PACKAGE LEAFLET: INFORMATION FOR THE USER

ARAVA

20 mg film-coated tablets

LEFLUNOMIDE

• This leaflet is a copy of the Summary of Product Characteristics and Patient Information Leaflet for a medicine, which outlines the conditions under which the medicine should be used and information on its known safety • The product information may be updated several times within its shelf life, and there could be differences between the version of information shown here and other information in the public domain or in the package insert • This leaflet may not contain all the information about the medicine or the information may not be the most up to date version for this product • If you have any questions or are not sure about anything, ask your doctor or pharmacist • Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

• Keep this leaflet • You may need to read it again • If you have any further questions, ask your doctor or pharmacist • This medicine has been prescribed for you only • Do not pass it on to others • It may harm them, even if their signs of illness are the same as yours • If you get any side effects, talk to your doctor or pharmacist • This includes any possible side effects not listed in this leaflet •

What is in this leaflet?

1. WHAT ARAVA IS AND WHAT IT IS USED FOR

Arava belongs to a group of medicines called anti-rheumatic medicines. It contains the active substance leflunomide.
Arava is used to treat adult patients with active rheumatoid arthritis or with active psoriatic arthritis.
Symptoms of rheumatoid arthritis include inflammation of joints, swelling, difficulty moving and pain. Other symptoms that affect the entire body include loss of appetite, fever, loss of energy and anaemia (lack of red blood cells).
Symptoms of active psoriatic arthritis include inflammation of joints, swelling, difficulty moving, pain and patches of red, scaly skin (skin lesions).

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE ARAVA

Do not take Arava

- if you have ever had an allergic reaction to leflunomide (especially a serious skin reaction, often accompanied by fever, joint pain, red skin stains, or blisters e.g. Stevens-Johnson syndrome) or to any of the other ingredients of this medicine (listed in section 6), or if you are allergic to teriflunomide (used to treat multiple sclerosis),
- if you have any liver problems,

- if you have moderate to severe kidney problems,
- if you have severely low numbers of proteins in your blood (hypoproteinaemia),
- if you suffer from any problem which affects your immune system (e.g. AIDS),
- if you have any problem with your bone marrow, or if you have low numbers of red or white cells in your blood or a reduced number of blood platelets,
- if you are suffering from a serious infection,
- if you are pregnant, think you may be pregnant, or are breast-feeding.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking Arava

- if you have ever suffered from interstitial lung disease
- if you have ever had tuberculosis or if you have been in close contact with someone who has or has had tuberculosis. Your doctor may perform tests to see if you have tuberculosis
- if you are male and wish to father a child. As it can not be excluded that Arava passes into semen, reliable contraception should be used during treatment with Arava. Men wishing to father a child should contact their doctor who may advise them to stop taking Arava and take certain medicines to remove Arava rapidly and sufficiently from their body. You will then need a blood test to make sure that Arava has been sufficiently removed from your body, and you should then wait for at least another 3 months before attempting to father a child.

Arava can occasionally cause some problems with your blood, liver, lungs, or nerves in your arms or legs. It may also cause some serious allergic reactions (including Drug Reaction with Eosinophilia and Systemic Symptoms [DRESS]), or increase the chance of a severe infection. For more information on these, please read section 4 (Possible side effects).

DRESS appears initially as flu-like symptoms and a rash on the face then an extended rash with a high temperature, increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia) and enlarged lymph nodes.

Your doctor will carry out blood tests at regular intervals, before and during treatment with Arava, to monitor your blood cells and liver. Your doctor will also check your blood pressure regularly as Arava can cause an increase in blood pressure.

Tell your doctor if you have unexplained chronic diarrhoea. Your doctor may perform additional tests for differential diagnosis.

Children and adolescents

Arava is not recommended for use in children and adolescents below 18 years of age.

Other medicines and Arava

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

This is especially important if you are taking:

- other medicines for rheumatoid arthritis such as antimalarials (e.g. chloroquine and hydroxychloroquine), intramuscular or oral gold, D-penicillamine, azathioprine and other immunosuppressive medicines (e.g. methotrexate) as these combinations are not advisable,
- warfarin and other oral medicines used to thin the blood, as monitoring is necessary to reduce the risk of side effects of this medicine
- teriflunomide for multiple sclerosis - repaglinide, pioglitazone, nateglinide, or rosiglitazone for diabetes
- daunorubicin, doxorubicin, paclitaxel, or topotecan for cancer
- duloxetine for depression, urinary incontinence or in kidney disease in diabetics
- alosetron for the management of severe diarrhoea
- theophylline for asthma
- tizanidine, a muscle relaxant
- oral contraceptives (containing ethinylestradiol and levonorgestrel)

- cefaclor, benzylpenicillin (penicillin G), ciprofloxacin for infections
- indomethacin, ketoprofen for pain or inflammation
- furosemide for heart disease (diuretic, water pill)
- zidovudine for HIV infection
- rosuvastatin, simvastatin, atorvastatin, pravastatin for hypercholesterolemia (high cholesterol)
- sulfasalazine for inflammatory bowel disease or rheumatoid arthritis
- a medicine called colestyramine (used to reduce high cholesterol) or activated charcoal as these medicines can reduce the amount of Arava which is absorbed by the body.

If you are already taking a nonsteroidal anti-inflammatory drug (NSAID) and/or corticosteroids, you may continue to take them after starting Arava.

Vaccinations

If you have to be vaccinated, ask your doctor for advice. Certain vaccinations should not be given while taking Arava, and for a certain amount of time after stopping treatment.

Arava with food, drink and alcohol

Arava may be taken with or without food.
It is not recommended to drink alcohol during treatment with Arava. Drinking alcohol while taking Arava may increase the chance of liver damage.

Pregnancy and breast-feeding

Do not take Arava if you are, or think you may be pregnant. If you are pregnant or become pregnant while taking Arava, the risk of having a baby with serious birth defects is increased.
Women of childbearing potential must not take Arava without using reliable contraceptive measures.
Tell your doctor if you plan to become pregnant after stopping treatment with Arava, as you need to ensure that all traces of Arava have left your body before trying to become pregnant. This may take up to 2 years. This may be reduced to a few weeks by taking certain medicines which speed up removal of Arava from your body.
In either case it should be confirmed by a blood test that Arava has been sufficiently removed from your body and you should then wait for at least another month before you become pregnant.
For further information on the laboratory testing please contact your doctor.
If you suspect that you are pregnant while taking Arava or in the two years after you have stopped treatment, you must contact your doctor immediately for a pregnancy test. If the test confirms that you are pregnant, your doctor may suggest treatment with certain medicines to remove Arava rapidly and sufficiently from your body, as this may decrease the risk to your baby.
Do not take Arava when you are breast-feeding, as leflunomide passes into the breast milk.

Driving and using machines

Arava can make you feel dizzy which may impair your ability to concentrate and react. If you are affected, do not drive, or use machines.

Arava contains lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. HOW TO TAKE ARAVA

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.
The usual starting dose of Arava is one 100 mg tablet once daily for the first three days. After this, most patients need a dose of:

- For rheumatoid arthritis: 10 or 20 mg Arava once daily, depending on the severity of the disease.
- For psoriatic arthritis: 20 mg Arava once daily.

Swallow the tablet whole and with plenty of water.
It may take about 4 weeks or longer until you start to feel an improvement in your condition.
Some patients may even still feel further improvements after 4 to 6 months of therapy.
You will normally take Arava over long periods of time.

If you take more Arava than you should

If you take more Arava than you should, contact your doctor or get other medical advice. If possible, take your tablets or the box with you to show the doctor.

If you forget to take Arava

If you forget to take a dose, take it as soon as you remember, unless it is nearly time for your next dose. Do not take a double dose to make up for a forgotten dose.
If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Tell your doctor immediately and stop taking Arava:

- if you experience weakness, feel light-headed or dizzy or have difficulty breathing, as these may be signs of a serious allergic reaction,
- if you develop a skin rash or ulcers in your mouth, as these may indicate severe, sometimes life-threatening reactions (e.g. Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, Drug Reaction with Eosinophilia and Systemic Symptoms [DRESS]), see section 2.

Tell your doctor immediately if you experience:

- pale skin, tiredness, or bruising, as these may indicate blood disorders caused by an imbalance in the different types of blood cells which make up blood,
- tiredness, abdominal pain, or jaundice (yellow discolouration of the eyes or skin), as these may indicate serious conditions such as liver failure, which may be fatal,
- any symptoms of an infection such as fever, sore throat or cough, as this medicine may increase the chance of a severe infection which may be life-threatening,
- a cough or breathing problems as these may indicate problems of the lung (interstitial lung disease or pulmonary hypertension);
- unusual tingling, weakness or pain in your hands or feet as these may indicate problems with your nerves (peripheral neuropathy).

Common side effects (may affect up to 1 in 10 people)

- a slight decrease in the number of white blood cells (leucopenia),
- mild allergic reactions,
- loss of appetite, weight loss (usually insignificant),
- tiredness (asthenia),
- headache, dizziness,
- abnormal skin sensations like tingling (paraesthesia),
- mild increase in blood pressure,
- colitis
- diarrhoea,
- nausea, vomiting,
- inflammation of the mouth or mouth ulcers,
- abdominal pain,
- an increase in some liver test results,
- increased hair loss,
- eczema, dry skin, rash, itching,

• tendonitis (pain caused by inflammation in the membrane surrounding the tendons usually in the feet or hands),
• an increase of certain enzymes in the blood (creatine phosphokinase),
• problems in the nerves of the arms or legs (peripheral neuropathy).

Uncommon side effects (may affect up to 1 in 100 people)
• a decrease in the number of red blood cells (anaemia) and a decrease in the number of blood platelets (thrombocytopenia),
• a decrease in the levels of potassium in the blood,
• anxiety,
• taste disturbances,
• urticaria (nettle rash),
• tendon rupture,
• an increase in the levels of fat in the blood (cholesterol and triglycerides),
• a decrease in the levels of phosphate in the blood.

Rare side effects (may affect up to 1 in 1,000 people)
• an increase in the numbers of blood cells called eosinophiles (eosinophilia); mild decrease in the number of white blood cells (leucopenia); decrease in the number of all blood cells (pancytopenia),
• severe increase in blood pressure,
• inflammation of the lung (interstitial lung disease),
• an increase in some liver results which may develop into serious conditions such as hepatitis and jaundice,
• severe infections called sepsis which may be fatal,
• an increase of certain enzymes in the blood (lactate dehydrogenase).

Very rare side effects (may affect up to 1 in 10,000 people)
• a marked decrease of some white blood cells (agranulocytosis),
• severe and potentially severe allergic reactions,
• inflammation of the small vessels (vasculitis, including cutaneous necrotizing vasculitis),
• inflammation of the pancreas (pancreatitis),
• severe liver injury such as liver failure or necrosis which may be fatal,
• severe sometimes life-threatening reactions (Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme).

Other side effects such as kidney failure, a decrease in the levels of uric acid in your blood, pulmonary hypertension, male infertility (which is reversible once treatment with this medicine is stopped), cutaneous lupus (characterized by rash/erythema on skin areas that are exposed to light), psoriasis (new or worsening) and DRESS may also occur with an unknown frequency.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

United Kingdom
You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

Ireland
You can also report side effects directly via HPRA
Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2;
Tel: +353 1 6764971; Fax: +353 1 6762517.
Website: www.hpra.ie; e-mail: medsafety@hpra.ie

Malta
You can also report side effects directly via ADR Reporting www.medicinesauthority.gov.mt/adrportal
By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE ARAVA

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the packaging. The expiry date refers to the last day of that month.
Blister: Store in the original package.
Bottle: Keep the bottle tightly closed.
Do not throw away any medicines 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. CONTENTS OF THE PACK AND OTHER INFORMATION

What Arava contains

- The active substance is leflunomide. One filmcoated tablet contains 20 mg of leflunomide.
- The other ingredients are: maize starch, povidone (E1201), crospovidone (E1202), silica colloidal anhydrous, magnesium stearate (E470b), and lactose monohydrate in the tablet core, as well as talc (E553b), hypromellose (E464), titanium dioxide (E171), macrogol 8000 and yellow ferric oxide (E172) in the film-coating.

What Arava looks like and contents of the pack

Arava 20 mg film-coated tablets are yellowish to ochre and triangular.
Imprint on one side: ZBO.
The tablets are packed in blisters or bottles.
Packs of 30, 50 and 100 tablets are available.
Not all pack size may be marketed.

Marketing Authorisation Holder

Sanofi-Aventis Deutschland GmbH
D-65926 Frankfurt am Main
Germany

Manufacturer

Sanofi Winthrop Industrie
56, Route de Choisy au Bac
F-60205 Compiegne Cedex
France

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

Ireland
sanofi-aventis Ireland Ltd.
T/A SANOFI
Tel: +353 (0) 1 403 56 00

Malta
Sanofi Malta Ltd.
Tel: +356 21493022

United Kingdom
Sanofi
Tel: +44 (0) 845 372 7101

This leaflet was last revised in 12/2015.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu/.