Approved Patient Information Leaflet for NATPEM

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

NATPEM 100 mg concentrate for solution for infusion

NATPEM 500 mg concentrate for solution for infusion

NATPEM 1000 mg concentrate for solution for infusion

Pemetrexed

Sugar free.

Read all of this leaflet carefully before you start using NATPEM:

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist, nurse or other health care provider.
- NATPEM 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 NATPEM is and what it is used for

NATPEM is a medicine used in the treatment of cancer.

NATPEM 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.

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

NATPEM 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.

NATPEM 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 NATPEM

NATPEM should not be administered to you:

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

Warnings and precautions:

Take special care with NATPEM:

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

Children and adolescents:

NATPEM should not be used in children or adolescents, since there is no experience with NATPEM in children and adolescents under 18 years of age.

Other medicines and NATPEM:

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

Tell your doctor or pharmacist if you are currently using:

- Vaccines, or will receive vaccination soon.
- Aminoglycoside antibiotics (used to treat bacterial infections).

- 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 drugs (NSAIDs, e.g. ibuprofen, aspirin, piroxicam or rofecoxib, used to treat pain and inflammation). There are many sorts of NSAIDs with different durations of activity. Based on the planned date of your infusion of NATPEM 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.

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 health care provider for advice before taking NATPEM.

Women must use effective contraception during treatment with NATPEM.

Do not breastfeed while you are receiving NATPEM.

If you are male, you will be advised by your doctor not to father a child during and up to 6 months following treatment with NATPEM. You should therefore use effective contraception during treatment with NATPEM 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:

NATPEM may make you feel tired. Therefore, be careful when driving a vehicle or using machines until you know how NATPEM will affect you.

It is not always possible to predict to what extent NATPEM may interfere with the daily activities of a patient. Patient should ensure that they do not engage in the above activities until they are aware of the measure to which NATPEM affects them.

3. How to use NATPEM

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

You will not be expected to give yourself NATPEM. NATPEM will always be prepared and given to you by a doctor or health care provider who are trained to administer NATPEM.

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.

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

When receiving NATPEM in combination with cisplatin:

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

Additional medicines that will be prescribed to you by your doctor:

To lower your chances of side effects of NATPEM, you must also take folic acid and vitamin B_{12} prior to and during treatment with NATPEM.

Your doctor will also prescribe corticosteroids during your treatment with NATPEM. Corticosteroid medicines lower your chances of getting skin reactions with NATPEM.

If you have any further questions on the use of NATPEM, ask your doctor or health care provider.

If you receive more NATPEM than you should:

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

If you forget to take NATPEM:

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

4. Possible side effects

NATPEM can have side effects.

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

If any of the following happens, stop taking NATPEM 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 NATPEM. 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 experience side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects 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 NATPEM.

5. How to store NATPEM

- Store at or below 25 °C.
- Keep the vial in the outer carton until required for use.
- When prepared as directed, infusion solutions of NATPEM contain no preservatives. Chemical and physical in-use stability of the infusion solution were demonstrated for 24 hours at refrigerated temperature (2 °C – 8 °C). From a microbiological point of view, NATPEM 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 not be longer than 24 hours at 2 °C – 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.
- STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
- Do not use after the expiry date printed on the carton.

- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What NATPEM contains:

NATPEM 100: Each 4 mL vial of NATPEM contains 100 mg pemetrexed.

NATPEM 500: Each 20 mL vial of NATPEM contains 500 mg pemetrexed.

NATPEM 1000: Each 40 mL vial of NATPEM contains 1 000 mg pemetrexed.

Each vial contains 25 mg/mL pemetrexed.

The other ingredients are citric acid (E330), l-arginine (pH adjuster), l-cysteine and propylene glycol.

What NATPEM looks like and contents of the pack:

Clear, colourless to slightly yellow to brown, brown-yellow or green-yellow solution, free from particles.

7 mL / 20 mL / 50 mL type I, clear, colourless glass vial, sealed with a round bromobutyl rubber stopper, an aluminium cap and a blue flip-top, packed in an outer carton.

Pack size: one vial.

Holder of certificate of registration:

Adcock Ingram Limited

1 New Road

Erand Gardens

Midrand 1685

South Africa

Tel. nr: 011 635 0000

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