PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Teriflunomide Medomie

Film-coated tablets

Composition

Each tablet contains:
The active ingredient and its quantity: Teriflunomide 14 mg
Each tablet also contains 79 mg lactose.

Inactive ingredients and allergens: see section 2 ("Important information about some of the ingredients of the medicine") and section 6 ("Further Information").

Read this leaflet carefully in its entirety before using the medicine.

This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed for you only, do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.
The medicine is not intended for children and adolescents below the age of 18 years.

In addition to the leaflet, Teriflunomide Medomie also has a Patient Safety Information Card. This card contains important safety information that you must know and abide by before starting treatment and during treatment with Teriflunomide Medomie.
Read the Patient Safety Information Card and the Patient Leaflet before commencing use of the preparation. Keep the card for further reading, if necessary.

1. WHAT IS THE MEDICINE INTENDED FOR?

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

Teriflunomide Medomie 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 disability.

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.

How does Teriflunomide Medomie work
Teriflunomide Medomie 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.

Therapeutic group:
The active ingredient teriflunomide belongs to the group of medicines that selectively suppress the immune system.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient teriflunomide or to any of the other ingredients contained in the 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 regarding use of the medicine
Before treatment with Teriflunomide Medomie, tell the 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 Teriflunomide Medomie treatment. Please read section 4.
- You have high blood pressure (hypertension), whether controlled with medicines or not. Teriflunomide Medomie can cause a rise in blood pressure. Your doctor will check your blood pressure before starting treatment and regularly during the treatment. Please read section 4.
- You have an infection. Before you take Teriflunomide Medomie, your doctor will confirm that you have enough white blood cells and platelets in the blood. Since Teriflunomide Medomie lowers the number of white blood cells, 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 any infection. Herpes virus infections, including oral herpes or herpes zoster, may occur during teriflunomide treatment. In some cases, serious complications have occurred. Inform your doctor immediately if you suspect that you have any symptoms of herpes virus infections. Please read section 4.
- You have severe skin reactions.
- You have respiratory symptoms.
- You experience weakness, numbness and pain in the hands and feet.
- You are about to receive a vaccine.
- You take leflunomide with Teriflunomide Medomie.
- You are switching to or from Teriflunomide Medomie 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 Medomie is not intended for children and adolescents below the age of 18 years.

Tests and follow up
Before starting to use the medicine, the doctor will refer you for blood tests and women for a pregnancy test.

Drug interactions
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.
In particular, inform the 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 hypercholestrolemia (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.

Use of the medicine and food
The medicine can be taken with or without food.

Pregnancy, breastfeeding and fertility
Do not take Teriflunomide Medomie if you are pregnant or think that you may be pregnant. If you are pregnant or became pregnant while taking Teriflunomide Medomie, the risk of you having a baby with 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 Medomie, since you must confirm 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 Medomie 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 attending doctor that the blood level of Teriflunomide Medomie 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 Medomie or during the two years following termination of treatment, stop taking Teriflunomide Medomie 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 Medomie 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 Medomie. 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 Medomie levels in your blood are low enough – your doctor will check this.
- Consult the doctor about the best contraceptive method for you and about any possible need for a change in contraception.

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

Driving and using machinery

Teriflunomide Medomie 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 the ingredients of the medicine
Teriflunomide Medomie 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 Medomie contains sodium. This medicine contains less than 1 mmol (23 mg) sodium per tablet, i.e., it is considered “sodium-free”.

3. HOW SHOULD YOU USE THE MEDICINE?
Treatment with Teriflunomide Medomie will be supervised by a doctor who is experienced in the treatment of multiple sclerosis. Always use the preparation according to the doctor’s instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

Dosage
The dosage and treatment regimen will be determined by the doctor only. The usual dosage is generally one film-coated tablet (14 mg) per day.
Do not exceed the recommended dose.

Method of administration
Teriflunomide Medomie 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 Medomie can be taken with or without food.

If you accidentally took a higher dosage
If you took an overdose or if a child accidentally swallowed some medicine, immediately refer to your doctor or proceed to a hospital emergency room and bring the package of the medicine with you. You may experience side effects similar to those described in chapter 4.

If you forgot to take the medicine
If you forget to take this medicine at the designated time, do not take a double dose. Take the next dose at the regular time and consult the doctor.

Adhere to the treatment regimen as recommended by the doctor. Even if there is an improvement in your health, do not discontinue treatment with the medicine without consulting the doctor.

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

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take medicine. Wear glasses if you need them.
If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS
As with any medicine, use of Teriflunomide Medomie 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 1 in 100 people):
- 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 (frequency cannot be estimated from the available data):
- 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 can occur at the following frequencies:
Very common side effects (may affect more than 1 in 10 people):
- 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 1 in 10 people):
- Flu, upper respiratory tract infection, urinary tract infection, bronchitis, sinusitis, sore throat and discomfort when swallowing, bladder infection, gastrointestinal viral infection, tooth infection, laryngitis, fungal infection in the leg
- Herpes virus infections, including oral herpes and herpes zoster, with symptoms such as blisters, burning sensation, itching, skin numbness or pain, usually on one side of the upper body or face, and other symptoms, such as fever and weakness
- 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
- Nausea (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 1 in 100 people):
- 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 1 in 1,000 people):
- Inflammation or injury of the liver

Not known (frequency cannot be estimated from the available data):
- Respiratory hypertension

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link “Reporting Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Storage conditions
Store in the original package. Store at a temperature below 25°C.
Do not discard any medicine via wastewater or household waste.
Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Lactose monohydrate, maize starch (corn starch), sodium starch glycolate, hydroxy propyl cellulose, magnesium stearate, colloidal silicon dioxide, hypromellose, titanium dioxide, macrogol, brilliant blue FCF aluminum lake, iron oxide yellow.

What the medicine looks like and the contents of the package:
Film-coated, blue, pentagon-shaped tablets, with an embossment of "14" on one side and "T" engraved on the other side.

Pack: 28 film-coated tablets.

Registration Holder's name and address: Medomie Pharma Ltd., P.O.B. 816, Givatayim 5358305, Israel

Manufacturer's name and address:
MSN Laboratories private limited, Telangana 509228, India

This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, please ask your doctor.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 171-29-37077-99

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