

## Package leaflet: Information for the user

### Pemetrexed Teva 25 mg/ml 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**

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

### **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 medicinal products” (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 hospital pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

### **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 treatment with Pemetrexed Teva.

#### **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.

## **3. How to use Pemetrexed Teva**

Pemetrexed Teva will always be given to you by a healthcare professional. Your condition will be closely monitored during treatment. This routinely involves blood tests, including checks on your liver and kidney function. Your dose may be changed or treatment delayed depending on results from these test.

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 diluted the Pemetrexed Teva concentrate with 5% w/v glucose 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 B<sub>12</sub> (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 B<sub>12</sub> 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).

Other side effects with Pemetrexed Teva may include:

*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 lost 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
- Abnormal 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

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:

HPRA Pharmacovigilance Website: [www.hpra.ie](http://www.hpra.ie)

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.

Unopened vials: Store in a refrigerator (2 °C–8 °C). Keep the vial in the outer carton in order to protect from light.

Infusion Solutions: The product should be used immediately. When prepared as directed, chemical and physical in-use stability 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.

Each ml of concentrate contains 25 mg pemetrexed (as pemetrexed diacid).

Pemetrexed Teva 25 mg/ml: Each vial of 4 ml concentrate contains 100 milligrams of pemetrexed (as pemetrexed diacid).

Pemetrexed Teva 25 mg/ml: Each vial of 20 ml concentrate contains 500 milligrams of pemetrexed (as pemetrexed diacid).

Pemetrexed Teva 25 mg/ml: Each vial of 40 ml concentrate contains 1000 milligrams of pemetrexed (as pemetrexed diacid).

The other ingredients are mannitol (E 421), citric acid, trometamol and water for injections.

### **What Pemetrexed Teva looks like and contents of the pack**

Pemetrexed Teva is a concentrate for solution for infusion (sterile concentrate) in a vial. It is a colourless to yellow or green yellow solution.

Each pack of Pemetrexed Teva consists of either:

One 100 mg/4 ml clear glass vial closed with bromobutyl stopper with fluoropolymer coating and aluminium cap. The vials are sleeved (provided with a protective transparent cover).

One 500 mg/20 ml glass vial closed with bromobutyl stopper with fluoropolymer coating and aluminium cap. The vials are sleeved (provided with a protective transparent cover).

One 1000 mg/40 ml glass vial closed with bromobutyl stopper with fluoropolymer coating and aluminium cap. The vials are sleeved (provided with a protective transparent cover).

Not all pack sizes may be marketed.

### **Marketing Authorisation Holder and Manufacturer**

#### **Marketing authorisation holder**

Teva B.V.  
Swensweg 5  
2031GA Haarlem  
Netherlands

#### **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

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

Austria:	Pemetrexed ratiopharm 25 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Belgium:	<b>Dutch:</b> Pemetrexed Teva 25 mg/ml concentraat voor oplossing voor infusie <b>French:</b> Pemetrexed Teva 25 mg/ml solution a diluer pour perfusion <b>German:</b> Pemetrexed Teva 25 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Croatia	Pemetreksed Pliva 25 mg/ml koncentrat za otopinu za infuziju
Denmark:	Pemetrexed Teva
Estonia:	Pemetrexed Teva
France:	Pemetrexed Teva 25 mg/ml solution à diluer pour perfusion
Germany:	Pemetrexed-ratiopharm 25 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Hungary:	Pemetrexed Teva 25 mg/ml koncentrátum oldatos infúzióhoz
Iceland:	Pemetrexed Teva 25 mg/ml innrennslisþykkni, lausn
Ireland:	Pemetrexed Teva 25 mg/ml Concentrate for Solution for Infusion
Latvia:	Pemetrexed Teva 25 mg/ml koncentrāts infūziju šķīduma pagatavošanai
Lithuania:	Pemetrexed Teva 25 mg/ml koncentratas infuziniam tirpalui
Luxembourg:	Pemetrexed Teva 25 mg/ml solution a diluer pour perfusion
Netherlands:	Pemetrexed Teva 25 mg/ml, concentraat voor oplossing voor infusie
Portugal:	Pemetrexed Zidrium
Romania:	Pemetrexed Teva 25 mg/ml concentrat pentru soluție perfuzabilă
Slovenia:	Pemetreksed Teva 25 mg/ml koncentrat za raztopino za infundiranje
Spain:	Pemetrexed Teva 25 mg/ml concentrado para solución para perfusión
Sweden:	Pemetrexed Teva

**This leaflet was last revised in February 2021.**

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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 dilution of pemetrexed for intravenous infusion administration.
2. Calculate the dose and the volume of Pemetrexed Teva 25 mg/ml concentrate for solution for infusion needed.

3. Pemetrexed Teva must only be diluted with 5% glucose solution, without preservative. The appropriate volume of pemetrexed concentrate must be diluted to 100 ml with 5 % glucose solution and administered as an intravenous infusion over 10 minutes.
4. 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.  
  
Pemetrexed Teva contains trometamol as an excipient. Trometamol is incompatible with cisplatin resulting in degradation of cisplatin. This medicinal product must not be mixed with other medicinal products. Intravenous lines should be flushed after administration of Pemetrexed Teva.
5. Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration. If particulate matter is observed, do not administer.
6. 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.