**INSTRUCTIONS FOR USE**

**AUBAGIO 14 MG FILM-COATED TABLETS**

**For oral use.**

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***Active ingredient:*** 14 mg teriflunomide

***Excipients:*** Lactose monohydrate (from cow's milk), maize starch, microcrystalline cellulose, sodium starch glycolate (Type A), hydroxypropylcellulose, magnesium stearate, hypromellose, titanium dioxide (E171), talc, macrogol 8000, indigo carmine aluminum lake (E132)

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

***Read this ENTIRE INSTRUCTIONS FOR USE carefully before you start using this medicine, because it contains important information for you.***

- ***Keep these instructions for use. You may need to read them again later.***
- ***If you have any further questions, please ask your doctor or pharmacist.***
- ***This medicine has been prescribed for you personally, do not pass it on to others.***
- ***If you go to a doctor or hospital while using this medicine, tell your doctor that you are using this medicine.***
- ***Follow these instructions exactly. Do not use high or low doses other than the dose recommended for you.***

**In these Instructions for Use:**

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## 1. What is AUBAGIO and what is it used for?

AUBAGIO are pentagonal film-coated tablets, from pale blue to pastel blue, with "14" embossed on one side and the corporate logo on the other side. It is available in aluminum blister packs of 28 tablets.

AUBAGIO contains the active substance teriflunomide.

AUBAGIO is used to treat relapsing-remitting MS (multiple sclerosis) in adults.

**What is multiple sclerosis?**

MS is a long-term disease that affects the central nervous system (CNS). The CNS consists of the brain and spinal cord. In multiple sclerosis, inflammation destroys the protective sheath (called myelin) around the nerves in the CNS. This loss of myelin is called demyelination. This prevents nerves from functioning properly.

People with relapsing multiple sclerosis will experience recurrent attacks (relapses) of physical symptoms caused by their nerves not working properly. These symptoms vary from person to person but include:

- difficulty walking
- vision problems
- balance problems

After a relapse ends, some symptoms may disappear completely, but over time, some problems may remain between relapses. This can lead to some physical disabilities that can disrupt your daily activities.

AUBAGIO helps protect the immune system against attacks on the central nervous system by limiting the proliferation of certain white blood cells (lymphocytes). This limits the inflammation that leads to nerve damage in MS.

## 2. Before you use AUBAGIO

**Do NOT use AUBAGIO in the following situations:**

If you:

- Are allergic to the active substance or any of the other ingredients of this medicine (listed in section 6),
- Experience severe skin rash or peeling, blistering, and/or sores in your mouth after taking AUBAGIO or leflunomide,
- Have severe liver problems,
- Are **pregnant**, think you may be pregnant, or are breastfeeding,
- Have a serious problem affecting your immune system (e.g., AIDS),
- Have a serious problem with your bone marrow or have low red (anemia) or white blood cell (leukopenia, neutropenia) or platelet counts,
- Have a severe infection,
- Have severe kidney problems requiring dialysis,
- Have very low protein levels in your blood (hypoproteinemia),

If you are not sure, please consult your doctor or pharmacist before taking AUBAGIO.

**Use AUBAGIO CAUTIOUSLY in the following situations**

Talk to your doctor or pharmacist before taking AUBAGIO in the following situations. If you:

- Have liver problems and/or consume significant amounts of alcohol; your doctor will perform blood tests before and during treatment to check how your liver is functioning. If test results indicate a problem with your liver, your doctor may stop your AUBAGIO treatment (See Section 4).
- Have high blood pressure (hypertension) controlled or uncontrolled by medication. AUBAGIO can cause an increase in blood pressure. Your doctor will regularly monitor your blood pressure during treatment (See Section 4).
- Have an infection. Before taking AUBAGIO, your doctor will ensure you have enough white blood cells and platelets in your blood. Since AUBAGIO reduces the number of white blood cells in the blood, this may affect your ability to cope with infection. If you think you have an infection, your doctor may order blood tests to check your white blood cells (See Section 4).
- Since a decrease in white blood cell count may occur during AUBAGIO treatment, a complete blood count should be performed before and during treatment as needed. The risk of blood count abnormalities increases in patients with pre-existing low blood values.
- Your AUBAGIO treatment should be immediately discontinued if certain severe widespread major skin reactions occur.
- Lung inflammation, including symptoms such as shortness of breath or persistent cough, called interstitial lung disease, has been reported during AUBAGIO treatment. If you experience symptoms such as sudden breathing difficulties accompanied by cough and fever, consult your doctor immediately. Your doctor may decide to discontinue your AUBAGIO treatment and, if necessary, initiate procedures to rapidly eliminate the drug from your body.
- If you experience symptoms such as weakness, numbness, and pain in your hands and feet or other parts of your body (peripheral neuropathy), tell your doctor. Your doctor may decide to discontinue your AUBAGIO treatment and, if necessary, initiate procedures to rapidly eliminate the drug from your body.
- Are going to be vaccinated.
- Are using leflunomide together with AUBAGIO.
- Are switching from AUBAGIO treatment to another treatment or from another treatment to AUBAGIO treatment.
- Need a special blood test to measure calcium levels. Calcium levels may appear falsely low.
- After AUBAGIO treatment, it may take a long time, from 8 months to 2 years, for the drug to be eliminated from your body, depending on your individual characteristics. If necessary, your doctor may apply accelerated elimination procedures to remove the drug after treatment.
- Your AUBAGIO treatment should be immediately discontinued if inflammatory oral sores (ulcerative stomatitis) occur.

**Respiratory reactions**

Tell your doctor if you have unexplained cough and dyspnea (shortness of breath). Your doctor may perform additional tests.

If these warnings apply to you at any time, please consult your doctor.

**Using AUBAGIO with food and drink**

You can take AUBAGIO with or without food.

**Pregnancy**

*Consult your doctor or pharmacist before using this medicine.*

Do not use AUBAGIO if you are pregnant or think you may be pregnant. If you become pregnant or get pregnant while using AUBAGIO, there is an increased risk of giving birth to a baby with birth defects. Women of childbearing potential should not use AUBAGIO without using reliable birth control measures.

Tell your doctor if you plan to become pregnant after AUBAGIO treatment, as most of AUBAGIO needs to be eliminated from the body before you try to conceive. The natural elimination of the drug from the body can take up to 2 years. This period can be reduced to a few weeks by taking certain medications that accelerate the elimination of AUBAGIO from the body.

In both cases, it must be confirmed by a blood test that AUBAGIO has been sufficiently eliminated from the body, and your treating doctor must confirm that the blood level of AUBAGIO is low enough to allow you to become pregnant.

For detailed information on laboratory tests, please contact your doctor.

If you suspect you are pregnant while taking AUBAGIO or within two years after finishing treatment, you should immediately contact your doctor for a pregnancy test. If the test confirms you are pregnant, your doctor may recommend treatment with specific medications to rapidly and sufficiently eliminate AUBAGIO from your body, as this may reduce the risk to your baby.

**Contraception**

You must use an effective method of contraception during AUBAGIO treatment and afterwards. Teriflunomide remains in your blood for a long time after discontinuation. Continue to use effective contraception after discontinuing treatment.

- Continue until AUBAGIO levels in your blood are sufficiently low – your doctor will check this.
- Talk to your doctor about the best birth control method for you and any potential need to change your birth control method.

AUBAGIO may interact with oral contraceptives (containing ethinylestradiol or levonorgestrel) and may alter their effects. Tell your doctor if you are using any of these medicines.

*If you notice that you are pregnant during your treatment, consult your doctor or pharmacist immediately.*

**Breastfeeding**

*Consult your doctor or pharmacist before using this medicine.*

Do not use AUBAGIO while breastfeeding, as teriflunomide passes into breast milk.

**Driving and using machines**

AUBAGIO may make you feel dizzy and may affect your ability to concentrate and react. Do not drive or use machines if you are affected.

**Important information about some of the excipients in AUBAGIO**

AUBAGIO contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

AUBAGIO contains less than 1 mmol (23 mg) sodium per “dose”; that is to say, it is essentially “sodium-free”.

**Using with other medicines**

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

Especially tell your doctor or pharmacist if you are using any of the following:

- Leflunomide, methotrexate, and other medicines that affect the immune system (generally referred to as immunosuppressants or immunomodulators)
- Rifampicin (a medicine used to treat tuberculosis and other infections)

- Carbamazepine, phenobarbital, phenytoin for epilepsy
- St. John's wort (a herbal medicine for depression)
- Repaglinide, pioglitazone, nateglinide or rosiglitazone for diabetes
- Daunorubicin, doxorubicin, paclitaxel or topotecan for cancer
- Duloxetine for depression, urinary incontinence, or kidney disease in diabetics
- Alosetron for the treatment of severe diarrhea
- Theophylline for asthma
- Tizanidine, a muscle relaxant
- Warfarin, a blood thinner used to prevent blood clots (i.e., making it more fluid)
- Oral contraceptives (containing ethinylestradiol or levonorgestrel)
- Cefaclor, benzylpenicillin (penicillin G), ciprofloxacin for infections
- Indomethacin, ketoprofen for pain or inflammation
- Furosemide, a diuretic for heart disease
- Cimetidine to reduce gastric acid (stomach acid)
- Zidovudine for HIV infection (AIDS)
- Rosuvastatin, simvastatin, atorvastatin, pravastatin for hypercholesterolemia (high cholesterol)
- Sulfasalazine for inflammatory bowel disease or rheumatoid arthritis
- Cholestyramine to relieve itching in high cholesterol or liver disease
- Activated charcoal to reduce the absorption of drugs or other substances

*If you are currently using or have recently used any prescription or non-prescription medication, please inform your doctor or pharmacist about them.*

**3. How to use AUBAGIO?**

**Instructions for proper use and dose/frequency of administration:**

AUBAGIO treatment will be monitored by a doctor experienced in the treatment of multiple sclerosis.

Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

The recommended dose is one 14 mg film-coated tablet daily.

**Route and method of administration:**

AUBAGIO is taken orally. AUBAGIO is taken as a single daily dose at any time of the day.

You should swallow the tablet whole with water.

AUBAGIO can be taken before or after meals.

**Different age groups:**

**Use in children:**

AUBAGIO should not be used in children and adolescents under 18 years of age. This is because the effects of the drug in this age group are unknown.

**Use in the elderly:**

AUBAGIO should be used with caution in patients 65 years of age and older.

**Specific usage situations:**

**Kidney/Liver failure:**

No dose adjustment is required for patients with kidney failure not on dialysis. AUBAGIO should not be used in patients with severe kidney problems requiring dialysis.

AUBAGIO should not be used in patients with severe liver failure.

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

**If you use more AUBAGIO than you should:**

If you take too much AUBAGIO, call your doctor immediately. You may experience side effects similar to those described in Section 4.

*If you have used more AUBAGIO than you should, talk to a doctor or pharmacist.*

**If you forget to use AUBAGIO**

Do not take a double dose to make up for a forgotten tablet. Take the next dose at the prescribed time. *Do not take a double dose to make up for forgotten doses.*

**Effects that may occur when treatment with AUBAGIO is discontinued**

Do not stop taking AUBAGIO or change your dose without first talking to your doctor.

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

**4. What are the possible side effects?**

Like all medicines, AUBAGIO can cause side effects in people who are sensitive to the substances contained in it.

Side effects are listed in the following categories:
Very common: May be seen in at least 1 in 10 patients.
Common: May be seen in less than 1 in 10 patients, but more than 1 in 100 patients.
Uncommon: May be seen in less than 1 in 100 patients, but more than 1 in 1,000 patients.
Rare: May be seen in less than 1 in 1,000 patients, but more than 1 in 10,000 patients.
Very rare: May be seen in less than 1 in 10,000 patients.
Not known: Cannot be estimated from the available data.

The following side effects may occur with this medicine:

**If any of the following occur, stop using AUBAGIO and IMMEDIATELY notify your doctor or go to the emergency department of the nearest hospital:**

**Common**

- Pancreatitis, including symptoms such as severe pain in the upper abdomen (which may also be felt in your back), nausea or vomiting.

**Uncommon**

- Allergic reactions, including symptoms such as rash, hives, swelling of the lips, tongue or face, or sudden difficulty breathing.
- Severe skin reactions, including symptoms such as skin rash, blisters on the skin, fever or sores in the mouth.
- Sepsis (a potentially life-threatening type of infection) or severe infections, which may include symptoms of high fever, chills, shivers, decreased urine flow, or mental confusion.
- Inflammation in the lungs, including symptoms such as shortness of breath or persistent cough.

**Not known**

Severe liver disease, including symptoms such as yellowing of your skin or the whites of your eyes, darker than normal urine, unexplained nausea and vomiting, or abdominal pain.

If you notice any of the above side effects, tell your doctor immediately.

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

**Tell your doctor if you notice any of the following:**

**Very common**

- Headache
- Diarrhea, nausea
- Increase in ALT in tests (increase in blood levels of certain liver enzymes)
- Hair thinning

**Common**

- Flu, upper respiratory tract infection, urinary tract infection, bronchitis (inflammation of the bronchi), sinusitis (inflammation of the sinuses), sore throat and difficulty swallowing, cystitis (inflammation of the urinary bladder), viral gastroenteritis (stomach and intestinal infection caused by viruses, accompanied by diarrhea and vomiting), oral herpes (cold sores in the mouth area), tooth infection, laryngitis (inflammation of the larynx), athlete's foot infection.
- Laboratory values: Decrease in red blood cell count (anemia), changes in liver and white blood cell test results (See Section 2), increase in a muscle enzyme (creatine phosphokinase) have been observed.
- Mild allergic reactions

- Feeling anxious
- Weakness, numbness, tingling sensation or pain in the lower back or leg (sciatica); numbness, burning or pain sensation in the hand 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)
- Need to urinate more often than usual
- Painful menstruation
- Pain
- Feeling drained and weak (asthenia)
- Weight loss

**Uncommon**

- Decrease in platelet count (thrombocytopenia)
- Increased sensation or sensitivity, especially in the skin; stabbing or throbbing pain along one or more nerves, problems with nerves in the arms or legs (peripheral neuropathy)
- Nail disorders, severe skin reactions
- Pain occurring after injury (post-traumatic pain)
- Psoriasis
- Inflammation of the mouth/lips
- Abnormal fat levels in the blood (lipids)
- Inflammation of the large intestine (colitis)

**Rare**

- Liver inflammation or damage

**Not known**

- Pulmonary hypertension

*If you experience any side effects not mentioned in these instructions for use, inform your doctor or pharmacist.*

**Reporting of side effects**

If you experience any side effects, whether listed in these instructions for use or not, talk to your doctor, pharmacist or nurse. You can also report side effects to the Turkish Pharmacovigilance Centre (TÜFAM) by clicking on the "Drug Side Effect Notification" icon on www.titck.gov.tr or by calling the side effect notification line at 0 800 314 00 08. By reporting side effects, you will contribute to obtaining more information about the safety of the medicine you are using.

**5. How to store AUBAGIO?**

*Keep AUBAGIO out of the sight and reach of children and in its original packaging.*

Store below 30 ºC at room temperature.

**Use in accordance with the expiry date.**

*Do not use AUBAGIO after the expiry date stated on the carton/protective sleeve/blister.* The expiry date refers to the last day of that month.

Do not dispose of expired or unused medicines in the trash! Hand them over to the collection system specified by the Ministry of Environment and Urbanization.

***Marketing Authorization Holder:***
Sanofi Sağlık Ürünleri Ltd. Şti.
Şişli-İstanbul

***Manufacturer:***
Opella Healthcare International SAS
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France

*This instructions for use was approved on …/…/….*