PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Pemetrexed 100 mg powder for concentrate for solution for infusion
Pemetrexed 500 mg powder for concentrate for solution for infusion
Pemetrexed 1000 mg powder for concentrate for solution for infusion

pemetrexed

Read all of this leaflet carefully before you are given 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, please ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Pemetrexed is and what it is used for

Pemetrexed contains the active substance pemetrexed, which belongs to the group of medicines used in the treatment of cancer. It is used:
- 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
- in combination with cisplatin for the initial treatment of patients with advanced stage of lung cancer
- as a treatment for patients with lung cancer at an advanced stage if their disease has responded to treatment or it remains largely unchanged after initial chemotherapy
- as 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 Pemetrexed

Do not use Pemetrexed
- 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 Pemetrexed
- if you have recently received or are about to receive a vaccine against yellow fever.

Warnings and precautions
Talk to your doctor or pharmacist before using Pemetrexed
- if you currently have or have previously had problems with your kidneys, as you may not be able to receive Pemetrexed.
  Before each infusion you will have samples of your blood taken to see if you have sufficient kidney and liver function and to check that you have enough blood cells to receive Pemetrexed.

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 treatment before and after receiving cisplatin to prevent vomiting.
- if you have had or are going to have radiation therapy, as there may be an early or late radiation reaction with Pemetrexed
- if you have been recently vaccinated, as this can possibly cause bad effects with Pemetrexed
- if you have heart disease or a history of heart disease
- if you have an accumulation of fluid around your lungs, your doctor may decide to remove the fluid before giving you Pemetrexed.

Children and adolescents
This medicine should not be used in children or adolescents, since there is no experience with this medicine in children or adolescents under 18 years of age.

Other medicines and Pemetrexed
Tell your doctor or hospital pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.
Please tell your doctor or hospital pharmacist 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 Pemetrexed SUN 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 inform your doctor if you are taking medicines called proton pump inhibitors (omeprazole, esomeprazole, lansoprazole, pantoprazole, and rabeprazole) used to treat heartburn and acid regurgitation.

Pregnancy, breast-feeding and fertility
Pregnancy
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. The use of Pemetrexed should be avoided during pregnancy. Your doctor will discuss with you the potential risk of receiving Pemetrexed during pregnancy. Women must use effective contraception during treatment with Pemetrexed and for 6 months after receiving the last dose.

Breast-feeding
If you are breast-feeding, tell your doctor. Breast-feeding must be discontinued during treatment with Pemetrexed.

Fertility
Men are advised not to father a child during and up to 3 months following treatment with Pemetrexed and should therefore use effective contraception during treatment with Pemetrexed and for up to 3 months afterwards. If you would like to father a child during the treatment or in the 3 months following receipt of treatment, seek advice from your doctor or pharmacist. Pemetrexed can affect your ability to have children. Talk to your doctor to seek advice about sperm storage before starting your therapy.

Driving and using machines
Pemetrexed may make you feel tired. Be careful when driving a car or using machines.

Pemetrexed contains sodium

Pemetrexed 100 mg contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.
Pemetrexed 500 mg contains approximately 54 mg sodium (main component of cooking /table salt) in each vial. This is equivalent to 2.7% of the recommended maximum daily dietary intake of sodium for an adult.

Pemetrexed 1000 mg contains approximately 108 mg sodium (main component of cooking /table salt) in each vial. This is equivalent to 5.4% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Pemetrexed

The recommended dose of Pemetrexed is 500 milligrams for every square meter 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 pharmacist, nurse or doctor will have mixed the Pemetrexed powder with 9 mg/ml (0.9 %) sodium chloride solution for injection before it is given to you.

You will always receive Pemetrexed by infusion into one of your veins. The infusion will last approximately 10 minutes.

When using Pemetrexed in combination with cisplatin
- the doctor or 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 Pemetrexed 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 Pemetrexed 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 Pemetrexed. You must take at least 5 doses during the seven days before the first dose of Pemetrexed. You must continue taking the folic acid for 21 days after the last dose of Pemetrexed. You will also receive an injection of vitamin B_{12} (1000 micrograms) in the week before administration of Pemetrexed and then approximately every 9 weeks (corresponding to 3 courses of Pemetrexed treatment). Vitamin B_{12} 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, pharmacist or nurse.

4. Possible side effects

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

Serious side effects
Tell your doctor straight away about any of the following serious side effects:

Very common (may affect more than 1 in 10 people)
- pain, redness, swelling or sores in mouth
- allergic reaction: skin rash. Rarely, skin reactions may be severe and could lead to death
- low level of haemoglobin (anaemia). You could experience tiredness, feeling faint, becoming easily breathless or you could look pale

Common (may affect up to 1 in 10 people)
- fever or infection: if you have a temperature of 38ºC 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
- chest pain
- allergic reaction: burning or prickling sensation and fever
- low counts of platelets. You could experience bleeding from the gums, nose or mouth or any bleeding that would not stop, reddish or pinkish urine, unexpected bruising

Uncommon (may affect up to 1 in 100 people)
- fast heart rate
- blood clots in the blood vessels of the lungs (pulmonary embolism). You could experience sudden breathlessness, intense chest pain or cough with bloody sputum

Rare (may affect up to 1 in 1,000 people)
- allergic reaction: severe rash, or itching, or blistering (Stevens-Johnson Syndrome or Toxic epidermal necrolysis).

Other side effects
Tell your doctor as soon as possible about any of the following side effects:

Very common (may affect more than 1 in 10 people)
- infection
- pharyngitis (a sore throat)
- low number of neutrophil granulocytes (a type of white blood cell)
- low white blood cells
- low haemoglobin level
- pain, redness, swelling or sores in your mouth
- loss of appetite
- vomiting
- diarrhoea
- nausea
- skin rash
- flaking skin
- abnormal blood tests showing reduced functionality of kidneys
- fatigue (tiredness)

Common (may affect up to 1 in 10 people)
- blood infection
- fever with low number of neutrophil granulocytes (a type of white blood cell)
- low platelet count
- allergic reaction
- loss of body fluids
- taste change
- damage to the motor nerves which may cause muscle weakness and atrophy (wasting) primary in the arms and legs
- damage to the sensory nerves that may cause loss of sensation, burning pain and unsteady gait

- dizziness
- inflammation or swelling of the conjunctiva (the membrane that lines the eyelids and covers the white of the eye
- dry eye
- watery eyes
- dryness of the conjunctiva (the membrane that lines the eyelids and covers the white of the eye) and cornea (the clear layer in front of the iris and pupil
- swelling of the eyelids
- eye disorder with dryness, tearing, irritation, and/or pain
- cardiac failure (condition that affects the pumping power of your heart muscles)
- irregular heart rhythm
- indigestion
- constipation
- abdominal pain
- liver: increases in the chemicals in the blood made by the liver
- increased skin pigmentation
- itchy skin
- rash on the body where each mark resembles a bullseye
- hair loss
- hives
- kidney stop working
- reduced functionality of kidney
- fever
- pain
- excess fluid in body tissue, causing swelling
- chest pain
- inflammation and ulceration of the mucous membranes lining the digestive tract

Uncommon (may affect up to 1 in 100 people)
- reduction in the number of red, white blood cells and platelets
- stroke
- type of stroke when an artery to the brain is blocked
- bleeding inside the skull
- angina (chest pain caused by reduced blood flow to the heart)
- heart attack
- narrowing or blockage of the coronary arteries
- increased heart rhythm
- deficient blood distribution to the limbs
- blockage in one of the pulmonary arteries in your lungs
- inflammation and scarring of the lining of the lungs with breathing problems
- passage of bright red blood from the anus
- bleeding in the gastrointestinal tract
- ruptured bowel
- inflammation of the lining of the oesophagus
- inflammation of the lining of the large bowel, which may be accompanied by intestinal or rectal bleeding (seen only in combination with cisplatin)
- inflammation, edema, erythema, and erosion of the mucosal surface of the esophagus caused by radiation therapy
- inflammation of the lung caused by radiation therapy

Rare (may affect up to 1 in 1,000 people)
- destruction of red blood cells
- anaphylactic shock (severe allergic reaction)
- inflammatory condition of the liver
- redness of the skin

- skin rash that develops throughout a previously irradiated area

Very rare (may affect up to 1 in 10,000 people)
- infections of skin and soft tissues
- Stevens-Johnson syndrome (a type of severe skin and mucous membranes reaction that may be life threatening)
- toxic epidermal necrolysis (a type of severe skin reaction that may be life threatening)
- autoimmune disorder that results in skin rashes and blistering on the legs, arms, and abdomen
- inflammation of the skin characterized by the presence of bullae which are filled with fluid
- skin fragility, blisters and erosions and skin scarring
- redness, pain and swelling mainly of the lower limbs
- inflammation of the skin and fat beneath the skin (pseudocellulitis)
- inflammation of the skin (dermatitis)
- skin to become inflamed, itchy, red, cracked, and rough
- intensely itchy spots

Not known (frequency cannot be estimated from the available data)
- form of diabetes primarily due to pathology of the kidney
- disorder of the kidneys involving the death of tubular epithelial cells that form the renal tubules.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Pemetrexed SUN

Your doctor, pharmacist or nurse knows how to store Pemetrexed properly.

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 the vial and carton after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

After opening the vial, the product should be used immediately in order to avoid microbial contamination. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C – 8°C, unless reconstitution/ dilution has taken place in controlled and validated aseptic conditions. Allow the refrigerated solution to reach room temperature before administration.

6. Contents of the pack and other information

What Pemetrexed contains
- The active substance is pemetrexed. Each vial contains 100, 500 or 1000 milligrams of pemetrexed (as pemetrexed disodium heptahydrate). 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, hydrochloric acid and/or sodium hydroxide (for pH adjustment) (see section 2 for further information).

What Pemetrexed looks like and contents of the pack
Pemetrexed is a powder for concentrate for solution for infusion in a vial. It is a white to either light yellow or green-yellow lyophilized powder.
Pemetrexed is supplied in packs containing one vial.

Marketing Authorisation Holder and Manufacturer
Sun Pharmaceutical Industries Europe B.V.
Polarisavenue 87
2132 JH Hoofddorp
The Netherlands

This medicinal product is authorised in the Member states of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names

Germany:	Pemetrexed SUN 100 mg/ 500 mg / 1000 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung
Italy:	Pemetrexed SUN 100 mg/ 500 mg/ 1000 mg polvere per concentrato per soluzione per infusione
Netherlands:	Pemetrexed SUN 100 mg/ 500 mg/ 1000 mg poeder voor concentraat voor oplossing voor infusie
Poland:	Pemetreksed SUN 100 mg/ 500 mg/ 1000 mg proszek do sporządzania koncentratu roztworu do infuzji
Romania:	Pemetrexed SUN 100 mg/ 500 mg/ 1000 mg pulbere pentru concentrat pentru soluţie perfuzabilă
Spain:	Pemetrexed SUN 100 mg polvo para concentrado para solución para perfusión EFG Pemetrexed SUN 500 mg polvo para concentrado para solución para perfusión EFG Pemetrexed SUN 1000 mg polvo para concentrado para solución para perfusión
United Kingdom (Northern Ireland):	Pemetrexed SUN 100 mg/ 500 mg/ 1000 mg powder for concentrate for solution for infusion

This leaflet was last revised in 01/2025.

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. Pemetrexed 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.

   Pemetrexed 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.

   Pemetrexed 1000 mg:
   Reconstitute each 1000 mg vial with 40 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. The osmolality of the reconstituted solution is between 480 and 570 mOsm/kg. **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.