PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: **S4**

PEMETREXED 500 mg/20 mL FRESENIUS

25 mg/mL concentrate for solution for infusion

Pemetrexed

Sugar free

Read all of this leaflet carefully before PEMETREXED 500 mg/20 mL FRESENIUS is administered to you

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse, or other health care provider.

What is in this leaflet

1. What PEMETREXED 500 mg/20 mL FRESENIUS is and what it is used for

PEMETREXED 500 mg/20 mL FRESENIUS is a medicine that prevents growth of certain cancer cells.

PEMETREXED 500 mg/20 mL FRESENIUS is given alone or in combination with cisplatin (another anticancer medicine) in the treatment of certain types of lung cancers.

2. What you need to know before PEMETREXED 500 mg/20 mL FRESENIUS is administered to you

PEMETREXED 500 mg/20 mL FRESENIUS should not be administered to you

- if you are hypersensitive (allergic) to pemetrexed or any of the other ingredients of PEMETREXED 500 mg/20 mL (listed in section 6);
- if you have just had a yellow fever vaccine.

Warnings and precautions

Tell your doctor or healthcare provider before being given the injection:

Special care should be taken with PEMETREXED 500 mg/20 mL FRESENIUS:

- if you have problems with your kidneys, as you may not be able to receive PEMETREXED 500 mg/20 mL FRESENIUS
- if you have taken anti-inflammatory medicines within 5 days before your treatment with PEMETREXED 500 mg/20 mL FRESENIUS starts, as this may lead to kidney problems
- if you have dehydration, hypertension of diabetes, as you may be at risk of kidney problems while receiving PEMETREXED 500 mg/20 mL FRESENIUS
- if you have heart disease or a history of heart disease, as you may be at risk of serious heart conditions while receiving PEMETREXED 500 mg/20 mL FRESENIUS
- if you have recently been vaccinated, as this may cause suppression of the immune system
- if you are a male planning to father a child, as PEMETREXED 500 mg/20 mL FRESENIUS can have genetically damaging effects. Do not to father a child during the treatment and up to 6 months thereafter. Use contraceptive measures or abstinence. Seek counselling on sperm

storage before starting treatment as PEMETREXED 500 mg/20 mL FRESENIUS may cause irreversible infertility

- if you are a woman planning to become pregnant, as PEMETREXED 500 mg/20 mL FRESENIUS may harm your unborn baby. Use effective contraception and avoid becoming pregnant during treatment with PEMETREXED 500 mg/20 mL FRESENIUS
- if you had radiation therapy prior to treatment with PEMETREXED 500 mg/20 mL FRESENIUS, or if you are going to have radiation therapy during or after treatment with PEMETREXED 500 mg/20 mL FRESENIUS, as this may lead to inflammation of the lungs
- if you have ever had, or are going to have radiation therapy, as there may be an early or late radiation reaction with PEMETREXED 500 mg/20 mL FRESENIUS.

While you are treated with PEMETREXED 500 mg/20 mL FRESENIUS:

PEMETREXED 500 mg/20 mL FRESENIUS may suppress your bone marrow function. Your doctor may therefore perform regular blood tests to monitor changes in your blood count (see "**Possible side effects**"), to determine what your dosage should be and what the dose intervals should be.

To limit blood-related side effects, your doctor may instruct you to take folic acid and vitamin B_{12} before your treatment with PEMETREXED 500 mg/20 mL FRESENIUS starts.

To prevent the incidence and severity of skin reactions, your doctor may instruct you to take a corticosteroid like dexamethasone before your treatment with PEMETREXED 500 mg/20 mL FRESENIUS starts. Tell your doctor immediately if you develop skin reactions.

If you are also receiving cisplatin, your doctor will ensure that you are properly hydrated and that you receive appropriate treatment before and after receiving cisplatin to prevent nausea and vomiting.

Children and adolescents

You should not receive PEMETREXED 500 mg/20 mL FRESENIUS if you are under 18 years of age because it is unlikely to be safe.

Other medicines and PEMETREXED 500 mg/20 mL FRESENIUS

Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

Tell your doctor if you are taking, or have received any of the following:

- Medicines that may affect the kidneys such as aminoglycosides, loop diuretics, platinum compounds, ciclosporin, probenecid and penicillin.
- Anti-inflammatory medicines such as ibuprofen and aspirin, especially in high doses.
- Medicines to prevent blood clotting.
- Yellow fever vaccine or other vaccines.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist, or other healthcare provider for advice before taking PEMETREXED 500 mg/20 mL FRESENIUS.

Pregnancy

PEMETREXED 500 mg/20 mL FRESENIUS may harm your unborn baby. Use effective contraception and avoid becoming pregnant during treatment with PEMETREXED 500 mg/20 mL FRESENIUS.

Breastfeeding

It is not known if PEMETREXED 500 mg/20 mL FRESENIUS appears in breastmilk. You should not breastfeed your baby while receiving PEMETREXED 500 mg/20 mL FRESENIUS because it could affect your baby.

Fertility

PEMETREXED 500 mg/20 mL FRESENIUS can have genetically damaging effects. Do not to father a child during the treatment and up to 6 months thereafter. Use contraceptive measures or abstinence. Seek counselling on sperm storage before starting treatment as PEMETREXED 500 mg/20 mL FRESENIUS may cause irreversible infertility.

Driving and using machines

PEMETREXED 500 mg/20 mL FRESENIUS may make you feel tired, cause eyesight problems or neuropathy (a condition affecting peripheral nerves, causing pain, weakness, and numbness in specific areas) (see "**Possible side effects**"). Do not drive or use tools or machines if this happens.

It is not always possible to predict to what extent PEMETREXED 500 mg/20 mL FRESENIUS may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which PEMETREXED 500 mg/20 mL FRESENIUS affects them.

3. How PEMETREXED 500 mg/20 mL FRESENIUS will be administered to you

You will not be expected to give yourself PEMETREXED 500 mg/20 mL FRESENIUS. It will be given to you by a person who is qualified to do so.

The usual dose of PEMETREXED 500 mg/20 mL FRESENIUS 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 500 mg/20 mL FRESENIUS solution with 0,9 % sodium chloride injection or with 5 % glucose intravenous infusion before it is given to you.

You will always receive PEMETREXED 500 mg/20 mL FRESENIUS by infusion into one of your veins. The infusion will last approximately 10 minutes.

When using PEMETREXED 500 mg/20 mL FRESENIUS 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 500 mg/20 mL FRESENIUS has finished. The infusion of cisplatin will last approximately 2 hours.

You should usually receive your infusion once every 3 weeks.

If you have the impression that the effect of PEMETREXED 500 mg/20 mL FRESENIUS is too strong or too weak, tell your doctor or pharmacist.

Additional medicines:

Corticosteroids: your doctor will prescribe you steroid tablets (equivalent to 4 mg of dexamethasone twice a day) that you will need to take on the day before, on the day of, and the day after

PEMETREXED 500 mg/20 mL FRESENIUS 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 1 000 mcg) that you must take once a day while you are taking PEMETREXED 500 mg/20 mL FRESENIUS.

You must take at least 5 doses during the seven days before the first dose of PEMETREXED 500 mg/20 mL FRESENIUS. You must continue taking the folic acid for 21 days after the last dose of PEMETREXED 500 mg/20 mL FRESENIUS.

You will also receive an injection of vitamin B_{12} (1 000 mcg) in the week before administration of PEMETREXED 500 mg/20 mL FRESENIUS and then approximately every 9 weeks (corresponding to 3 courses of PEMETREXED 500 mg/20 mL FRESENIUS treatment).

Vitamin B_{12} and folic acid are given to you to reduce the possible toxic effects of the anticancer treatment.

If you receive more PEMETREXED 500 mg/20 mL FRESENIUS than you should

Since a healthcare provider will administer PEMETREXED 500 mg/20 mL FRESENIUS, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you forget to receive PEMETREXED 500 mg/20 mL FRESENIUS

Since a healthcare provider will administer PEMETREXED 500 mg/20 mL FRESENIUS, it is unlikely that the dose will be missed.

4. Possible side effects

PEMETREXED 500 mg/20 mL FRESENIUS can have side effects.

Not all side effects reported for PEMETREXED 500 mg/20 mL FRESENIUS are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving PEMETREXED 500 mg/20 mL FRESENIUS, please consult your healthcare provider for advice.

If any of the following happens, stop taking PEMETREXED 500 mg/20 mL FRESENIUS and tell your doctor immediately or go to the casualty department at your nearest hospital:

• Swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing.

• Rash or itching.

• Fainting.

These are all very serious side effects. If you have them, you may have had a serious reaction to PEMETREXED 500 mg/20 mL FRESENIUS. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

• sepsis (blood poisoning);

• signs of recurrent infections such as fever, sweating or sore throat;

• bleeding or bruising more easily than normal;

• stroke (sudden numbness or weakness in the face, arm or leg, especially on one side of your body, sudden confusion or trouble speaking);

• bleeding within your skull (causing symptoms such as headache, blurred vision, weakness);

• heart problems which can cause shortness of breath or ankle swelling (cardiac failure)

• changes in the way your heart beats (beating faster or slower);

• chest pain;

• heart attack (pain in your chest, back, jaw and other areas of your upper body that lasts more than a few minutes or that goes away and comes back, shortness of breath);

• yellowing of your skin and eyes, dark urine, and tiredness which may be symptoms of liver problems;

• painful, blistering or peeling skin rash, such as Stevens-Johnson syndrome or toxic epidermal necrolysis;

• passing less urine than is normal for you;

• difficulty breathing, sudden breathlessness, intense chest pain or cough with bloody sputum (it may indicate a blood clot in the blood vessels of your lungs);

• stomach pain, inflammation of your colon that can cause discomfort and bloody stools, passage of bright red blood from your anus.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

• infection, sore throat;

• tiredness, feeling faint, becoming easily breathless (decreased haemoglobin levels);

• loss of fluid (dehydration);

• damage to your motor nerves (muscle weakness and atrophy (wasting) primary in the arms and legs)

• damage to your sensory nerves (loss of sensation, burning pain and unsteady gait);

• dizziness;

• inflammation or swelling of the conjunctiva (the membrane that lines your eyelids and covers the white of your eye);

• dry eyes or watery eyes;

• dryness of your conjunctiva (the membrane that lines the eyelids and covers the white of your eye) and cornea (the clear layer in front of your iris and pupil);

• swelling of your eyelids;

• redness or sores in your mouth, throat, on your lips;

• loss of appetite, vomiting (being sick), diarrhoea, nausea (feeling sick), indigestion, constipation, stomach pain, change in taste

• inflammation and ulceration of the mucous membranes lining the digestive tract;

• changes in liver function results when blood tests are done;

• increased skin pigmentation;

• hair loss (temporary);

• red, often itchy spots, similar to the rash of measles which starts on your limbs and sometimes on your face and the rest of your body (erythema multiforme);

• abnormal blood tests showing reduced functionality of kidneys;

• tiredness, fever, pain.

Less frequent side effects:

• deficient blood distribution to your limbs;

• inflammation and pain in the tube that connects the throat and stomach (oesophagus);

• redness of your skin;

• scaly, flaky, itchy, and red skin rash with fluid-filled blisters (bullous dermatitis);

• inflammation of the skin and fat beneath the skin (pseudocellulitis);

• eczema (inflamed, itchy, cracked, and rough skin);

• inflammation, swelling, redness and erosion of the mucosal surface of your oesophagus caused by radiation therapy;

• inflammation of your lungs caused by radiation therapy;

• skin rash that develops throughout a previously irradiated area.

Frequency unknown:

• a form of diabetes primarily due to kidney problems (nephrogenic diabetes insipidus).

• renal tubular necrosis (a kidney disorder involving damage to the tubule cells of the kidney).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of PEMETREXED 500 mg/20 mL FRESENIUS.

Patients are asked to report any suspected adverse drug reactions to their healthcare provider or Holder of the Certificate of Registration at the following email address: safety.fksa@fresenius-kabi.com and to the relevant medicine's regulatory authority in the country where the product is marketed.

5. How to store PEMETREXED 500 mg/20 mL FRESENIUS

Store all medicines out of reach of children.

Unopened vial: Store at or below 25 °C.

Diluted solution

PEMETREXED 500 mg/20 mL FRESENIUS contains no antibacterial preservative. For the diluted solution, chemical and physical in-use stability has

been demonstrated for 21 days when stored between 2 °C and 8 °C and 7 days when stored at or below 25 °C.

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 store in a bathroom.

Do not use after the expiry date stated on the label.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What PEMETREXED 500 mg/20 mL FRESENIUS contains

The active substance in each 1 mL is 25 mg pemetrexed as pemetrexed diacid.

The other ingredients are hydroxypropylbetadex, hydrochloric acid (for pH adjustment), trometamol (for pH adjustment) and water for injection.

Sugar free.

What PEMETREXED 500 mg/20 mL FRESENIUS looks like and contents of the pack

PEMETREXED 500 mg/20 mL FRESENIUS is a colourless to slightly yellowish or yellow-greenish solution.

The diluted product is a clear, colourless or yellow-greenish solution free from visible particles.

20 mL concentrate in a 30 mL clear glass vial.

Pack of 1 vial in a carton

Holder of Certificate of Registration

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Access to the corresponding Professional Information

The professional information will be printed and packaged with the product.