

PACKAGE LEAFLET

Package leaflet: Information for the user

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

pemetrexed

Read all of this leaflet carefully before you start using 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 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 Pemetrexed Teva is and what it is used for**
2. **What you need to know before you use Pemetrexed Teva**
3. **How to use Pemetrexed Teva**
4. **Possible side effects**
5. **How to store Pemetrexed Teva**
6. **Contents of the pack and other information**

1. **What Pemetrexed Teva is and what it is used for**

Pemetrexed Teva is a medicine used in the treatment of cancer.

Pemetrexed Teva 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.

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

Pemetrexed Teva 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.

Pemetrexed Teva 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 Pemetrexed Teva**

Do NOT use Pemetrexed Teva if you:

- are allergic to pemetrexed or any of the other ingredients of this medicine (listed in section 6).
- are breast-feeding; you **MUST** discontinue breast-feeding during treatment with Pemetrexed Teva (see Pregnancy, breast-feeding and fertility).
- have recently received or are about to receive a vaccine against yellow fever.

Warnings and precautions

Talk to your doctor or hospital pharmacist before using Pemetrexed Teva.

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 Pemetrexed Teva.

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 Pemetrexed Teva. 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 Pemetrexed Teva.

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

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 Pemetrexed Teva.

Children and adolescents

There is no relevant use of Pemetrexed Teva in the paediatric population.

Other medicines and Pemetrexed Teva

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 Pemetrexed Teva 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.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Pregnancy, breast-feeding and fertility

Pregnancy

If you are pregnant, or thinking about becoming pregnant, **tell your doctor**. The use of Pemetrexed Teva should be avoided during pregnancy. Your doctor will discuss with you the potential risk of taking Pemetrexed Teva during pregnancy. Women **MUST** use effective contraception during treatment with Pemetrexed Teva.

Breast-feeding

If you are breast-feeding, **tell your doctor**.

Breast-feeding **MUST** be discontinued during Pemetrexed Teva treatment.

Fertility

Men are advised not to father a child during and up to 6 months following treatment with Pemetrexed Teva and should therefore use effective contraception during treatment with Pemetrexed Teva 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

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

Pemetrexed Teva contains sodium

Pemetrexed Teva 100 mg contains less than 1 mmol sodium (approximately 11 mg) per vial. To be taken into consideration by patients on a controlled sodium diet.

Pemetrexed Teva 500 mg contains approximately 2.3 mmol sodium (approximately 54 mg) per vial. To be taken into consideration by patients on a controlled sodium diet.

Pemetrexed Teva 1000 mg contains approximately 4.7 mmol sodium (approximately 109 mg) per vial. To be taken into consideration by patients on a controlled sodium diet.

3. How to use Pemetrexed Teva

The dose of Pemetrexed Teva 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 the Pemetrexed Teva powder with 9 mg/ml (0.9%) sodium chloride solution for injection before it is given to you.

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

When using Pemetrexed Teva 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 Pemetrexed Teva 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 Teva 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 Teva. You must take at least 5 doses during the seven days before the first dose of Pemetrexed Teva. You must continue taking the folic acid for 21 days after the last dose of Pemetrexed Teva. You will also receive an injection of vitamin B₁₂ (1000 micrograms) in the week before administration of Pemetrexed Teva and then approximately every 9 weeks (corresponding to 3 courses of Pemetrexed Teva 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 Pemetrexed Teva 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 (being sick)
- Pain, redness, swelling or sores in your mouth
- Nausea (feeling sick)
- 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.

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 Pemetrexed Teva / 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 Pemetrexed Teva 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 Pemetrexed Teva 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
- Haemolytic anaemia (anaemia due to destruction of red blood cells)
- Hepatitis (inflammation of the liver)
- Anaphylactic shock (severe allergic reaction).

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

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 Pemetrexed Teva

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 the vials 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 (2°C - 8°C).

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

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

6. Contents of the pack and other information

What Pemetrexed Teva contains

- The active substance is pemetrexed.

Pemetrexed Teva 100 mg: Each vial contains 100 milligrams of pemetrexed (as pemetrexed disodium).

Pemetrexed Teva 500 mg: Each vial contains 500 milligrams of pemetrexed (as pemetrexed disodium).

Pemetrexed Teva 1000 mg: Each vial contains 1000 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), sodium hydroxide and hydrochloric acid (for pH adjustment).

What Pemetrexed Teva looks like and contents of the pack

Pemetrexed Teva 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 Pemetrexed Teva consists of one glass vial closed with rubber stopper and aluminium cap. The vials are sleeved (provided with a protective transparent cover).

Marketing Authorisation Holder and Manufacturer

[To be completed nationally]

Manufacturer

Pharmachemie B.V.,
Swensweg 5,
2031 GA Haarlem,
The Netherlands

Teva Pharmaceutical Works Private Limited Company

Táncsics Mihály út 82,

H-2100 Gödöllő,

Hungary

Pliva Croatia Ltd.,

Prilaz baruna Filipovica 25,

10000 Zagreb,

Croatia

Teva Operations Poland Sp. z.o.o.

Ul. Mogilska 80,
31-546 Krakow
Poland

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The following information is intended for 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 Teva vials needed.
3. Pemetrexed Teva 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. (Each vial contains an excess of pemetrexed to facilitate delivery of the label amount).

Pemetrexed Teva 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 Teva 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. 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 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.

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.