

1.3.2 PROPOSED PATIENT INFORMATION LEAFLET

Scheduling status: **S4**

APIMEX 100 powder for concentrate for solution for infusion

APIMEX 500 powder for concentrate for solution for infusion

Pemetrexed

Contains sugar (mannitol)

APIMEX 100 contains 106 mg mannitol per vial and APIMEX 500 mg contains 500 mg mannitol per vial.

Read all of this leaflet carefully before you are given APIMEX

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

1. What APIMEX is and what it is used for

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

APIMEX 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.

APIMEX 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 APIMEX

Do not use APIMEX

- if you are hypersensitive (allergic) to pemetrexed or any of the other ingredients of APIMEX (listed in section 6).

Warnings and precautions

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 APIMEX;
- if you have heart disease or a history of heart disease;
- if you have recently been vaccinated, as this can cause adverse effects with APIMEX (see “Other medicines and APIMEX ”);
- if you have an accumulation of fluid around your lungs, your doctor may decide to remove the fluid before giving you APIMEX ;
- 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 APIMEX ;

- if you are taking NSAIDs (nonsteroidal anti-inflammatory drugs) (see “Other medicines and APIMEX”).
- While you are treated with APIMEX 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).

Children and adolescents

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

Other medicines and APIMEX

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

Make sure your doctor knows if you are taking, or have received:

- vaccines, particularly yellow fever vaccine;
- nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, aspirin, piroxicam, rofecoxib;
- anticoagulants (medicines to prevent blood clotting), such as warfarin;
- aminoglycoside antibiotics such as streptomycin, kanamycin, tobramycin, amikacin and penicillin;
- probenecid (medicine to prevent gouty arthritis);
- ‘water pills’, such as furosemide.

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 APIMEX.

Safety in pregnancy and lactation has not been established.

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

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

Breastfeeding

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

Fertility

Men should not to father a child during and up to 6 months following treatment with APIMEX. Effective contraception should be used during treatment with APIMEX 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.

Driving and using machines

APIMEX may make you feel tired and dizzy (see section 4). Do not drive or use tools or machines if this happens. APIMEX could interfere with your ability to drive safely or handle tools or machinery safely.

APIMEX contains potassium

APIMEX 100 mg powder for concentrate for solution for infusion contains approximately 18 mg (less than 1 mmol) potassium per vial and is essentially 'potassium free'.

APIMEX 500 mg powder for concentrate for solution for infusion contains approximately 91,5 mg (2,34 mmol) potassium per vial. Tell your doctor if you have a reduced kidney function or if you are on a controlled potassium diet.

3. How to use APIMEX

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

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

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

Your doctor will work out what dose you should receive. He/she will consider your diagnosis, your weight and height and kidney function.

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

After appropriate preparation and further dilution with a sterile saline or dextrose solution, APIMEX 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 APIMEX 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 APIMEX 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 APIMEX 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 APIMEX . You should take at least 5 doses during the 7 days before the first dose of APIMEX . You must continue taking the folic acid for 21 days after the last dose of APIMEX . You will also receive an injection of vitamin B12 (1 000 micrograms) in the week before administration of APIMEX and then approximately every 2 to 3 months (corresponding to 3 courses of APIMEX treatment). Vitamin B12 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 APIMEX is too strong or too weak, tell your doctor or pharmacist.

If you receive more APIMEX than you should

Since a healthcare provider will administer APIMEX, 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 APIMEX.

If you forget to use APIMEX

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

4. Possible side effects

APIMEX can have side effects.

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

If the following happens, stop using APIMEX 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).

- 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 become severe and could be fatal.
- Sudden breathlessness, intense chest pain or cough with bloody sputum. These symptoms may indicate a blood clot in the blood vessels of the lungs.
- 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).
- Chest pain or an irregular heart rate.
- Hepatitis (inflammation of the liver). Some signs may be nausea and vomiting, abdominal pain or discomfort and clay-coloured bowel movements.
- Acute renal failure (decreased urinary output, swelling, fatigue).

These are all very serious side effects. Your doctor may stop giving you APIMEX. You may require urgent medical attention or further hospitalisation.

Tell your doctor if you notice any of the following:

Frequent side effects:

- low haemoglobin level (anaemia)
- low white blood cells
- dehydration (feeling tired and thirsty)
- loss of sensation

- taste change
- red, inflamed eyes (conjunctivitis)
- diarrhoea
- vomiting
- nausea
- loss of appetite
- constipation
- pain, redness, swelling or sores in your mouth
- pain in the abdomen
- liver problems: abnormal blood tests
- hair loss
- increased skin pigmentation
- kidney disorders: abnormal blood tests
- fatigue (tiredness)
- oedema (excess fluid in body tissue, causing swelling)
- fever.

Less frequent side effects:

- dizziness
- watery eyes
- inflammation of the lining of the oesophagus (gullet) if you have also received radiation therapy
- 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
- Some patients have experienced a heart attack, stroke or “mini-stroke” while receiving APIMEX usually in combination with another anticancer therapy

- 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 APIMEX therapy.

Frequency unknown:

- muscle cramps, joint pains
- 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/Publications/Index/8>. By reporting side effects, you can help provide more information on the safety of APIMEX.

5. How to store APIMEX

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 APIMEX were demonstrated for 96 hours at refrigerated temperature and controlled room temperature at 25 °C.

APIMEX 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 APIMEX is not past its expiry date before giving you the injection.

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 APIMEX contains

- The active substance is pemetrexed.

APIMEX 100: Each vial contains 100 milligrams of pemetrexed (as pemetrexed dipotassium).

APIMEX 500: Each vial contains 500 milligrams of pemetrexed (as pemetrexed dipotassium).

APIMEX contains approximately 18 mg potassium per 100 mg vial or 91,5 mg potassium 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 APIMEX looks like and contents of the pack

A white to off-white lyophilised cake or powder having a blue or green tinge.

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

APIMEX 100 is packed in 10 ml clear glass, tubular lyo vial, with a grey chlorobutyl double-vent lyo rubber stopper and a grey aluminum flip-off seal. Single vial packs.

Not all pack sizes may be marketed.

APIMEX 500 is packed in 50 ml clear glass, tubular lyo blow-back vial, with a grey chlorobutyl double-vent lyo rubber stopper and a red aluminum flip-off seal. Single vial packs.

Not all pack sizes may be marketed.

Holder of the Certificate of Registration

Astral Pharma (Pty) Ltd

125 Meade Street

George

6529

South Africa

This leaflet was last revised in

24/11/2020

Registration numbers

Apimex 100 mg: 52/26/01222

Apimex 500 mg: 52/26/0123

Access to the corresponding Professional Information

To be confirmed