Teva Pharmaceuticals (Pty) Ltd.	**Product:** Abitrexate 2,5 mg Tablets **Dosage Form:** Tablets **Strength:** 2,5 mg methotrexate as the sodium salt
Reg. No.: 37/26/0466	

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

ABITREXATE 2,5 mg TABLETS

ABITREXATE 10 mg, (Tablets)

Methotrexate

Contains sugar (lactose monohydrate, 77,758 mg per 2,5 mg tablet and 150,032 mg per 100 mg tablet)

Read all of this leaflet carefully before you start taking ABITREXATE

- 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.
- 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 take ABITREXATE

3. How to take 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 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, as in ABITREXATE blocks an enzyme needed by the cell to live. This interferes with the growth of cancer cells, which are eventually destroyed. Since the growth of normal body cells may also be affected by methotrexate, other effects will also occur. Some of these may be serious and must be reported to your doctor. Other effects, like hair loss, may not be serious but may cause concern. Some effects may not occur for months or years after the medicine is used.

Before you begin treatment with ABITREXATE, you and your doctor should talk about the good this medicine will do as well as the risk of using it.

ABITREXATE is available only with your doctor's prescription.

2. What you need to know before you take ABITREXATE

Important warning about the dose of ABITREXATE:

Take ABITREXATE only once a week for the treatment of psoriasis and rheumatoid arthritis requiring dosing once a week.

Taking too much of **ABITREXATE** may be fatal.

Please read "**How to take ABITREXATE**" of this leaflet very carefully.

If you have any questions, please talk to your doctor or pharmacist before you take **ABITREXATE**.

Do not take ABITREXATE:

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

- if you are pregnant or breastfeeding your baby.
- if you suffer from a problem of excessive drinking (alcoholism).
- if you have severe liver problems, including alcoholic liver disease and recent or active hepatitis (inflammation of the liver).
- if you have severe kidney problems.
- if you have any serious blood disorders including severe anaemia or abnormal numbers of blood cells such as low white cells leucopenia) or low small blood cell numbers (platelets) causing (thrombocytopenia).
- if you have symptoms which may suggest an active infectious disease (e.g. fever, chills, achiness).
- if you have a medical condition or are receiving medication which lowers your resistance to infection.
- while you are being treated with ABITREXATE, and after you stop treatment with it, do not have any immunisations (vaccinations) without your doctor's approval.

Also tell your doctor and pharmacist if you are allergic to any other substances, such as foods, preservatives, or dyes.

Warnings and precautions

Take special care with ABITREXATE:

- if you are being treated for psoriasis or rheumatoid arthritis, ABITREXATE 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, 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 are taking other medicines or alcohol that can harm the liver.
- 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 impaired respiratory function.
- 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 or ultraviolet (UV) radiation concurrently.

Acute bleeding from the lungs in patients with underlying rheumatologic disease has been reported with ABITREXATE. 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 ABITREXATE 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 ABITREXATE.

Some patients who take ABITREXATE may become more sensitive to sunlight than they are normally. When you first begin taking ABITREXATE 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, diclofenac, ibuprofen, indomethacin, ketoprofen, mefenamic, indomethacin acid, naproxen, phenylbutazone, piroxicam, sulindac, tolmentin, etc.) without first checking with your doctor. These medicines may increase the effects of ABITREXATE, which could be harmful.

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.

ABITREXATE temporarily affects sperm and egg production, which is reversible in most cases. ABITREXATE can cause miscarriage and severe birth defects. You must avoid becoming pregnant when using ABITREXATE and for at least six months after treatment has stopped. See also section “Pregnancy, breastfeeding and fertility”.

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.

Other medicines and ABITREXATE

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

Although certain medicines should not be used together at all, in other cases two different medicines may be used together even if an interaction might occur. In these cases, your doctor may want to change the dose, or other precautions may be necessary. When you are taking ABITREXATE, it is especially important that your doctor and pharmacist know you are taking any other prescription or non-prescription (over the counter) medicine:

- vaccinations (see "do not take ABITREXATE")
- antibiotics including penicillins, sulphonamides, trimethoprim/ sulfamethoxazole (as cotrimoxazole), neomycin, ciprofloxacin, doxycycline, tetracyclines, chloramphenicol
- colestyramine (reduces the levels of cholesterol in the blood and improves the itching associated with liver disease)
- nitrous oxide-based anaesthetics
- olanzapine used for the treatment of schizophrenia
- p-aminobenzoic acid, retinoids, e.g. acitretin (for psoriasis or skin disorders)
- corticosteroids used for the treatment of arthritis, allergic reactions or skin diseases
- cytostatics (medication against cancer), e.g. cisplatin

- NSAIDs (non-steroidal anti-inflammatory drugs) e.g. ibuprofen, indomethacin, azapropazone or aspirin (for relief of pain or inflammation) including any preparations of these bought without a prescription. Taking these products together with ABITREXATE can increase its toxic effects.
- probenecid, sulfinpyrazone (for gout)
- phenytoin, carbamazepine and valproate (for seizures)
- pyrimethamine (medicine against malaria)
- digoxin (used to treat heart failure)
- immunosuppressant drugs such as leflunomide (used for suppression of inflammatory conditions) or ciclosporin
- theophylline (for asthma)
- omeprazole, pantoprazole (for stomach ulcers, heartburn, reflux)
- diuretics (e.g. loop diuretics like furosemide, hydrochlorothiazide or triamterene - water pills)
- thiazides (a group of diuretics used for the treatment of fluid retention e.g. bendroflumethiazide)
- vitamin preparations containing folic acid or its derivatives
- oral hypoglycaemics (lower blood sugar levels e.g. metformin).
- mercaptopurine (used to treat acute lymphocytic leukaemia)
- radiotherapy
- acitretin (a treatment for psoriasis)
- levetiracetam (a medicine used to treat seizures in epilepsy)

They should also be told if you have ever been treated with x-rays or cancer medicine or if you drink alcohol.

Taking ABITREXATE with food and drink

You should not drink alcohol whilst you are taking ABITREXATE.

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 healthcare provider for advice before taking ABITREXATE**.**

You should not take ABITREXATE if you are pregnant or breastfeeding your baby (see "Do not take ABITREXATE").

Male fertility:

The available evidence does not indicate an increased risk of malformations or miscarriage if the father takes methotrexate less than 30 mg/week. However, a risk cannot be completely excluded. ABITREXATE may be genotoxic. This means that the medicine may cause genetic mutation. ABITREXATE can affect sperm production with the potential to cause birth defects. Therefore, you should avoid fathering a child or to donate semen whilst taking methotrexate and for at least 6 months after treatment is stopped.

Driving and using machines

ABITREXATE may make you feel tired, dizzy or may give you blurred vision. You should not drive a vehicle or use machines when you first start to take ABITREXATE until you know how you are affected.

It is not always possible to predict to what extent ABITREXATE may interfere with your daily activities. You should ensure that you do not engage in driving a vehicle or use machines until you are aware of the measure to which ABITREXATE affects you.

ABITREXATE contains lactose

ABITREXATE contains lactose. Patients with the rare hereditary conditions of lactose or galactose intolerance should not take ABITREXATE.

3. How to take ABITREXATE

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

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

Recommended dose in treating psoriasis: Single weekly doses of 10 to 25 mg.

Take ABITREXATE only once a week.

Recommended dose in treating rheumatoid arthritis: One (2,5 mg) to two (5 mg) tablets every 12 hours for 3 doses and your doctor will increase the dose with 2,5 mg per week up to 20 mg per week.

Take ABITREXATE only once a week.

ABITREXATE may be given by mouth. ABITREXATE should be administered under the supervision of a medical doctor experienced in the use of chemotherapeutic medicines. The exact amount of medicine has been carefully worked out. Taking too much may increase the chance of side effects, while taking too little may not improve your condition.

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 and keep your kidneys working well.

Your doctor will tell you how long your treatment with ABITREXATE will last. If you have the impression that the effect of ABITREXATE is too strong or too weak, tell your doctor or pharmacist.

If you vomit shortly after taking a dose of ABITREXATE, check with your doctor. You will be told whether to take the dose again or to wait until the next scheduled dose.

If you take more ABITREXATE than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you missed a dose of ABITREXATE

If you miss a dose of ABITREXATE do not take the missed dose at all and do not double the next one. Instead go back to your regular dosing schedule and check with your doctor.

Effects when treatment with ABITREXATE is stopped

ABITREXATE commonly causes nausea and vomiting. Even if you begin to feel ill, do not stop using ABITREXATE without first checking with your doctor. Ask your doctor, nurse or pharmacist for ways to lessen these effects.

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 taking ABITREXATE, please consult your other healthcare provider for advice.

Along with their effects, medicines like ABITREXATE can sometimes cause unwanted effects such as blood problems, kidney problems, stomach or liver problems, loss of hair, and other side effects. These and other side effects are described below. Also because of the way these medicines act on the body, there is a chance that they might cause other unwanted effects that may not occur until months or years after the medicine is used. These delayed effects may include certain types of cancer, such as leukaemia. Discuss these possible effects with your doctor.

If any of the following happens, stop taking ABITREXATE and 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,
- rash or itching,
- fainting,
- yellowing of the skin and eyes also called jaundice.

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:

Frequently:

- ABITREXATE can make you more likely to catch infections. If you think you have an infection, a sore throat, mouth ulcers, fever, chills, or achiness during treatment you should tell your doctor immediately.

Less frequently:

- ABITREXATE can cause inflammation of the lung with breathlessness, symptoms of which include persistent cough, experience of pain or difficulty in breathing or becoming breathless at rest, chest pain or fever.
- Spitting or coughing blood*.
- Severe skin rash that causes blistering. These may be signs of a condition known as Stevens Johnson Syndrome. Your doctor will stop your treatment in these cases.
- Fits.

*(has been reported for methotrexate used in patients with underlying rheumatologic disease)

Unknown frequency:

- Bleeding from the lungs*
- Chest pain or tightness of chest, with difficulty in breathing (heart attack)
- Lung infection

*(has been reported for methotrexate used in patients with underlying rheumatologic disease)

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

Tell your doctor if you notice any of the following:

Frequently:

- Inflammation or sore mouth
- Loss of appetite, nausea, vomiting, loose stools, dark, sticky stools
- a Reduction in the number of white cells in the blood

- Raised liver enzymes
- Headache, tiredness
- Hair loss

Less frequently:

- Herpes zoster (shingles) which is a viral disease characterised by a painful skin rash with blisters
- Large number of cancer cells die within a short period, releasing their contents into the blood
- A serious infection affecting the whole body (sepsis) characterised by fever, chills, rapid breathing and low blood pressure, infections due to weakened immune system
- Increased liver function tests
- Sensation of numbness or tingling / having less sensitivity to stimulation than normal
- Blood clots
- A lump in your neck, groin or armpits with associated backache, weight loss or night sweats
- Swelling of the gums, vomiting of blood
- Stomach or intestinal ulcers, bleeding or inflammation of the intestine, inflammation of the pancreas
- Complication of inflammatory bowel disease
- Decrease in the number of red or white blood cells and blood platelets
- Weakened immune system
- Excessive growth of white blood cells
- Drug-induced liver damage
- Raised blood sugar levels (Diabetes mellitus)
- Depression, confusion
- Sleepiness
- Inability to move one half of the body, muscular weakness

- Difficulty and unclear with speech
- Irritation, lack of energy
- Involuntary muscle movement
- Eye inflammation, blurred vision
- Excess fluid between the heart and the sac surrounding the heart, known as the pericardium or inflammation of the heart sac
- Nose bleeding
- Low blood pressure
- Tenderness and swelling of the lower extremities (clot in the veins), vasculitis (pain or redness of the blood vessels)
- Lung infection, inflammation of the walls of the air sacs
- Pain or difficulty in passing urine, blood in urine
- Elevation of urea and/or creatinine in the blood, inflammation of the bladder
- Loss of interest in, or inability to have sex
- Menstrual disorders, infertility, vaginal ulcers or bleeding, enlargement of breasts
- Affected sperm and egg production
- Sensitivity to light, skin ulcers and painful erosions of inflamed areas, in psoriasis patients, appearance of lightened patches on the skin
- Acne, hives, a discoloration of the skin resulting from bleeding underneath, typically caused by bruising, widened tiny blood vessels cause threadlike red lines or patterns on the skin
- Infection of hair follicles
- Muscle pain, joint pain
- Weakening or softening of bones, stress fractures

- Increase in rheumatic nodules

Unknown frequency:

- Painful inflammation and ulceration of the mucous membranes of the digestive tract
- Blood disorders such as larger as normal red blood cells, disease of the lymph nodes, lower than normal white blood cells, depression of the immune system
- Deficiency of all type of blood cells, increase in white blood cells
- Mood changes
- Sleeplessness, a mental disorder characterised by a disconnection from reality
- Vision impairment
- Ringing in the ears
- Asthma, severe weakness of the muscles of respiration
- Skin sensitivity
- Bone damage in the jaw (secondary to excessive growth of white blood cells)
- Kidney failure
- Miscarriage, damage to your unborn baby
- Increased risk of dying of tissue and bone during radiotherapy
- Redness and shedding of skin
- Detachment of the nail from the nail bed, a chronic, very itchy skin rash made up of bumps and blisters, a small red or purple spot caused by bleeding into the skin, a chronic skin condition featuring lumps in places such as the armpits or groin
- Darkened patches or spots on the skin, an infection of the tissue folds around the nails
- General feeling of illness, fever, chills

- Swelling.

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 all medicines out of reach of children.

Tablets: Store at or below 25 °C in well-closed containers and protect from light. Do not remove the blisters from the carton until required for use.

Do not store in bathroom, near the kitchen sink, or in other damp places. Heat or moisture may cause the medicine to break down.

Do not keep outdated or medicines no longer needed. Be sure that any discarded medicine is out of the 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 2,5 mg TABLETS contain 2,5 mg of methotrexate as the sodium salt.

ABITREXATE 10 mg tablets contain 10 mg of methotrexate as the sodium salt.

Inactive ingredients: Tablets: Microcrystalline cellulose PH102, potato starch, magnesium stearate, lactose monohydrate and colloidal silicon dioxide.

What ABITREXATE looks like and contents of the pack

ABITREXATE 2,5 mg TABLETS are flat-faced, yellow, bevel-edged and scored with a diameter of 6,5 mm, code MTX2 ½ on one side, PCH on the other side.

ABITREXATE 10 mg tablets are flat-faced, yellow, bevel-edged and scored with a diameter of 9 mm code MTX10 on one side.

ABITREXATE tablets are available in blister strips containing 10 tablets.

ABITREXATE tablets are available in white high-density polyethylene (HDPE) bottles with white pilferproof closures.

Each bottle contains 30 and 100 tablets.

Holder of Certificate of Registration

Teva Pharmaceuticals (Pty) Ltd

Maxwell Office Park,

Magwa Crescent West,

Waterfall City,

Midrand,

Gauteng,

2090

Tel No. +27 (0) 11 055 0200

This leaflet was last revised in

21 March 2021

Registration number

ABITREXATE 2,5 mg TABLETS: 37/26/0466

ABITREXATE 10 mg: S/26/0338