PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Teriflunomide Taro
Film-coated tablets

Active ingredient
Each tablet contains:
teriflunomide 14 mg

Inactive ingredients and allergens in the medicine: see section 2 under "Important information about some of this medicine's ingredients" and section 6 "Additional information".

Read the entire leaflet carefully before you start using this medicine.
This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

In addition to the leaflet, Teriflunomide Taro also has a patient safety information card. This card contains important safety information that you need to know and that you should follow before you start and during treatment with Teriflunomide Taro.

Read the patient safety information card and patient information leaflet before using this medicine. Keep the card in case you need to read it again.

1. WHAT IS THE MEDICINE INTENDED FOR?

Teriflunomide Taro is intended for the treatment of adults with relapsing-remitting multiple sclerosis, in order to reduce the frequency of relapses and to delay the progression of physical disability.

Therapeutic group: selective immunosuppressive medicines.

Teriflunomide Taro contains the active ingredient teriflunomide, a substance that acts on the immune system to limit its attack on the nervous system.

How does Teriflunomide Taro work
Teriflunomide Taro helps protect the CNS from attacks by the immune system by inhibiting the increase in levels of certain white blood cells (lymphocytes). This reduces the inflammation that causes nerve damage in MS.

What is multiple sclerosis
Multiple sclerosis (MS) is a chronic disease that affects the central nervous system (CNS). The CNS is made up of the brain and spinal cord.
In MS, the inflammation destroys the protective sheath (called myelin) that surrounds the nerve fibers of the CNS. Loss of myelin is called demyelination, and it disrupts the normal activity of the nerves.

People with relapsing-remitting MS will have recurrent relapses of physical symptoms resulting from the abnormal activity of the nerves. These symptoms vary from patient to patient, but usually involve:

- Difficulty walking
- Vision problems
- Balance problems

The symptoms may fully disappear after the relapse is over, but with time, certain problems may persist between relapses. This can cause physical disabilities that may interfere with your daily activities.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient teriflunomide or to any of the other ingredients in this medicine (see section 6).
- You developed a severe skin rash or skin peeling, blistering and/or mouth sores in the past after taking teriflunomide or leflunomide.
- You have severe liver problems.
- You are pregnant, think you are pregnant or are breastfeeding.
- You are suffering from a serious problem that affects your immune system, e.g., acquired immunodeficiency syndrome (AIDS).
- You have a serious problem with your bone marrow, or you have a significant reduction in levels of red or white blood cells or a reduced level of platelets in the blood.
- You are suffering from a serious infection.
- You have severe kidney problems that require dialysis.
- You have very low blood protein levels (hypoproteinemia).

If you are uncertain, or if you have questions regarding use of this medicine, speak to your doctor or pharmacist before taking this medicine.

Special warnings about using this medicine

Before using Teriflunomide Taro, tell your doctor if:

- You have liver problems and/or if you normally drink large quantities of alcohol; your doctor will perform blood tests before and during the treatment to check your liver function. If your test results indicate that you have a liver problem, your doctor may stop the treatment with Teriflunomide Taro. See section 4.
- You have high blood pressure (hypertension), whether controlled with medicines or not. Teriflunomide Taro can cause a rise in blood pressure. Your doctor will check your blood pressure before starting treatment and regularly during the treatment. See section 4.
- You have an infection. Before you take Teriflunomide Taro, your doctor will confirm that you have enough white blood cells and platelets in your blood. Teriflunomide Taro lowers the number of white blood cells, and your ability to fight the infection may be affected. Your doctor may refer you for blood tests to check your white blood cell level, if you think you have an infection. See section 4.
- You have severe skin reactions.
- You have respiratory symptoms.
- You feel weakness, numbness and pain in the hands and feet.
- You are about to receive a vaccine.
- You take leflunomide with Teriflunomide Taro.
- You are switching to or from Teriflunomide Taro treatment.
- You are due to undergo a specific blood test (calcium level). The test results may falsely indicate low levels of calcium.

Respiratory reactions
Tell your doctor if you have an unexplained cough or shortness of breath. Your doctor may perform additional tests.

Children and adolescents
Teriflunomide Taro is not intended for children and adolescents below the age of 18.

Tests and follow-up
Before you start taking this medicine, the doctor will refer you for blood tests and women of child-bearing age for a pregnancy test.

Drug interactions
If you are taking or have recently taken, other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.
Particularly, inform your doctor or pharmacist if you are taking any of the medicines listed below:
- Leflunomide, methotrexate and other medicines that affect the immune system (usually known as immunosuppressants or immunomodulators).
- Rifampicin - a medicine used to treat tuberculosis and other infections.
- Carbamazepine, phenobarbital, phenytoin - to treat epilepsy.
- *Hypericum perforatum* (St. John's wort) – a medicinal herb to treat depression.
- Repaglinide, pioglitazone, nateglinide or rosiglitazone – to treat diabetes.
- Daunorubicin, doxorubicin, paclitaxel, or topotecan - to treat cancer.
- Duloxetine, to treat depression, urinary incontinence or renal disease in diabetic patients.
- Alosetron to treat acute diarrhea.
- Theophylline for asthma.
- Tizanidine - a muscle relaxant.
- Warfarin, an anticoagulant used as a blood thinner (i.e., makes it more fluid) to prevent blood clots.
- Oral contraceptives (which contain ethinylestradiol and levonorgestrel).
- Cefaclor, benzylpenicillin (penicillin G), ciprofloxacin - for infections.
- Indomethacin, ketoprofen - for pain and inflammation.
- Furosemide for heart disease.
- Cimetidine to reduce gastric acidity.
- Zidovudine for HIV infection.
- Rosuvastatin, simvastatin, atorvastatin, pravastatin - for hypercholesterolemia (high cholesterol).
- Sulfasalazine, for inflammatory bowel disease or arthritis.
- Cholestyramine for high cholesterol or to relieve itchiness in liver disease.
- Active charcoal to reduce absorption of medicines or other substances.

Using this medicine and food
This medicine can be taken with or without food.

Pregnancy, breastfeeding and fertility
Do not take Teriflunomide Taro if you are **pregnant** or think that you may be **pregnant**. If you are pregnant or became pregnant while taking Teriflunomide Taro, the risk of the baby having birth defects increases. Women of child-bearing age must not take this medicine without using reliable contraceptives.

Refer to the doctor if you are planning to become pregnant after stopping treatment with Teriflunomide Taro, since you must ensure that most of the active ingredient of this medicine

has cleared from your body before you try to become pregnant. Natural clearance of the active ingredient from the body may take two years. This time can be shortened to a few weeks by taking certain medicines that speed up the clearance of Teriflunomide Taro from the body.
In any case, confirm via blood test that an adequate amount of the active ingredient has been cleared from your body and receive confirmation from your doctor that the blood level of Teriflunomide Taro is low enough to allow you to become pregnant.

For further information about laboratory tests, refer to your doctor.

If you suspect you are pregnant when taking Teriflunomide Taro or during the two years following termination of treatment, stop taking Teriflunomide Taro and refer to your doctor **immediately** to do a pregnancy test. If the test confirms that you are pregnant, your doctor may suggest treatment with certain medicines so that Teriflunomide Taro can be rapidly and adequately cleared from your body, as this may reduce the risk to your baby.

Contraceptives
You must use effective contraceptives during and after treatment with Teriflunomide Taro. Teriflunomide remains in your blood for a long time after you stop taking the medicine. Continue using effective contraceptives after stopping treatment.
- Do so until the Teriflunomide Taro levels in your blood are low enough - your doctor will check this.
- Consult your doctor about the best contraceptive method for you and about any possible need for a change in contraception.

Breastfeeding
Do not take Teriflunomide Taro when you are breastfeeding, since teriflunomide passes into the breast milk.

Driving and using machines
Teriflunomide Taro may cause you to feel dizzy, which may impair your ability to concentrate and react. Therefore, if you feel dizzy, do not drive or operate machines during treatment.

Important information about some of this medicine's ingredients
Teriflunomide Taro **contains lactose** (a kind of sugar). If you have been told by the doctor that you have an intolerance to certain sugars, consult your doctor before taking this medicine.
Teriflunomide Taro contains less than 1 mmol (23 mg) sodium per tablet, i.e., it is considered "sodium-free".

3. HOW TO USE THIS MEDICINE?

Treatment with Teriflunomide Taro will be supervised by a doctor who is experienced in the treatment of multiple sclerosis.
Always use this medicine according to your doctor's instructions.
Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine. Only your doctor will determine your dose and how you should take this medicine.
The usual dosage is usually one film-coated tablet (14 mg) per day.
Do not exceed the recommended dose.

Method of administration
Teriflunomide Taro is a medicine to be taken orally, one tablet per day, at any time of the day.
Do not chew! Swallow the tablet whole with water.
Teriflunomide Taro can be taken with or without food.

If you have accidentally taken a higher dose
If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you. You may experience side effects as described in section 4.

If you forget to take the medicine
If you forget to take the medicine at the scheduled time, do not take a double dose. Take the next dose at the usual time and consult your doctor.
Adhere to the treatment as recommended by your doctor.
Even if your health improves, do not stop taking the medicine without consulting your doctor.

If you stop taking this medicine
Do not stop taking Teriflunomide Taro or change the dosage without first consulting your doctor.

Do not take medicines in the dark! Check the label and the dose <u>every time</u> you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

Like with all medicines, using Teriflunomide Taro may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Serious side effects
Some side effects could be or could become serious, if you experience any of these, **refer to your doctor immediately**.

Uncommon (may affect up to one in 100 users):
- Inflammation of the pancreas which might include symptoms of pain in the abdominal area, nausea, or vomiting.
- Allergic reactions which might include symptoms of rash, hives, swelling of the lips, tongue or face or sudden difficulty breathing.
- Severe skin reactions which might include symptoms of skin rash, blistering, fever, or mouth ulcers.
- Severe infections or sepsis (a potentially life-threatening type of infection) which might include symptoms of high fever, shaking, chills, reduced urine flow, or confusion.
- Inflammation of the lungs which might include symptoms of shortness of breath or persistent cough.

Not known (the frequency of which has not yet been determined):
- Serious liver disease which might include symptoms of yellowing of the skin or the whites of the eyes, darker urine than usual, unexplained nausea and vomiting or abdominal pain.

Additional side effects

Very common side effects (may affect more than one in 10 users):
- Headache
- Diarrhea, nausea

- Increased ALT values (increase in the blood levels of certain liver enzymes), demonstrated in blood tests
- Hair thinning

Common side effects (may affect up to one in 10 users):
- Flu, upper respiratory tract infection, urinary tract infection, bronchitis, sinusitis, sore throat and discomfort when swallowing, bladder infection, gastrointestinal viral infection, oral herpes, tooth infection, laryngitis, fungal infection in the leg
- Lab values: reduced red blood cell count (anemia), changes in liver function test results and white blood cell count (see section 2), as well as an increase in muscle enzyme (creatine phosphokinase) have been observed
- Moderate allergic reactions
- Feeling anxious
- Paresthesia (pins and needles), feeling weak, numbness, tingling or pain in the lower back or leg; numbness, burning, tingling or pain in the palms and fingers (carpal tunnel syndrome)
- Palpitations
- Increased blood pressure
- Vomiting, toothache, upper abdominal pain
- Rash, acne
- Tendon, joint, bone pain, muscle pain (musculoskeletal pain)
- Urge to urinate more frequently than usual
- Heavy menstrual bleeding
- Pain
- Lack of energy or feeling weak
- Weight loss

Uncommon side effects (may affect up to one in 100 users):
- Decreased number of platelets (thrombocytopenia)
- Increased sensation or increased sensitivity, especially of the skin, stabbing or throbbing pain along one or more nerve paths, nerve problems in the arms or legs (peripheral neuropathy)
- Nail disorders, severe skin reactions
- Post-traumatic pain
- Psoriasis
- Inflammation of mouth or lips
- Abnormal levels of fats (lipids) in the blood
- Inflammation of the colon (colitis)

Rare side effects (may affect up to one in 1,000 users):
- Inflammation or injury of the liver

Not known (the frequency of these effects has not been established yet):
- Respiratory hypertension

If you experience any side effect, if any side effect gets worse or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link “Reporting Side Effects of Drug Treatment” on the Ministry of Health homepage (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by the doctor.
Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
Storage conditions
Store in the original package at a temperature below 25°C.
Do not throw away the medicine via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. ADDITIONAL INFORMATION

In addition to the active ingredient, this medicine also contains:
Lactose monohydrate, maize starch, microcrystalline cellulose, sodium starch glycolate, Opadry Blue 03M505004 (HPMC 2910/hypromellose, titanium dioxide, FD&C Blue#2/indigo carmine aluminium lake, glycerol, talc, FD&C Blue#1/brilliant blue FCF aluminium lake, FD&C Red#40/allura red aluminium lake), hydroxypropyl cellulose, colloidal anhydrous silica, magnesium stearate.

What the medicine looks like and the contents of the package:
Film-coated, blue, round, biconvex tablets, with an embossment of "14" on one side.

The pack contains 28 film-coated tablets.

Registration holder and importer's name and address: Taro International Ltd., 14 Hakitor St., Haifa Bay 2624761

Revised in May 2023 according to MOH guidelines.

Registration number of the medicine in the Ministry of Health's National Drug Registry: 171-24-36269-00