PATIENT INFORMATION LEAFLET FOR PEMJECT

SCHEDULING STATUS S4

PEMJECT 500 mg powder for solution for infusion

Pemetrexed

PEMJECT contains sugar (mannitol, 500 mg)

Read all of this leaflet carefully before you receive PEMJECT.

- 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 PEMJECT is and what it is used for
2. What you need to know before you receive PEMJECT
3. How PEMJECT should be administered
4. Possible side effects
5. How to store PEMJECT
6. Contents of the pack and other information

1. What PEMJECT is and what it is used for

PEMJECT is used for the treatment of cancer.

PEMJECT 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.

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

PEMJECT 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.

PEMJECT 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 receive PEMJECT

PEMJECT should not be administered to you:

- If you are hypersensitive (allergic) to pemetrexed or any other ingredient of PEMJECT (see section 6).
- If you have recently received or are about to receive a vaccine against yellow fever.

Warnings and precautions

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

Special care should be taken with PEMJECT:

- If you currently have or have previously had problems with your kidneys. 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 PEMJECT. 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.
- To lower your chances of side effects of PEMJECT, you must also take folic acid and vitamin B_{12} prior to and during treatment with PEMJECT.
- Your doctor will prescribe a medicine called a corticosteroid during your treatment with PEMJECT. Corticosteroid medicines lower your chances of getting skin reactions with PEMJECT.
- Please tell your doctor if you are taking any medicine for pain or inflammation

(swelling) including medicines purchased without a doctor's prescription. Do not take a long-acting anti-inflammatory medicine during the period 5 days before to at least 2 days after receiving PEMJECT, including the day you receive your treatment. If you are unsure that your anti-inflammatory has a long duration of activity, discuss it with your doctor or pharmacist before receiving PEMJECT. In addition, if you have problems with your kidneys, tell your doctor or pharmacist, as you may not be able to take short-acting anti-inflammatory medicines during the period at least 2 days before to at least 2 days after receiving PEMJECT, including the day you receive your treatment.

- If you have an accumulation of fluid around your lungs, your doctor may decide to remove the fluid before giving you PEMJECT.
- If you are also receiving cisplatin with PEMJECT, 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 heart disease or a history of heart disease, please tell your doctor.
- If you have been recently vaccinated, please tell your doctor, as this can possibly cause bad effects with PEMJECT.
- If you are a sexually mature male, you should not father a child during treatment with PEMJECT and up to 6 months thereafter. Men should seek counselling on sperm storage before starting treatment since PEMJECT may cause irreversible infertility.
- If you are a woman of childbearing potential, you should use effective contraception during treatment with PEMJECT.
- If you had or are going to have radiation therapy, please tell your doctor, as there may be an early or late radiation reaction with PEMJECT.

If any of the above applies to you (or you are not sure), consult your doctor, pharmacist or healthcare professional before you are given PEMJECT.

Children and adolescents

PEMJECT has not been studied in children. There is no relevant use of PEMJECT in the

paediatric population.

Other medicines and PEMJECT

Always tell your health care professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

Tell your doctor or pharmacist if you are currently using any of the following medicines which could delay the removal of PEMJECT from your kidneys, and thereby prolong the effects of PEMJECT or increase the occurrence of side effects:

- Aminoglycoside and penicillin antibiotics (used to treat bacterial infections)
- Probenecid (used to treat gout)
- Loop diuretics (used to treat hypertension and oedema due to congestive heart failure or kidney problems).
- Platinum compounds (e.g. cisplatin, used to treat cancer).
- Ciclosporin (used to prevent organ rejection after a kidney, heart, or liver transplant; to treat severe psoriasis or to treat severe rheumatoid arthritis).
- Nonsteroidal anti-inflammatory medicines (NSAIDs, e.g. ibuprofen, piroxicam or high doses of aspirin, used to treat pain and inflammation).

Tell your doctor or pharmacist if you are currently using any of the following medicines, since PEMJECT may affect how well these medicines work:

- Oral anticoagulant medicines (used to stop your blood from clotting).
- Vaccines (medicines to make your immune system learn to fight an infectious disease).

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking PEMJECT. PEMJECT should be avoided during pregnancy due to possible harm to the unborn baby. Women are therefore advised not to become pregnant

while being treated with PEMJECT. Women must use effective contraception during treatment with PEMJECT.

You should not breastfeed your baby during PEMJECT treatment.

Men are advised not to father a child during and up to 6 months following treatment with PEMJECT and should use effective contraception during treatment with PEMJECT and for up to 6 months afterwards. If you would like to father a child during the treatment or in the 6 months following treatment, seek advice from your doctor or pharmacist.
You may want to seek counselling on sperm storage before starting PEMJECT.

Driving and using machines

PEMJECT may make you feel tired. Therefore, you should not drive or use machines until you know how PEMJECT will affect you.

3. How PEMJECT should be administered

You will not be expected to give yourself PEMJECT. PEMJECT will always be prepared and given to you by a healthcare professional qualified to do so.
The usual dose of PEMJECT is 500 mg for every square metre of your body's surface area. Your height and body mass 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. Your healthcare professional will have mixed the PEMJECT powder with 0,9 % sodium chloride solution for injection before it is given to you. You will always receive PEMJECT by infusion into one of your veins. The infusion will last approximately 10 minutes.

When receiving PEMJECT in combination with cisplatin

Your healthcare professional will work out the dose you need based on your height and body

mass. Cisplatin is also given by infusion into one of your veins, and is given approximately 30 minutes after the infusion of PEMJECT has finished. The infusion of cisplatin will last approximately 2 hours.

You should usually receive your infusion every 3 weeks.

Additional medicines

Corticosteroids:

Your doctor will prescribe 4 mg of dexamethasone orally, twice a day, that you will need to take on the day before, on the day of, and the day after PEMJECT treatment. A corticosteroid 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 – 1000 *µg*) that you must take once a day while you are receiving PEMJECT. You must take at least 5 doses during the 7 days before the first dose of PEMJECT. You must continue taking the folic acid for 21 days after the last dose of PEMJECT. You will also receive an injection of vitamin B_{12} (1 000 *µg*) in the week before administration of PEMJECT and then approximately every 9 weeks (corresponding to 3 cycles of PEMJECT 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 PEMJECT, ask your doctor or pharmacist.

If you have been given more PEMJECT than you should receive

Since a healthcare professional will administer PEMJECT, they will decide how much PEMJECT you need and for how long each day. However, in the event of an overdose, your doctor will manage the overdose.

Signs of an overdose may include changes in your blood which could make you feel unwell,

inflammation and sores in the digestive tract, numbness of the hands and feet, rash or infection with or without fever, diarrhoea and stomach pain or bloating.

If you miss a dose of PEMJECT

Since a health care provider will administer PEMJECT, it is unlikely that the dose will be missed.

4. Possible side effects

PEMJECT can have side effects.

Not all side effects reported for PEMJECT are included in this leaflet.

Should your general health worsen or if you experience any untoward effects while receiving PEMJECT, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, stop receiving PEMJECT and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of your hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing,
- Rash or itching,
- If you experience tiredness, feeling faint, becoming breathless easily or if you look pale (since you might have less haemoglobin in your red blood cells than normal)

These are all very serious side effects. If you have them, you may have had a serious reaction to PEMJECT. 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:

- Angina (chest pain caused by decreased blood flow to your heart), changes in the way your heart beats (if you notice it is beating faster or slower), heart attack (pressure, tightness, pain, or a squeezing or aching sensation in your chest or arms that may spread to your neck, jaw or back).

- Difficulty breathing, shortness of breath, including a dry cough, interstitial pneumonitis (scarring of the air sacs of the lung).
- Sepsis (severe infection in your blood which may lead to death).
- Serious kidney or liver problems including kidney failure and hepatitis (inflammation of the liver). Symptoms may include a reduced amount of urine, swelling of your legs, ankles and feet from retention of fluids and yellowing of your skin and eyes (jaundice), pain in your upper right abdomen and sleepiness.
- Stroke with symptoms of numbness or paralysis in the face, leg, or arm, most likely on just one side of the body
- Serious skin conditions (blistering skin diseases) including Stevens-Johnson syndrome and toxic epidermal necrolysis
- Tissue death of the extremities (gangrene) due to loss of blood supply or bacterial infection in open wounds.

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:

- Recurrent infections including fever or sore throat, infection without decreased levels of white blood cells.
- If you experience bleeding from the gums, nose or mouth or any bleeding that does not stop, reddish or pinkish urine, unexpected bruising (due to changes in your blood)
- The development of fever, often with other signs of infection, in patients with an abnormally low number of neutrophil granulocytes (a type of white blood cell) in the blood
- Dehydration
- Loss of sensation, taste disturbance, muscle weakness and wasting, numbness and tingling feeling of the extremities
- Conjunctivitis (inflammation in the eyes), decreased tear production and/or increased tear evaporation, increased secretion of tears

- Nausea (feeling sick), vomiting (being sick), redness, swelling or sores in your mouth, sore throat, severe weight loss, painful inflammation and ulceration of the mucous membranes lining the digestive tract, diarrhoea, constipation, indigestion, heartburn, abdominal pain
- Rash, hair loss (temporary), hives, skin peeling, severe itching, patches of skin becomes darker in colour than the normal surrounding skin
- Kidneys and liver: abnormal blood tests
- Unusual weakness or tiredness, raised body temperature, chest pain, fever, pain, oedema (excess fluid in body tissue, causing swelling).

Less frequent side effects:

- Chest pain.
- Too few blood cells (all types) which would be confirmed in a blood test.
- Colitis (inflammation of the lining of the large bowel, which may be accompanied by intestinal or rectal bleeding).
- 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.

Side effects of unknown frequency:

- Redness of the skin or mucous membranes of the lower limbs, occurring with skin injury, infection, or inflammation.
- A type of diabetes primarily due to problems of the kidney (chronic excessive thirst and excessive urine production)
- Damage to a part of your kidneys due to a lack of oxygen and blood flow to the kidneys, resulting in dehydration or excessive thirst, small amount of urine output, swelling and fluid retention, nausea and vomiting.

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 or pharmacist.

This includes any possible side effect not listed in this leaflet. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of PEMJECT.

5. How to store PEMJECT

Store all medicines out of reach of children.

Store at or below 30 °C.

Do not freeze.

From a microbiological point of view, PEMJECT 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 4 hours at or below 25 °C or 24 hours at 2 to 8 °C, unless reconstitution and dilution have taken place in controlled validated aseptic conditions.

6. Contents of the pack and other information

What PEMJECT contains:

The active substance is 500 mg pemetrexed.

When reconstituted, PEMJECT solution contains 25 mg/ml pemetrexed.

The other ingredient is mannitol.

What PEMJECT looks like and contents of the pack:

PEMJECT powder for solution for infusion is a white or off-white loose lump or powder.

After reconstitution PEMJECT is a clear, light yellow, green solution.

PEMJECT is contained in a 50 mL type I, clear, colourless glass vial, sealed with a 20 mm grey bromobutyl rubber stopper, secured with a 20 mm aluminium seal with a blue flip-off

cap, packed in an outer carton.

Holder of Certificate of Registration

Lamar International (Pty) Ltd

2 Waterford Mews

Waterford Place

Century City

7441

Cape Town

South Africa

Registration number

51/26/1066