PATIENT INFORMATION LEAFLET

Scheduling status: S4

PEXALI® 100, powder for concentrate for solution for infusion

PEXALI® 500, powder for concentrate for solution for infusion

Pemetrexed

Contains sugar (mannitol)

PEXALI 100 contains 106,4 mg mannitol per vial and PEXALI 500 contains 500 mg mannitol per vial.

Read all of this leaflet carefully before you are given PEXALI

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- PEXALI has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What PEXALI is and what it is used for

Pemetrexed is an anticancer medicine that inhibits the growth of cancer cells and may reduce tumour size.

PEXALI is used in the treatment for malignant pleural mesothelioma (a type of cancer which affects the lining of the chest cavity). It is given in combination with cisplatin, which is another anticancer medicine.

PEXALI may also be given for advanced stage lung cancer (a certain type, called non-small cell lung cancer) after other anticancer medicines have been used.

2. What you need to know before you use PEXALI

Do not use PEXALI

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

Warnings and precautions

Special care should be taken with PEXALI.

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

- if you currently have, or have previously had, problems with your kidneys, as you may not be able to receive PEXALI;
- if you have heart disease or a history of heart disease;
- if you have recently been vaccinated, as this can cause adverse effects with PEXALI (see “Other medicines and PEXALI”);
- if you have an accumulation of fluid around your lungs, your doctor may decide to remove the fluid before giving you PEXALI;

- 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 PEXALI;
- if you are taking NSAIDs (nonsteroidal anti-inflammatory drugs) (see "Other medicines and PEXALI").

While you are treated with PEXALI your doctor will perform regular blood tests to monitor changes in your blood count (see section 4). 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 may make sure that you are properly hydrated and receive appropriate treatment before and after receiving cisplatin to prevent vomiting (feeling sick).

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

Children and adolescents

PEXALI is not indicated for treatment of children under 18 years.

Other medicines and PEXALI

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 the following medicines which may delay the removal of PEXALI or increase the occurrence of side effects:

- nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, aspirin, piroxicam, rofecoxib. If your kidney function is impaired, NSAIDs should be avoided at least 2 days before, on the day of, and at least 2 days after PEXALI administration;
- Ciclosporin (an immunosuppressant medicine);

- Aminoglycoside antibiotics such as streptomycin, kanamycin, tobramycin, amikacin and penicillin;
- probenecid (medicine to prevent gouty arthritis);
- platinum compounds (such as cisplatin, carboplatin) also used in cancer treatment;
- 'water pills' (loop diuretics) such as furosemide.

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

- anticoagulants (medicines to prevent blood clotting), such as warfarin.
  Your doctor may require more frequent blood tests as oral anticoagulants and anticancer medicines may have an interaction.
- vaccines, particularly yellow fever vaccine
- any other vaccines (medicines to make your immune system learn to fight an infectious disease).

Pregnancy, breastfeeding and fertility

Pregnancy

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 receiving PEXALI.

PEXALI should be avoided during pregnancy due to the potential risk to the foetus. Your doctor will explain to you the potential risk of receiving PEXALI during pregnancy.

Women should avoid becoming pregnant during treatment with PEXALI and must use effective contraception during the treatment.

Breastfeeding

You should not breastfeed your baby while receiving PEXALI because it could affect your baby.

Fertility

Men should not father a child during and up to 6 months following treatment with PEXALI. Effective contraception should be used during treatment with PEXALI 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 get expert advice on sperm storage before you start chemotherapy with PEXALI.

Driving and using machines

PEXALI may make you feel tired and dizzy (see section 4).

Therefore, you should not drive or use machines until you know how PEXALI will affect you**.**

PEXALI contains sodium

PEXALI 100 contains 11 mg (less than 1 mmol) sodium per 100 mg vial and is essentially 'sodium-free'.

PEXALI 500 contains approximately 54 mg of sodium per vial.

You should take this into consideration if you are on a controlled sodium diet.

3. How to receive PEXALI

Do not share medicines prescribed for you with any other person.

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

PEXALI will be administered to you in a specialised unit in hospital.

The usual dose of PEXALI is 500 mg/m^2.

Your doctor will work out what dose you should receive. He/she will consider your diagnosis, your weight and height and kidney function. The dose may be adjusted, or treatment may be delayed depending on your blood cell counts and your general condition.

Your doctor will decide how long your treatment with PEXALI solution for infusion will last.

After appropriate preparation and further dilution with a sterile saline solution, PEXALI will be infused (dripped) into a large vein. The infusion will last approximately 10 minutes. You should usually receive your infusion every 21 days (3 weeks).

Additional medicines

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

Corticosteroids:

It is recommended that you take steroid tablets (equivalent to 4 mg of dexamethasone twice a day) on the day before, on the day of, and on the day after PEXALI 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:

You should also take oral folic acid or a multivitamin containing folic acid (350 to 1 000 micrograms) once a day while you are receiving PEXALI. You should take at

least 5 doses during the 7 days before the first dose of PEXALI. You must continue taking the folic acid for 21 days after the last dose of PEXALI. You will also receive an injection of vitamin B_{12} (1 000 micrograms) in the week before administration of PEXALI and then approximately every 2 to 3 months (corresponding to 3 courses of PEXALI treatment). Vitamin B_{12} and folic acid are given to you to reduce the possible toxic effects of the anticancer treatment.

If you have the impression that the effect of PEXALI is too strong or too weak, tell your doctor of pharmacist.

If you receive more PEXALI than you should

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

Tell your healthcare provider at once if you think you may have been given too much PEXALI.

If you forget to use PEXALI

Since a healthcare provider will administer PEXALI, it is unlikely that the dose will be missed.

4. Possible side effects

PEXALI can have side effects.

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

If the following happens, stop using PEXALI and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Allergic reactions: swelling of the tongue and/or throat, difficulty in swallowing, difficulties in breathing, facial swelling, severe dizziness and a very fast heartbeat with heavy sweating.
- Allergic skin reactions: severe skin rash, burning or prickling sensation, fever, hives, itching, blistering and peeling of the skin (Stevens-Johnson syndrome or toxic epidermal necrolysis).

These are all very serious side effects. If you have them, you may have had a serious reaction to PEXALI. You may need urgent medical attention or further hospitalisation.

Tell your doctor immediately if you notice any of the following:

- 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 become severe and could be fatal.
- Skin infections (red, swollen, warm skin). You may have a bacterial infection and need additional medicines.
- Red, inflamed skin (erythema multiforme – an allergic skin condition).
- Sudden breathlessness, intense chest pain or cough with bloody sputum. These symptoms may indicate a blood clot in the blood vessels of the lungs.
- Heart attacks, chest pain (angina), irregular heart rate.
- Strokes or “mini-strokes”, usually in combination with another anticancer therapy.
- Bleeding from the gums, nose or mouth or any bleeding that would not stop, reddish or pinkish urine, unexpected bruising (due to a low platelet count).
- Colitis (inflammation of the lining of the large bowel, which may be accompanied by intestinal or rectal bleeding).

- Drowsiness, thirst, nausea and decreased or no urine (this could be due to damage to the cells in the small tubes of the kidneys).
- Acute renal failure (decreased urinary output, swelling, fatigue).

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:

- low haemoglobin level (anaemia)
- decreased white blood cells
- decreased platelets (blood clotting problems)
- dehydration (feeling tired and thirsty) (in combination with cisplatin)
- loss of sensation (sensory neuropathy)
- taste change
- red, inflamed eyes (conjunctivitis) (in combination with cisplatin)
- nausea
- vomiting
- diarrhoea
- anorexia (eating disorder)
- constipation
- pain, redness, swelling or sores in your mouth
- dyspepsia (heartburn) (in combination with cisplatin)
- hair loss
- skin rash
- peeling of the skin
- kidney disorders (shown by abnormal blood tests)
- fatigue (tiredness)
- liver problems: abnormal blood tests

- increased skin pigmentation
- oedema (excess fluid in body tissue, causing swelling)
- fever.

Less frequent side effects:

- dizziness
- muscle weakness (motor neuropathy)
- haemolytic anaemia (red blood cells are destroyed faster than they can be made)
- peripheral arterial disease (a circulatory problem in which narrowed arteries cause bad circulation and could cause death of tissues in hands or feet)
- conjunctivitis (red, sore eyes), watery eyes
- inflammation of the lining of the oesophagus (gullet) if you have also received radiation therapy
- interstitial pneumonitis (scarring and inflammation of the tissue that surrounds the lung's air sacs, blood vessels and airways)
- 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
- pancytopenia – combined low counts of white cells, red cells and platelets
- radiation pneumonitis (scarring of the air sacs of the lung associated with radiation therapy) may occur in patients who are also treated with radiation either before, during or after their PEXALI therapy.

Frequency unknown:

- skin infections
- thirst with large volumes of urine (diabetes insipidus)
- lower limb swelling with pain and redness.

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**. By reporting side effects, you can help provide more information on the safety of PEXALI.

5. How to store PEXALI

Store all medicines out of reach of children.

Store the vial in the original container, at or below 25 °C. Do not freeze.

Reconstituted and infusion solutions: The product should be used immediately. When prepared as directed, chemical and physical in-use stability of reconstituted and infusion solutions of PEXALI were demonstrated for up to 24 hours after reconstitution of the original vial when refrigerated between 2 to 8 °C and at or below 25 °C.

PEXALI is for single use only; any unused solution must be disposed of in accordance with local requirement.

The expiry date is stated on the label and carton. Your healthcare professional will make sure that PEXALI is not past its expiry date before giving you the injection.

6. Contents of the pack and other information

What PEXALI contains

- The active substance is pemetrexed.

PEXALI 100: Each vial contains 100 milligrams of pemetrexed (as pemetrexed disodium 2,5 hydrate).

PEXALI 500: Each vial contains 500 milligrams of pemetrexed (as pemetrexed disodium 2,5 hydrate).

PEXALI contains:

- about 11 mg sodium per 100 mg vial (essentially 'sodium-free')
- approximately 54 mg of sodium per 500 mg vial.

The other ingredients are mannitol, hydrochloric acid and sodium hydroxide.

Further dilution by a healthcare provider is required prior to administration.

What PEXALI looks like and contents of the pack

White to faint yellow lyophilized cake or powder.

The reconstituted solution is a clear, colourless solution without visible particles.

PEXALI 100: 10 ml clear, colourless, Type I glass vial with a grey butyl rubber stopper and sealed with an aluminium-plastic flip-off cap. Single vial packs.

PEXALI 500: 50 ml clear, colourless, Type I glass vial with a grey butyl rubber stopper and sealed with an aluminium-plastic flip-off cap. Single vial packs.

Not all pack sizes may be marketed.

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