PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

MEXATE 2,5 mg tablets

Methotrexate

Contains sugar: 6 mg lactose monohydrate and 49 mg anhydrous lactose.

Read all of this leaflet carefully before you start taking MEXATE.

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

1. What MEXATE is and what it is used for

MEXATE tablets contain the active ingredient methotrexate. Methotrexate is referred to as a cytotoxic medicine. It is most commonly used to kill cells in tumours.

MEXATE tablets can be used to treat rheumatoid arthritis. It is usually used for patients who have tried other treatments, but their illness has not improved. In the treatment of rheumatoid arthritis, methotrexate is thought to stop or reduce inflammation by altering the body's defences.

MEXATE tablets can also be used to treat severe, uncontrolled psoriasis. It is usually used for patients who have tried other treatments, but their condition has not improved. Methotrexate helps patients with psoriasis by killing the cells in the skin, which are growing too quickly. It is these fast-growing cells which cause the raised patches of skin in psoriasis.

MEXATE is used to treat a wide range of tumours, in particular:

- acute leukaemias
- soft tissue and bone sarcomas
- solid tumours like breast, lung, head and neck, bladder, cervical, ovarian and testicular cancer.

MEXATE can be given alone or in combination with other medicines.
You should consult your doctor if you are unsure why you have been given MEXATE tablets.

2. What you need to know before you take MEXATE

Important warning about the dose of MEXATE:

- Take MEXATE only once a week for the treatment of psoriasis and rheumatoid arthritis.
- Taking more tablets of MEXATE than prescribed may be fatal.
- Please read section 3 of this leaflet very carefully.
- If you have any questions, please talk to your doctor or pharmacist before you take MEXATE.

Do not take MEXATE:

- If you are allergic to methotrexate, or any of the other ingredients of MEXATE (listed in section 6).
- If you are pregnant, trying to become pregnant or breastfeeding. Methotrexate, as in MEXATE, may harm your baby (see section "Pregnancy, breastfeeding and fertility"). You and your

partner should avoid conception (becoming pregnant or fathering children) for at least three months after your treatment with MEXATE has stopped.

- If you have severe liver problems, including fibrosis, cirrhosis, alcoholic liver disease and recent or active hepatitis.
- If you have severe kidney problems, including conditions requiring kidney dialysis.
- If you have any serious blood problems including severe anaemia and clotting problems.
- If you have a medical condition or are receiving medicine which lowers your resistance to infection.
- If you are taking antibiotics which prevent the production of folic acid (vitamin B_9), such as cotrimoxazole, which are used to treat bacterial infections.
- If you have an active infectious disease (e.g. fever, chills, joint pain).
- If you have an impaired immune system.
- During MEXATE therapy concurrent vaccination with live vaccines must not be carried out.

Warnings and precautions

MEXATE SHOULD BE USED ONLY BY DOCTORS EXPERIENCED IN THE THERAPY TO TREAT CANCER.

Take special care with MEXATE:

- If you are being treated for psoriasis or rheumatoid arthritis, MEXATE should be taken once weekly (same day per week).
- If you have excess fluid between the lungs and chest wall (pleural effusion) causing breathlessness, or in the abdomen causing swelling of the stomach (ascites), these may affect the levels of methotrexate in your blood.
- If you are weak, an elderly person or have mental problems.
- If you are dehydrated since it could cause kidney toxicity.
- If you have any sign of infection, e.g. sore throat.
- If you have any mild or moderate liver or kidney problems or blood disorders.
- If you have a history of alcohol abuse.

- If you have diabetes mellitus and are being treated with insulin.
- If you are overweight.
- If you have a history of taking medicines that can harm the liver.
- If you have respiratory problems.
- If you have stomach ulcers or suffer from inflammation and ulceration of the gut.
- If you have severe mouth ulcers.
- If you have diarrhoea.
- If you are receiving radiotherapy (X-rays) or ultraviolet (UV) radiation concurrently.

Acute bleeding from the lungs in patients with underlying rheumatological disease has been reported with MEXATE. If you experience symptoms of spitting or coughing up blood you should contact your doctor immediately.

It is very important that your doctor check your progress at regular visits to make sure that MEXATE is working properly and to check for unwanted effects. It is also essential that examinations of blood and tests of kidney and liver function should be made before, during and after each course of treatment with MEXATE.

Some patients who take MEXATE may become more sensitive to sunlight than they are normally. When you first begin taking MEXATE avoid too much sun and do not use a sunlamp until you see how you react to the sun, especially if you tend to burn easily. In case of a severe burn, check with your doctor.

Do not take medicine for inflammation or pain (aspirin or other salicylates, e.g. ibuprofen, indometacin, phenylbutazone) without first checking with your doctor. These medicines may increase the effects of MEXATE, which could be harmful.

MEXATE can lower the number of white blood cells in your blood temporarily, increasing the chance of getting an infection. It can also lower the number of platelets, which are necessary for

proper blood clotting. If this occurs, there are certain precautions you can take, especially when your blood count is low, to reduce the risk of infection or bleeding.

MEXATE temporarily affects sperm and egg production, which is reversible in most cases. MEXATE can cause miscarriage and severe birth defects. You must avoid becoming pregnant when taking MEXATE and for at least six months after treatment has stopped (see section "Pregnancy, breastfeeding and fertility").

If possible, avoid people with infections. Contact your doctor immediately if you think you are getting an infection or if you get a fever or chills, cough or hoarseness, lower back or side pain, or painful or difficult urination.

Contact your doctor immediately if you notice any unusual bleeding or bruising; black, tarry stools; blood in urine or stools; or pinpoint red spots on your skin.

Other medicines and MEXATE:

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

The following medicines may cause an interaction with MEXATE when they are taken at the same time:

- vaccinations (see "Do not take MEXATE")
- aspirin, ibuprofen, indometacin (NSAIDs, nonsteroidal anti-inflammatory medicines) which are used for pain or inflammation
- antibiotics (used to treat bacterial infections, e.g. chloramphenicol, penicillin, sulphonamides, co-trimoxazole, trimethoprim, doxycycline, ciprofloxacin and tetracyclines)
- colestyramine (used to lower high cholesterol levels in your blood)
- thiazides (a group of diuretics used for the treatment of fluid retention, e.g. bendroflumethiazide)

- oral hypoglycaemics (used to treat high blood sugar levels that are caused by diabetes, e.g. metformin)
- mercaptopurine (used to treat acute lymphocytic leukaemia)
- *p*-aminobenzoic acid, acitretin (used to treat psoriasis or skin disorders)
- corticosteroids (used to treat arthritis, allergic reactions or skin diseases)
- cytostatics (used to treat cancer, e.g. cisplatin)
- diphenylhydantoins, phenytoin, carbamazepine, valproate (used to treat epilepsy [fits/seizures])
- pyrimethamine (used to treat malaria)
- digoxin (used to treat heart failure)
- immunosuppressants (used to treat inflammatory conditions, e.g. leflunomide or ciclosporin)
- theophylline (used to treat asthma)
- omeprazole, pantoprazole (used to treat stomach ulcers, heartburn or reflux)
- diuretics (e.g. loop diuretics like furosemide, hydrochlorothiazide or triamterene – water pills)
- thiazide diuretics (used to treat fluid retention)
- probenecid, sulfinpyrazone (used to treat gout)
- vitamin preparations containing folic acid or similar products
- nitrous oxide (a gas used in general anaesthesia)
- olanzapine (used to treat schizophrenia)
- levetiracetam (used to treat seizures in epilepsy).

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

MEXATE with food, drink and alcohol:

MEXATE can be taken with or without food. Alcohol should be avoided while taking MEXATE tablets.

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 MEXATE.

You should not take MEXATE if you are pregnant or breastfeeding your baby (see “Do not take MEXATE”).

Pregnancy:

Do not use MEXATE during pregnancy. MEXATE can cause birth defects, harm the unborn child or cause miscarriage. It is associated with malformations of the skull, face, heart and blood vessels, brain and limbs. It is therefore very important that MEXATE is not given to pregnant women or to women who are planning to become pregnant.

For non-oncological indications, in women of childbearing age the possibility of a pregnancy must be ruled out, e.g. by pregnancy tests, before treatment is started.

Do not use MEXATE if you are trying to become pregnant. You must avoid becoming pregnant during treatment with MEXATE and for at least 6 months after the end of treatment.

Therefore, you must ensure that you are taking effective contraception for the entire period (see “Take special care with MEXATE”).

Breastfeeding:

You should not take MEXATE if you are breastfeeding. Ask your doctor for advice if you are breastfeeding.

Male fertility:

Methotrexate, as in MEXATE, can cause genetic mutations (genotoxic effect). Methotrexate, as in MEXATE, can affect the production of sperm, which is associated with the possibility of birth defects.

You should avoid fathering a child or to donate semen during treatment with MEXATE and for at least 6 months after the end of treatment. As treatment with MEXATE at higher doses commonly

used in cancer treatment can cause infertility and genetic mutations, it may be advisable for male patients treated with methotrexate doses higher than 30 mg/week to consider sperm preservation before the beginning of treatment (see also section “Take special care with MEXATE”).

Driving and using machines:

MEXATE may cause dizziness, fatigue, drowsiness, eye irritation or blurred vision, which could affect your ability to drive a vehicle or use machinery. If you experience these symptoms, do not perform any tasks that require your attention, until you know how MEXATE will affect you. The full list of side effects is listed in section 4.

MEXATE contains lactose:

MEXATE tablets contain sugar (lactose monohydrate and anhydrous lactose). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking MEXATE tablets.

3. How to take MEXATE

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

Always take MEXATE exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The usual dose is:

Treatment of cancer:

Adults, elderly patients and children:

Your doctor will calculate the dosage required from your body surface area (m^2) and the dose is expressed as mg/m^2.

These doses may be reduced if you are receiving other medicine. Your doctor will decide the correct dose for you. If you want more information, you should ask your doctor.

Treatment of psoriasis: Take MEXATE only once a week.

Adults: For severe psoriasis, the usual dose is 10 mg to 25 mg by mouth, once a week on the same day each week.

OR

Divided oral dose schedule: 2,5 mg at 12-hour intervals for three doses or at 8-hour intervals for four doses each week.

Do not exceed a maximum of 30 mg per week.

This should be adjusted according to your response to treatment and side effects.

Elderly: No dosage adjustment required.

Children: Not recommended for use in children.

Treatment of rheumatoid arthritis:

Adults: Oral, initially 2,5 mg to 5 mg every 12 hours for 3 doses once a week, the dosage being increased as necessary in increments of 2,5 mg per week up to a maximum of 20 mg per week.

OR

Oral, initially 10 mg once a week (on the same day each week), the dosage being increased as necessary up to 20 mg per week.

Your doctor will tell you how long your treatment with MEXATE will last.

If you have the impression that the effect of MEXATE tablets is too strong or too weak, talk to your doctor or pharmacist.

If you take more MEXATE than you should:

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre. Always take the labelled medicine package with you, whether there are any MEXATE tablets left or not.

Overdose symptoms may include easy bruising or bleeding, unusual weakness, mouth sores, nausea, vomiting, black or bloody stools, coughing up blood or vomit that looks like coffee grounds and decreased urinating.

Inappropriate intake resulting in overdose can sometimes lead to death.

If you forget to take MEXATE:

If you forget to take a dose, take it as soon as you remember if this is within two days. However, if you have missed a dose by more than two days, please contact your doctor for advice. Do not take a double dose to make up for forgotten individual doses.

If you stop taking MEXATE:

Do not stop taking MEXATE tablets unless your doctor tells you to. Should you need to stop taking MEXATE tablets, your doctor will decide which is the best method for you.

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

4. Possible side effects

MEXATE can have side effects.

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

If any of the following happens, stop taking MEXATE 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 MEXATE. You may need urgent medical attention or hospitalisation.

Tell your doctor if you notice any of the following:

Less frequent side effects:

- Infection, including serious infections.
- Sepsis (confusion or disorientation, shortness of breath, extreme pain or discomfort, clammy or sweaty skin).
- Lymphoma (enlarged lymph nodes, characterised by chills, weight loss, feeling very tired, swollen stomach, feeling full after only a small amount of food, chest pain or pressure, shortness of breath or cough).
- Abnormal red blood cell function.
- Immune disorder (low levels of serum immunoglobulin).
- High blood sugar levels (extreme thirst, extreme hunger and frequent urination).
- Mood alterations, loss of intellectual functions (such as reasoning, memory loss and other neurological abilities that is severe enough to interfere with daily functioning).
- Headache, weakness of one entire side of the body.
- Drowsiness, muscular weakness, speech problems (slurred speech, language disorders), unusual taste sensations.
- Blurred vision, serious visual changes, eye infection, blindness (transient), vision loss.
- Low blood pressure (dizziness and light-headedness).
- Fluid around the heart (chest pain, pressure, discomfort), pericarditis (sharp, piercing chest pain over the centre or left side of the chest, which is generally more intense when breathing in).
- Blood clot forming, usually in your legs.
- Inflammation of the blood vessels (pain, fever and unusual tiredness).
- Lung disease (dry cough or shortness of breath), sore throat.
- Eating disorder causing weight loss due to loss of appetite (anorexia), diarrhoea, inflamed and sore mouth, vomiting, inflammation of the pancreas, inflammation of the small intestines, blood in your stools, irritation, redness and swelling of your gums, dark stools, vomiting of blood.
- Increased liver enzymes, inflammation of the liver, serious liver diseases (yellow eyes or skin, appetite loss, fluid buildup in the legs or stomach).
- Hair loss (temporary).
- Severe skin rash that causes blistering, acne, problem skin, red spots on the skin,

discolouration of skin.

- Sensitivity to sunlight, hives, boils on skin, threadlike red lines or patterns on the skin.
- Muscle or joint pain.
- Weakening or softening of bones.
- Kidney problems, kidney failure, painful or difficult urination.
- Bladder infection (pelvic pain, increased urge to urinate, pain with urination), blood in the urine.
- Birth defects, abortion.
- Problems with menstrual cycle.
- Vaginal discharge, irritation or swelling of the vaginal tissues.
- Reduced ability to become pregnant and reduced ability to father children.
- Loss of interest in, or inability to have sex.

Frequency unknown:

- Lung infections (cough, fever, shaking chills, shortness of breath).
- Shingles (blistering, itching, painful and burning rash).
- Low levels of white and red blood cells and cells that clot blood.
- Inflammation of the air sacs of the lungs (alveolitis).
- Liver failure.
- Presence of abnormal quantities of protein in the urine, which may indicate damage to the kidneys.

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. This includes any possible side effects 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 MEXATE.

5. How to store MEXATE

- Store at or below 25 °C.
- Keep tablets in original container until required for use.
- 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 MEXATE contains:

The active substance in MEXATE is methotrexate.

Each tablet contains 2,5 mg methotrexate.

The other ingredients are:

Anhydrous lactose

Lactose monohydrate

Magnesium stearate

Microcrystalline cellulose

Pregelatinised starch.

What MEXATE looks like and contents of the pack:

Yellow, round, uncoated tablets, with ‘L2’ debossed on one side and a score line on the other side.

White 60 mL HDPE round bottle closed with a 33 mm white PP child-resistant cap (CRC).

Pack size: 100 tablets.

Holder of Certificate of Registration:

Zydus Healthcare SA (Pty) Ltd

Southdowns Office Park

Building B, Ground Floor

22 Karee Street

Centurion 0157

Tel: 012 748 6400

This leaflet was last revised in

Not applicable.

Registration number

54/26/0019

Date of registration

30 January 2024