickling sensation
- Infection including sepsis
- Fever
- Dehydration
- Kidney failure
- Irritation of the skin and itching
- Chest pain
- Muscle weakness
- Conjunctivitis (inflamed eye)
- Upset stomach
- Pain in the abdomen
- Taste change
- Liver: abnormal blood tests
- Watery eyes
- Increased skin pigmentation

Uncommon (may affect up to 1 in 100 people)

- Acute renal failure

- Fast heart rate
- Inflammation of the lining of the oesophagus (gullet) has been experienced with <Product Name> / radiation therapy.
- Colitis (inflammation of the lining of the large bowel, which may be accompanied by intestinal or rectal bleeding)
- Interstitial pneumonitis (scarring of the air sacs of the lung)
- Oedema (excess fluid in body tissue, causing swelling)
- Some patients have experienced a heart attack, stroke or “mini-stroke” while receiving this medicine usually in combination with another anticancer therapy
- Pancytopenia- combined low counts of white cells, red cells and platelets
- Radiation pneumonitis (scarring of the air sacs of the lung associated with radiation therapy) may occur in patients who are also treated with radiation either before, during or after their <Product Name> therapy
- Extremity pain, low temperature and discolouration have been reported.
- Blood clots in the lung blood vessels (pulmonary embolism)

Rare (may affect up to 1 in 1,000 people)

- Radiation recall (a skin rash like severe sunburn) which can occur on skin that has previously been exposed to radiotherapy, from days to years after the radiation
- Bullous conditions (blistering skin diseases)-including Stevens-Johnson syndrome and Toxic epidermal necrolysis
- Immune mediated haemolytic anaemia (antibody-mediated destruction of red blood cells)
- Hepatitis (inflammation of the liver)
- Anaphylactic shock (severe allergic reaction)

Not known: frequency cannot be estimated from the available data

- Lower limb swelling with pain and redness
- Increased urine output
- Thirst and increased water consumption
- Hyponatremia – increased sodium in blood
- Inflammation of the skin, mainly of the lower limb with swelling, pain and redness

You might have any of these symptoms and/or conditions. You must tell your doctor as soon as possible when you start experiencing any of these side effects.

If you are concerned about any side effects, talk to your doctor.

Reporting of side effects

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 side effects directly [via the national reporting system listed in Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store <Product Name>

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

“Do not use this medicine after the expiry date which is stated on the carton and vial after EXP. The expiry date refers to the last day of that month.”

This medicine does not require any special storage conditions.

Reconstituted and Infusion Solutions: The product should be used immediately. When prepared as directed, chemical and physical in-use stability of reconstituted and infusion solutions of pemetrexed were demonstrated for 24 hours at refrigerated temperature.

This medicine is for single use only; any unused solution must be disposed of in accordance with local requirement.

6. Contents of the pack and other information

What <Product Name> contains

The active substance is pemetrexed.

[product name] <100 mg> <powder for concentrate for solution for infusion>: Each vial contains 100 milligrams of pemetrexed (as pemetrexed disodium).

[product name] <500 mg> <powder for concentrate for solution for infusion>: Each vial contains 500 milligrams of pemetrexed (as pemetrexed disodium).

After reconstitution, the solution contains 25 mg/ml of pemetrexed. Further dilution by a healthcare provider is required prior to administration.

The other ingredients are mannitol (E421), hydrochloric acid (E507), (for pH-adjustment) and sodium hydroxide (E524), (for pH-adjustment).

What <Product Name> looks like and contents of the pack

<Product Name> is a powder for concentrate for solution for infusion in a vial. It is a white to either light yellow or green-yellow lyophilised powder.

Each pack of <Product Name> consists of one Pemetrexed powder for concentrate for solution for infusion vial.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

< [To be completed nationally]>

Manufacturer

< [To be completed nationally]>

This medicinal product is authorised in the Member States of the EEA under the following names:

< [To be completed nationally]>

This leaflet was last revised in < {MM/YYYY}> < {month YYYY}>

The following information is intended for medical or healthcare professionals only

Instructions for use, handling and disposal

1. Use aseptic techniques during the reconstitution and further dilution of pemetrexed for intravenous infusion administration
2. Calculate the dose and the number of Pemetrexed vials needed. Each vial contains an excess of pemetrexed to facilitate delivery of the label amount.

3. **<PRODUCT NAME 100 mg>:**

Reconstitute each 100 mg vial with 4.2 ml of 9 mg/ml (0.9%) sodium chloride solution for injection, without preservative, resulting in a solution containing 25 mg/ml pemetrexed.

<PRODUCT NAME 500 mg>:

Reconstitute each 500 mg vial with 20 ml of 9 mg/ml (0.9%) sodium chloride solution for injection, without preservative, resulting in a solution containing 25 mg/ml pemetrexed.

Gently swirl each vial until the powder is completely dissolved. The resulting solution is clear and ranges in colour from colourless to yellow or green-yellow without adversely affecting product quality. The pH of the reconstituted solution is between 6.6 and 7.8.
Further dilution is required.

4. The appropriate volume of reconstituted pemetrexed solution must be further diluted to 100 ml with 9 mg/ml (0.9 %) sodium chloride solution for injection, without preservative, and administered as an intravenous infusion over 10 minutes.
5. Pemetrexed infusion solutions prepared as directed above are compatible with polyvinyl chloride and polyolefin lined administration sets and infusion bags. Pemetrexed is incompatible with diluents containing calcium, including lactated Ringer's Injection and Ringer's Injection.
6. Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. If particulate matter is observed, do not administer.
7. Pemetrexed solutions are for single use only. Any unused product or waste material should be disposed of in accordance with local requirements for cytotoxic agents.

Preparation and administration precautions: As with other potentially toxic anticancer agents, care should be exercised in the handling and preparation of pemetrexed infusion solutions. The use of gloves is recommended. If a pemetrexed solution contacts the skin, wash the skin immediately and thoroughly with soap and water. If pemetrexed solutions contact the mucous membranes, flush thoroughly with water. Pemetrexed is not a vesicant. There is not a specific antidote for extravasation of pemetrexed. There have been a few reported cases of pemetrexed extravasation, which were not assessed as serious by the investigator. Extravasation should be managed by local standard practice as with other non-vesicants.

Marketing Authorization Holder:

<Logo of MAH>

<Address of MAH>