Approved Patient Information Leaflet

SCHEDULING STATUS:

S4

ABITREXATE 50 (contains 50 mg methotrexate)

ABITREXATE 500 (contains 500 mg methotrexate)

ABITREXATE 1 g (contains 1 g methotrexate)

ABITREXATE 5 g (contains 5 g methotrexate)

Sugar free.

Read this leaflet carefully before you are given ABITREXATE:

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- **ABITREXATE** 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 ABITREXATE IS AND WHAT IT IS USED FOR**
2. **WHAT YOU NEED TO KNOW BEFORE YOU USE ABITREXATE**
3. **HOW TO USE ABITREXATE**
4. **POSSIBLE SIDE EFFECTS**
5. **HOW TO STORE ABITREXATE**
6. **CONTENTS OF THE PACK AND OTHER INFORMATION**

1. What ABITREXATE is and what it is used for:

ABITREXATE contains methotrexate which belongs to the group of medicines known as antimetabolites. It is used to treat some kinds of cancer. It may also be used for other conditions as determined by your doctor, such as severe psoriasis and rheumatoid arthritis.

Methotrexate blocks an enzyme needed by the cell to live. This interferes with the growth of cancer cells, which are eventually destroyed.

2. What you need to know before you use ABITREXATE:

Do not use ABITREXATE:

Before you begin treatment with **ABITREXATE**, you and your doctor must talk about the good **ABITREXATE** will do as well as the risk of using it. **ABITREXATE** is available only with your doctor's prescription.

- 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 **ABITREXATE**.
- 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.

You should not be administered ABITREXATE:

- if you are hypersensitive (allergic) to methotrexate or any of the other ingredients of **ABITREXATE**
- if you are pregnant or breastfeeding your baby while receiving **ABITREXATE** (see **Pregnancy and breastfeeding**)
- if you currently have or have previously had any disease of the immune system, kidneys or liver, talk to your doctor before receiving **ABITREXATE**
- if you have a history of alcohol abuse
- if you have disorders of the blood-forming system

- if you have been recently vaccinated, please tell your doctor, as this can possibly cause serious effects with **ABITREXATE**. You should not be given live vaccines during treatment with **ABITREXATE**
- if you have severe or existing infections e.g. HIV or other immunodeficiency syndromes.
- If you are currently using any sulphonamide containing medicines

Warnings and precautions:

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

- you suffer from liver or kidney impairment
- you have a problem with your lung function
- you have abnormal accumulation of liquid in the abdomen or in the cavity between the lungs and the chest wall (ascites, pleural effusions)
- you are dehydrated or suffer from conditions leading to dehydration (vomiting, diarrhea, sore or inflamed mouth)
- you have inactive, prolonged infections (e.g tuberculosis, hepatitis B or C, shingles (herpes zoster))
- you have a stomach ulcer or ulcerative colitis (inflammation and ulceration of the gut).
- If you are taking a medicine called leflunomide, used to treat psoriasis

Take special care with ABITREXATE:

- Do not drink alcohol while using **ABITREXATE**. Alcohol can increase the chance of liver problems.
- Avoid too much sun exposure and do not use a sunlamp until you see how you react to the sun, especially if you tend to burn easily as the skin is more sensitive. In case of a severe burn, check with your doctor.
- Do not take medicine for inflammation or pain (aspirin, diclofenac, ibuprofen, ketoprofen,

mefenamic, indomethacin acid, naproxen, piroxicam, sulindac or other NSAIDS) without first checking with your doctor. These medicines may increase the effects of **ABITREXATE**, which could be harmful.

- If you have recently had chickenpox (including recent exposure) or Herpes zoster (shingles).
- **ABITREXATE** 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: If you can, avoid people with infections.

  Check with 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.
- Check with 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.
- Be careful when using a regular toothbrush, dental floss, or toothpick. Your medical doctor, dentist, or nurse may recommend other ways to clean your teeth and gums. Check with your medical doctor before having any dental work done.
- Do not touch your eyes or the inside of your nose unless you have just washed your hands and have not touched anything else in the meantime.
- Be careful not to cut yourself when you are using sharp objects such as a safety razor or fingernail or toenail cutters.
- Avoid contact sports or other situations where bruising or injury could occur.
- Contraception should be used by males and females until at least six months after treatment
- If you experience fatigue, loss of appetite, night sweats or enlarged lymph nodes contact your doctor

- If you are taking vitamins such as folic acid as this may decrease the effectiveness of **ABITREXATE**
- **ABITREXATE** use is not recommended in <3 years old

Other medicines and ABITREXATE:

Always tell your healthcare professional if you are taking any other medicine. This includes complementary or traditional medicines.

It is especially important to tell your doctor if you are using:

- Treatments for rheumatoid arthritis or psoriasis such as leflunomide, sulphasalazine (also used for ulcerative colitis).
- Salicylates such as acetylsalicylic acid, phenylbutazone, or amidopyrine derivatives (used to treat pain, fever and inflammation).
- Alcohol (should be avoided).
- Live vaccinations.
- Azathioprine (used to prevent rejection after an organ transplant).
- Retinoids (used to treat skin disorders such as psoriasis or severe acne).
- Anticonvulsant drugs such as phenytoin (prevent fits).
- Cancer treatments (such as bleomycin, doxorubicin, cyclophosphamide, vincristine, asparaginase and cytosine arabinoside
- Barbiturates (for sleeping and anxiety disorders and epilepsy).
- Tranquillisers (used to treat anxiety and sleeping disorders).
- Oral contraceptives.
- Probenecid and allopurinol (for gout).
- Antibiotics (such as sulphonamides, aminoglycosides and tetracyclines).

- Pyrimethamine (used to prevent and treat malaria).
- Vitamin preparations which contain folic acid.
- Proton-pump inhibitors such as omeprazole and pantoprazole (used to treat severe heartburn or ulcers).
- Theophylline (used to treat asthma).

• The effects of **ABITREXATE** may be enhanced by concurrent administration of chloramphenicol (used to treat eye infections), hydrocortisone and prednisone (steroids)

- 5-flourouracil (anticancer medicine)
- Antibiotics, like penicillin's, glycopeptides, ciprofloxacin and cefalotin can, in individual cases, reduce the renal clearance of **ABITREXATE**
- Concomitant use of trimethoprim/sulphamethoxazole and **ABITREXATE** should not occur as it can lead to bone marrow suppression (decreased production of blood cells)
- Avoid excessive coffee consumption during treatment with **ABITREXATE**
- Nitrous oxide (used for sedation and pain relief) should not be administered with **ABITREXATE**

Pregnancy and breastfeeding:

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before receiving **ABITREXATE**.

You must not use **ABITREXATE** during pregnancy. Men and women should use an effective method of birth control during treatment and during a further six months after treatment with **ABITREXATE** has been discontinued.

In women of child-bearing age, any existing pregnancy must be excluded with certainty by taking appropriate measures e.g. pregnancy test, prior to therapy.

Driving and using machinery:

Do not drive or operate any tools or machines until you know how **ABITREXATE** affects you.

ABITREXATE can make you feel sleepy.

3. How to use ABITREXATE:

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

ABITREXATE should be administered under the supervision of a medical doctor experienced in the use of chemotherapeutic agents.

The exact amount of medicine has been carefully worked out. Receiving too much may increase the chance of side effects, while receiving too little may not improve your condition.

If you have the impression that the effect of **ABITREXATE** is too strong or too weak, talk to your doctor.

ABITREXATE is often given together with certain other medicines. If you are using a combination of medicines, make sure that you take each one at the proper time and do not mix them. Ask your doctor, nurse, or pharmacist to help you plan a way to remember to take your medicines at the right times.

While you are using **ABITREXATE**, your doctor may want you to drink extra fluids so that you will pass more urine. This will help the medicine pass from the body, and will prevent kidney problems.

If you receive more ABITREXATE than you should:

Since a healthcare professional will administer this medicine, he/she will control the dosage.

However, in the event of overdosage, your doctor will manage the overdosage.

If you miss a dose of ABITREXATE:

If you miss a dose of **ABITREXATE y**ou should not receive the missed dose at all and not double

the next one. Instead check with your doctor.

4. Possible side effects:

ABITREXATE can have side effects.

Not all side effects reported for **ABITREXATE** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving **ABITREXATE**, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing (allergic reaction)
- rash or itching
- vomiting, nausea, blood in the vomit, diarrhoea, dark tarry stools
- blood in the urine
- neck stiffness, confusion or convulsions
- difficulty breathing, shortness of breath or a dry cough
- if you experience tiredness, feeling faint, becoming easily breathless or if you look pale (since you might have fewer red blood cells than normal)
- excessive peeling of the skin

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

- inflammation of the gums, sores in the mouth or on the lips
- muscular weakness or paralysis
- fever
- yellowing of the skin and eyes, also called jaundice
- pain or difficulty in passing urine
- retention of fluid, causing swelling in legs, ankles and feet
- blurred or decreased vision
- thirst and/or frequent urination.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you experience any of the following side effects that occur frequently:

- feeling unwell, chills
- headache
- drowsiness
- fatigue
- dizziness
- bleeding and perforation of the small intestine
- indigestion
- loss of appetite
- miscarriage
- foetus abnormalities
- loss of sex drive
- low sperm production
- abnormal periods, vaginal discharge

- infertility.

Tell your doctor if you experience any of the following side effects that occur less frequently:

- infections that occur due to a weak immune system (opportunistic infections)
- difficulty sleeping or falling asleep
- high blood sugar levels
- spinning sensation
- confusion
- depression
- brain disorder (leukoencephalopathy)
- mood alterations
- pain
- changes in sense of taste (metallic taste)
- meningism (inflammation of the lining of the brain causing paralysis or vomiting)
- low blood pressure
- inflammation of the blood vessels
- blood clot in the veins, lungs or brain
- malabsorption; swelling and inflammation in colon
- damage to tissue around your jaw
- sore or inflamed throat
- sensitivity to light
- changes to the colour of the skin
- hair loss

- abnormal bruising
- spider veins
- pain when urinating
- acne, boils
- joint or muscle pain
- inflammation and ulceration of the vagina

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 **ABITREXATE**.

5. How to store ABITREXATE:

Store at or below 25 ºC and keep in the outer container until required for use in order to protect the product from light.

Store all medicines out of reach of children.

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:

ABITREXATE 50 and **ABITREXATE 500**: Each 1 ml contains methotrexate 25 mg as the active substance.

ABITREXATE 1 g: Each 10 ml contains methotrexate 1 g as the active substance.

ABITREXATE 5 g: Each 50 ml contains methotrexate 5 g as the active substance.

The other ingredients are: Sodium chloride, water for injection.

What ABITREXATE looks like and contents of the pack:

Abitrexate 50 Injection:

Clear, yellow-brown solution, free of visible particles.

Abitrexate 500 Injection:

Clear, yellow-brown solution, free of visible particles.

Abitrexate 1 g Injection:

A clear orange to brown solution, free of visible particles.

Abitrexate 5 g Injection:

A clear orange to brown solution, free of visible particles.

CONTENTS OF PACK:

Abitrexate 50 Injection: Single 2 ml vial

Abitrexate 500 Injection: Single 20 ml vial

Abitrexate 1 g Injection: Single 10 ml vial

Abitrexate 5 g Injection: Single 50 ml vial

HOLDER OF THE CERTIFICATE OF REGISTRATION:

Teva Pharmaceuticals (Pty) Ltd

Maxwell Office Park

Magwa Crescent West, Waterfall City

Midrand

South Africa.

This leaflet was last revised in:

08 July 2022

Teva Pharmaceuticals (Pty) Ltd	**Product:** ABITREXATE 50/500/1 g/5 g Abitrexate 50 and Abitrexate 500: Each 1 ml contains methotrexate 25 mg. Abitrexate 1 g: Each 10 ml contains methotrexate 1 g. Abitrexate 5 g: Each 50 ml contains methotrexate 5 g.
	Date of Registration: 26 November 1986 **Approval date:** 08 July 2022

REGISTRATION NUMBER:

Abitrexate 50: T/26/63

Abitrexate 500: T/26/64

Abitrexate 1 g: T/26/57

Abitrexate 5 g: W/26/386