**Package leaflet: Information for the user**

**Pemetrexed Rowex 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 Rowex is and what it is used for

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

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

Pemetrexed Rowex 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 Rowex is also a treatment for patients with advanced stage of lung cancer whose disease has progressed after other initial chemotherapy has been used.
This medicinal product is for adults use only.

## 2. What you need to know before you are given Pemetrexed Rowex

**Do not use Pemetrexed Rowex**
- if you are allergic 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 Rowex
- 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 Pemetrexed Rowex.

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 Rowex.

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 Rowex. 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 Rowex.

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

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 Rowex.

**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 Rowex**
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 Rowex 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, breast-feeding and fertility**
*Pregnancy*
If you are pregnant, think you may be pregnant or are planning to have a baby, **tell your doctor**. The use of Pemetrexed Rowex should be avoided during pregnancy. Your doctor will discuss with you the potential risk of taking Pemetrexed Rowex during pregnancy.

Women must use effective contraception during treatment with Pemetrexed Rowex 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 Rowex.

*Fertility*
Men are advised not to father a child during and up to 3 months following treatment with Pemetrexed Rowex and should therefore use effective contraception during treatment with Pemetrexed Rowex 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 Rowex 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 Rowex may make you feel tired. Be careful when driving a car or using machines.

**Pemetrexed Rowex contains sodium and propylene glycol**
Pemetrexed Rowex 100 mg (vial with 4 ml)
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'. This medicine contains 200 mg propylene glycol in each vial.

Pemetrexed Rowex 500 mg (vial with 20 ml)
This medicine contains 55.6 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 3% of the recommended maximum daily dietary intake of sodium for an adult.
This medicine contains 1000 mg propylene glycol in each vial.

Pemetrexed Rowex 1000 mg (vial with 40 ml)
This medicine contains 111.2 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 6% of the recommended maximum daily dietary intake of sodium for an adult.
This medicine contains 2000 mg propylene glycol in each vial.

## 3. How to use Pemetrexed Rowex

Pemetrexed Rowex must only be administered under the supervision of a physician qualified in the use of anti-cancer chemotherapy.

The dose of Pemetrexed Rowex 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 concentrate with 9 mg/ml (0.9%) sodium chloride or with glucose 50 mg/ml (5%) solution for injection before it is given to you.

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

When using Pemetrexed 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 Rowex 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 milligrams of dexamethasone twice a day) that you will need to take on the day before, on the day of, and the day after Pemetrexed Rowex 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 Rowex. You must take at least 5 doses during the seven days before the first dose of Pemetrexed Rowex. You must continue taking the folic acid for 21 days after the last dose of Pemetrexed Rowex. You will also receive an injection of vitamin B12 (1000 micrograms) in the week before administration of Pemetrexed and then approximately every 9 weeks (corresponding to 3 courses of Pemetrexed 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** (respectively, common or very common): 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.
- 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 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 Rowex 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 stops 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, oedema, erythema, and erosion of the mucosal surface of the oesophagus 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 of 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 characterised 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 the national reporting system: HPRA Pharmacovigilance; website: www.hpra.ie. By reporting side effects, you can help provide more information on the safety of this medicine.

## 5. How to store Pemetrexed Rowex

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 box and label after EXP. The expiry date refers to the last day of that month.

Unopened vial
Do not store above 25°C. Store in the original package in order to protect from light.

After first opening
The product should be used immediately. Any unused portions have to be discarded.

After dilution
*100 mg vial*
The stability of the prepared infusion solution has been demonstrated for 3 days refrigerated at 2-8°C, protected from light.

*500 mg vial and 1000 mg vial*
The stability of the prepared infusion solution has been demonstrated for 7 days at room temperature protected from light and for 14 days at refrigerated at 2-8°C, protected from light.

From a microbiological point of view, the product should be used immediately. 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 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

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

## 6. Contents of the pack and other information

**What Pemetrexed Rowex contains**
The active substance is pemetrexed (as pemetrexed disodium hemipentahydrate).

Each ml concentrate for solution for infusion contains 25 mg pemetrexed (as pemetrexed disodium hemipentahydrate).

Each vial with 4 ml contains 100 mg of pemetrexed (as pemetrexed disodium hemipentahydrate).
Each vial with 20 ml contains 500 mg of pemetrexed (as pemetrexed disodium hemipentahydrate).
Each vial with 40 ml contains 1000 mg of pemetrexed (as pemetrexed disodium hemipentahydrate).

The other ingredients are sodium thiosulfate pentahydrate (E539), propylene glycol (E1520), hydrochloric acid (for pH adjustment), sodium hydroxide (E524) (for pH adjustment), water for injection.

**What Pemetrexed Rowex looks like and contents of the pack**
Pemetrexed Rowex is a concentrate for solution for infusion. It is a clear, colourless to yellow or green-yellow solution. Solution practically free of particles.

Pemetrexed Rowex is packed in type I glass vial with bromobutyl rubber stopper and aluminium crimp cap with light blue plastic flip-off.

Each vial contains 4 ml, 20 ml or 40 ml of concentrate for solution for infusion.
Each pack contains 1 vial (with sleeving or without sleeving).

**Marketing Authorisation Holder and Manufacturer**
**Marketing Authorisation Holder**
Rowex Ltd., Bantry, Co. Cork, Ireland.

**Manufacturer**
FAREVA Unterach GmbH, Mondseestrasse 11, 4866 Unterach am Attersee, Austria.

**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:**

| | |
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| Austria | Pemetrexed Sandoz 25 mg/ml – Konzentrat zur Herstellung einer Infusionslösung |
| Belgium | Pemetrexed Sandoz 25 mg/ml concentraat voor oplossing voor infusie |
| Bulgaria | Пеметрексед Сандоз 25 mg/ml концентрат за инфузионен разтвор |

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|---|---|
| Croatia | Pemetreksed Sandoz 25 mg/ml koncentrat za otopinu za infuziju |
| Denmark | Pemetrexed Hexal |
| Greece | Pemetrexed/EBEWE 25mg/ml πυκνό διάλυμα για παρασκευή διαλύματος προς έγχυση |
| Spain | Pemetrexed Ebewe 25mg/ml concentrado para solución para perfusión |
| Finland | Pemetrexed Hexal 25 mg/ml Infuusiokonsentraatti, liuosta varten |
| France | Pemetrexed GNR 25 mg/ml, solution à diluer pour perfusion |
| Ireland | Pemetrexed Rowex 25 mg/ml concentrate for solution for infusion |
| Iceland | Pemetrexed Hexal 25 mg/ml Koncentrat til infusionsvæske, opløsning |
| Italy | Pemetrexed Sandoz BV |
| Lithuania | Pemetrexed Ebewe 25mg/ml koncentratas infuziniam tirpalui |
| Norway | Pemetrexed Hexal |
| Poland | Pemetrexed Sandoz |
| Portugal | Pemetrexedo Sandoz |
| Romania | Pemetrexed Sandoz 25mg/ml concentrat pentru solutie perfuzabilă |
| Sweden | Pemetrexed Hexal 25 mg/ml Koncentrat till infusionsvätska, lösning |
| Slovenia | Pemetreksed Sandoz 25 mg/ml koncentrat za raztopino za infundiranje |
| The Netherlands | Pemetrexed Sandoz 25 mg/ml, concentraat voor oplossing voor infusie |
| United Kingdom (Northern Ireland) | Pemetrexed Sandoz 25 mg/ml Concentrate for solution for infusion |

**This leaflet was last revised in 01/2023.**

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The following information is intended for healthcare professionals only:

Special precautions for disposal and other handling.

***Pemetrexed solutions are for single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements for cytotoxic agents***.

1. Use aseptic technique during dilution of pemetrexed for intravenous infusion administration.
2. Calculate the dose and the number of Pemetrexed Rowex vials needed. Each vial contains an excess of pemetrexed concentrate to facilitate delivery of label amount.
3. The appropriate volume of pemetrexed concentrate must be further diluted to 100 ml with sodium chloride 9 mg/ml (0.9%) solution for injection (without preservative) or with glucose 50 mg/ml (5%) solution for injection (without preservative) 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.
5. Parenteral medicinal products must be inspected visually for particulate matter and discolouration prior to administration. If particulate matter is observed, do not administer.

**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 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.