PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

PEXITAZ 100 Powder for solution for infusion

PEXITAZ 500 Powder for solution for infusion

(Pemetrexed)

(Contains mannitol)

Read all of this leaflet carefully before you are given PEXITAZ.

- 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 PEXITAZ is and what it is used for

PEXITAZ is a medicine used in the treatment of cancer.

PEXITAZ 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.

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

PEXITAZ 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.

PEXITAZ 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 PEXITAZ

Do not use PEXITAZ:

- if you are hypersensitive (allergic) to pemetrexed or any of the other ingredients of PEXITAZ (listed in section 6).
- if you are pregnant or breastfeeding your baby.
- if you have recently received or are about to receive a vaccine against yellow fever.

Warnings and precautions

Tell your doctor or health care provider before being given the injection:

- 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 PEXITAZ.
- 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 PEXITAZ. 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 PEXITAZ.
- If you have been recently vaccinated, please tell your doctor, as this can possibly cause bad effects with PEXITAZ.
- 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 PEXITAZ.
- If you are taking any medicine for pain or inflammation (swelling), 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 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.
- If you experience skin reactions during your anticancer treatment, your doctor may then prescribe corticosteroids to reduce the frequency and severity of the skin reactions.

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

Children and adolescents

There is no relevant use of pemetrexed in the paediatric population.

Other medicines and PEXITAZ

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

Certain nephrotoxic medicine (medicine causing injury to the kidneys such as aminoglycosides (antibiotic), loop-diuretics (water tablets), platinum compounds (medicine used to treat cancer), ciclosporin medicine used in organ or bone marrow transplantation) may interact with PEXITAZ and cause a delay in the excretion of PEXITAZ from the body.

Concomitant administration of probenecid (medicine used for treatment of gout), penicillin (antibiotic), proton pump inhibitors (PPIs)) (medicine used for treatment of heartburn/indigestion) could potentially cause a delay in the excretion of PEXITAZ from the body.

Higher doses of anti-inflammatory medicines (taken for pain and inflammation) may decrease the elimination of PEXITAZ from the body. Depending on the advice of your physician, treatment with these medicines may need to be interrupted 2 to 5 days before administration of PEXITAZ.

Possible interaction between anticoagulants (blood thinning (medicines) and PEXITAZ may require more frequent blood

tests and monitoring.

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

Your doctor and pharmacist have more information on medicines to be careful with or avoid while receiving PEXITAZ

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 health care provider for advice before taking PEXITAZ.

Pregnancy

The use of PEXITAZ should be avoided during pregnancy due to possible harm to the baby. Your doctor will discuss with you the potential risk of taking PEXITAZ during pregnancy. Women are therefore advised not to become pregnant while being treated with PEXITAZ .Women must use effective contraception during treatment with PEXITAZ.

Breastfeeding

You should not breastfeed your baby during PEXITAZ

treatment.

Fertility

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

PEXITAZ may make you feel tired. You should not drive a car or use machines until you know how PEXITAZ will affect you.

PEXITAZ contains sodium

PEXITAZ 100 contains 11 mg (< 1 mmol) sodium per vial, i.e. it is essentially “sodium-free”.

PEXITAZ 500 contains approximately 54 mg (2,35 mmol) sodium per vial. You should take into consideration if you are on a controlled sodium diet.

3. How to use PEXITAZ

Do not share medicines prescribed for you with any other

person.

You will not be expected to give yourself PEXITAZ. It will be given to you by a person who is qualified to do so.

The usual dose of PEXITAZ 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 PEXITAZ powder with 9 mg/ml (0,9 %) sodium chloride solution for injection before it is given to you.

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

You should usually receive your infusion once every 3 weeks.

When using PEXITAZ 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 PEXITAZ has finished. The infusion of cisplatin will last approximately 2 hours.

Additional medicines:

Corticosteriods: 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 PEXITAZ 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 PEXITAZ. You must take at least 5 doses during the seven days before the first dose of PEXITAZ. You must continue taking the folic acid for 21 days after the last dose of PEXITAZ. You will also receive an injection of vitamin B_{12} (1000 micrograms) in the week before administration of PEXITAZ and then approximately every 9 weeks (corresponding to 3 courses of PEXITAZ treatment). Vitamin B_{12} and folic acid are given to you to reduce the possible toxic effects of the anticancer treatment.

Your doctor will tell you how long your treatment with PEXITAZ will last. If you have the impression that the effect of PEXITAZ is too strong or too weak, tell your doctor or pharmacist.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

If you are given more PEXITAZ than you should

Since a health care provider will administer PEXITAZ, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you experience any side effects after being given PEXITAZ, immediately tell your doctor or nurse or go to the Emergency Department at your nearest hospital. You may need urgent medical attention.

If you missed a dose of PEXITAZ

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

4. Possible side effects

PEXITAZ can have side effects.

Not all side effects reported for PEXITAZ are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking PEXITAZ, please consult your healthcare provider for advice.

If any of the following happens while you are being treated with PEXITAZ, tell your doctor immediately or go to the casualty department of your nearest hospital:

- severe allergic reaction (anaphylactic shock); signs and symptoms include:

  - skin reactions, including hives and itching and flushed or pale skin.

  - low blood pressure (hypotension).

  - constriction of your airways and a swollen tongue or throat, which can cause wheezing and trouble breathing.

  - a weak and rapid pulse.

  - nausea, vomiting or diarrhea.

  - dizziness or fainting
- skin rash/hives, itching, burning or prickling sensation, fever, swelling of hands, feet, ankles, face, lips and mouth or throat which may cause difficulty in swallowing or breathing (allergic reaction),
- 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),
- skin rash, which may form blisters and looks like small targets (central dark spots surrounded by a paler area, with a dark ring around the edge) [erythema

multiforme].

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

Frequent side effects:

- fever or infection: 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). Infection (sepsis) may be severe and could lead to death,
- pain, redness, swelling or sores in your mouth,
- tiredness, feeling faint, becoming easily breathless or if you look pale (since you might have less haemoglobin than normal),
- 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).

Less frequent side effects:

- chest pain or having a fast heart rate,

- sudden breathlessness, intense chest pain or cough with bloody sputum (may indicate a blood clot in the blood vessels of the lungs),
- inflammation of the liver characterised by yellow pigmentation to the skin, mucus membrane or eyes, pale coloured stools, dark coloured urine, skin itch, rash, pain (hepatitis),
- inflammation of the lining of the large bowel, which may be accompanied by intestinal or rectal bleeding,
- scarring of the air sacs of the lung (interstitial pneumonitis),
- some patients have experienced a heart attack, stroke or “mini-stroke” while receiving PEXITAZ usually in combination with another anticancer therapy,
- inflammation of the lining of the oesophagus (gullet) has been experienced with pemetrexed/ radiation therapy.

Frequency unknown:

- passing much more or much less urine than usual, which may be a symptom of a type of kidney problem (renal tubular necrosis).

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:

- loose stools (diarrhoea),
- feeling or being sick,
- indigestion,
- loss of appetite,
- tiredness,
- skin rash,
- hair loss,
- constipation,
- loss of sensation,
- kidney: abnormal blood tests,
- fever,
- dehydration,
- kidney failure,
- irritation of the skin and itching,
- inflamed eye (conjunctivitis),
- swelling of the eyelids
- taste change,
- liver: increased alanine and aspartate aminotransferase (blood test),
- excess fluid in body tissue, causing swelling (oedema),
- pain,

- increased skin pigmentation,
- muscle weakness,
- pain in the abdomen.

Less frequent side effects:

- watery eyes,
- pancytopenia- combined low counts of white cells, red cells and platelets,
- irregular heartbeat,
- increased gamma-glutamyl transferase,
- hives.

Frequency unknown:

- scarring of the air sacs of the lung associated with radiation therapy (radiation pneumonitis) may occur in patients who are also treated with radiation either before, during or after their pemetrexed therapy,
- extremity pain, low temperature and discolouration have been reported,
- skin rash like severe sunburn (radiation recall) which can occur on skin that has previously been exposed to radiotherapy, from days to years after the radiation,
- antibody-mediated destruction of red blood cells (immune mediated haemolytic anaemia),
- lower limb swelling with pain and redness,

- thirst and increased water consumption,
- increased sodium in blood,
- inflammation of the skin, mainly of the lower limb with swelling, pain and redness.

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 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 "**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 PEXITAZ.

5. How to store PEXITAZ

Store all medicines out of reach of children.

Store at or below 25 °C (Room temperature).

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

After reconstitution, PEXITAZ should be used immediately. When prepared as directed, chemical and physical in-use stability of reconstituted and infusion solutions of PEXITAZ were demonstrated for 24 hours at refrigerated temperature.

6. Contents of the pack and other information

What PEXITAZ contains

- The active ingredient is pemetrexed.
- The other ingredients are hydrochloric acid, mannitol (sugar), nitrogen pure, sodium hydroxide

PEXITAZ 100

Each vial contains 100 mg of pemetrexed (as pemetrexed disodium heptahydrate).

Contains sugar: mannitol

PEXITAZ 500

Each vial contains 500 mg of pemetrexed (as pemetrexed disodium heptahydrate).

Contains sugar: mannitol

The reconstituted **PEXITAZ** solution contains 25 mg/ml pemetrexed.

What PEXITAZ looks like and contents of the pack

PEXITAZ 100:

Powder for solution for infusion.

White to either light yellow or green yellow lyophilizsed powder.

Powder for solution for infusion.

White to either light yellow or green yellow lyophilizsed powder.

Each carton contains a 10 ml colourless tubular vial with grey rubber stopper and sealed with light green F/O both sides clear lacquer coated seal.

PEXITAZ 500:

Powder for solution for infusion.

White to either light yellow or green yellow lyophilizsed powder.

Each carton contains a 50 ml colourless moulded vial with grey rubber stopper and sealed with light green F/O both sides clear lacquer coated seal.

Holder of Certificate of Registration

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