

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr **ARAVA**[®]

Leflunomide Tablets

Read this carefully before you start taking **ARAVA** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **ARAVA**.

What is ARAVA used for?

ARAVA is used to treat adults who have active rheumatoid arthritis. Rheumatoid arthritis is an immune system disease causing inflammation of the joints.

How does ARAVA work?

ARAVA includes the medicinal ingredient, leflunomide. Leflunomide belongs to a group of drugs called immunosuppressants. In rheumatoid arthritis, the immune system produces a chemical in the body that causes inflammation. This causes pain, stiffness, and swelling around the joints. ARAVA works by reducing the body's ability to produce the chemical that is responsible for the inflammation. This helps control the symptoms of rheumatoid arthritis.

What are the ingredients in ARAVA?

Medicinal ingredients: leflunomide.

Non-medicinal ingredients: colloidal silicon dioxide, crospovidone, hydroxypropyl methylcellulose, Lactose monohydrate, maize starch, magnesium stearate, polyethylene glycol, povidone, talc, titanium dioxide, yellow ferric oxide (20 mg tablet only)

ARAVA comes in the following dosage forms:

Film coated tablets, 10 mg, 20 mg and 100 mg.

Do not use ARAVA if:

- you are pregnant, think you are pregnant or able to get pregnant but are not on reliable birth control. Pregnancy must be excluded before you start treatment with ARAVA;
- you are breastfeeding;
- you have a disease of the liver;
- you are allergic or have ever had an allergic reaction to leflunomide, teriflunomide

or any other ingredients in this medicine. Especially a serious skin reaction such as red rash, skin peeling, blisters;

- you have a disorder that impacts your immune system (e.g. AIDS);
- you have a bone marrow problem or if there is a significant decrease in the number of red cells, white cells, or platelets in your blood;
- you have a serious infection;
- you have a moderate to severe kidney disease;
- you have severely low numbers of proteins in your blood (hypoproteinemia);
- you are younger than 18 years of age.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ARAVA. Talk about any health conditions or problems you may have, including if you:

- have or had heart disease or heart valve problems
- have or had blood clots stuck in the lung (pulmonary thromboembolism) or lung disorders (i.e. interstitial lung disease).
- have ever had tuberculosis. If you have ever had tuberculosis, your healthcare professional will monitor you in case the tuberculosis becomes active again.

Other warnings you should know about:

Washout Procedures:

Serious side effects might occur and persist, even if the treatment with ARAVA has been stopped. To manage these side effects, your healthcare professional may remove ARAVA from your body by performing a Washout Procedure. Your healthcare professional may also perform a Washout Procedure if you switch to other drugs used to treat rheumatoid arthritis (i.e. Disease-Modifying Antirheumatic Drugs). This is because ARAVA can stay in your body for a long period of time after you stop taking it.

Stomach and Intestinal Problems (gastrointestinal):

Taking ARAVA may cause gastrointestinal side effects, some can be serious or fatal. Tell your healthcare professional if you have unexplained chronic diarrhoea or weight loss. Your healthcare professional may perform additional tests to determine if you have Colitis.

Nerve problems:

Taking ARAVA may cause nerve problems in your arms or legs. Speak to your healthcare professional immediately if you experience altered sensations, muscle weakness, numbness, tingling or burning in arms or legs. You are at a higher risk of experiencing nerve problems if you are:

- over 60 years of age

- taking neurotoxic medication
- diabetic

Lung Problems:

Taking ARAVA can cause diseases that inflame or scar lung tissue (Interstitial Lung Disease). Interstitial Lung Disease can be fatal. Speak to your healthcare professional if you experience any of the side effects. See [What are possible side effects from using ARAVA?](#)

The risk of developing Interstitial Lung Disease is higher if you:

- have a disease that affects the lungs and other parts of the respiratory system
- have or had taken drugs that cause Interstitial Lung Disease (i.e. Disease-Modifying Antirheumatic Drugs).

Skin Problems:

Severe skin reactions may occur when taking ARAVA. Speak to your healthcare professional immediately if you experience any of symptoms associated with the severe skin reactions.

This includes:

- Stevens-Johnson syndrome
- toxic epidermal necrolysis
- drug reaction with eosinophilia and systemic symptoms (DRESS)
- Skin ulcers

See [‘What are possible side effects from using ARAVA?’](#) for more information. Your healthcare professional may end your treatment and perform the ‘Washout Procedure’

Pregnancy and breastfeeding:**Female patients**

- If you are pregnant, able to get pregnant or think you are pregnant, there are specific risks you should discuss with your healthcare professional
- Do not take ARAVA if you are, or think you may be pregnant. It may harm your unborn baby and cause serious birth defects.
- Do not breastfeed while you are taking ARAVA
- If you are able to become pregnant:
 - Your healthcare professional will do a pregnancy test before you start taking ARAVA. This test must show that you are not pregnant
 - Use reliable birth control methods when taking ARAVA. Ask your healthcare professional about methods of birth control available to you.
- Speak to your healthcare professional if you plan to become pregnant after stopping treatment with ARAVA. ARAVA need to be eliminated from your body before trying to become pregnant.

- Once you stop taking ARAVA, you must wait a period of 2 years before trying to get pregnant.
- This waiting period may be shortened to a few weeks by taking a certain medicine. The medicine will speed up the removal of ARAVA from your body.
- Speak to your healthcare professional if you are taking an oral contraceptive pill. The medicine that speeds up the removal of ARAVA may lower the effect of your contraceptive pill. You may need another contraceptive method during this period.
- Two blood tests must be taken two weeks apart to show that ARAVA has been removed from your body.
- Contact your healthcare professional **immediately** if you suspect that you are pregnant while taking ARAVA or in the two years after you have stopped treatment.
 - You must have a pregnancy test at the first delay of your period. If the test confirms that you are pregnant, your healthcare professional will discuss the potential risks to your unborn baby.
 - Your healthcare professional may suggest treatment with certain medicines to remove ARAVA from your body. This treatment may reduce the risk to your baby.

Male patients

- Avoid fathering a child while you are taking ARAVA or two years after your treatment. It may harm your unborn baby and cause serious birth defects
- During your treatment with ARAVA, use a reliable birth control each time you have sex with a woman who is pregnant, may be pregnant or could get pregnant. Ask your healthcare professional about methods of birth control available to you.
- If you wish to father a child
 - During your treatment, your healthcare professional may stop treatment and advise you to take a certain medicine. The medicine will speed up the removal of ARAVA from your body.
 - After your treatment, inform your healthcare professional beforehand. You must wait a period of 2 years before trying to father a child. This waiting period may be shortened by taking a certain medicine that will remove ARAVA from your body.
 - Two blood tests must be taken to show that ARAVA has been removed from your body. You should then wait for another 3 months before you try to get your partner pregnant.
- If, during your treatment with ARAVA or you have taken it within the last 2 years, your sexual partner becomes pregnant or thinks she may be pregnant, tell your healthcare professional right away.

Check-ups and testing: You will have regular visits with your healthcare professional, before and during your treatment. They will:

- Check your liver function as ARAVA may cause liver problems
- Check your lungs and blood pressure
- Do blood tests to monitor blood cell levels.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with ARAVA:

- activated charcoal
- cholestyramine
- cimetidine (stomach acid medicine)
- duloxetine (anti-depressant)
- Certain disease modifying antirheumatic (DMARDs) including gold (taken by mouth or by injection into the muscle), penicillamine, methotrexate, or azathioprine
- phenytoin
- teriflunomide
- theophylline (asthma medicine)
- tizanidine (muscle relaxant medicine)
- warfarin
- medicines used to treat diabetes, such as: repaglinide, pioglitazone, rosiglitazone, nateglinide or tolbutamide
- oral contraceptives
- some medicines used to treat infections such as: antimalarial drugs, cefaclor, ciprofloxacin, penicillin G, rifampin, rifampicin, zidovudine
- medicines used to lower blood cholesterol, such as: rosuvastatin, atorvastatin, simvastatin, pravastatin
- anti-inflammatory drugs, such as: indomethacin, ketoprofen, sulfasalazine
- diuretics (water losing pills), such as: furosemide
- some medicines to treat cancer such as: paclitaxel, methotrexate, topotecan, daunorubicin, doxorubicin
- medicines used to relieve pain and inflammation such as nonsteroidal anti-inflammatory drugs (NSAIDs) or cortisone. ARAVA can be taken with these medicines. Your healthcare professional will give you specific instructions about these medicines.

What you should avoid while taking ARAVA:

- It is not recommended to drink alcohol during treatment with ARAVA.
- You must not receive any type of live vaccinations while taking ARAVA or within 6 months after stopping treatment. Check ahead with the clinic if you have to be vaccinated

How to take ARAVA:

- Always take ARAVA exactly as your healthcare professional has told you. Check with your healthcare professional if you are not sure.
- Swallow capsules whole, with water or another fluid.
- Take with or without food. Take it at the same time every day

Usual dose:

Recommended starting dose: 100 mg once daily for the first 3 days

Maintenance dose: 20 mg once daily. The dose may be reduced to 10 mg once daily, depending on the side effects experienced.

Overdose:

If you think you, or a person you are caring for, have taken too much ARAVA, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you missed a dose of this medication, take it as soon as you remember. But if it is almost time for your next dose, skip the missed dose and continue with your next scheduled dose. Go back to the regular dosing schedule. Do not take two doses at the same time. **What are possible side effects from using ARAVA?**

These are not all the possible side effects you may have when taking ARAVA. If you experience any side effects not listed here, tell your healthcare professional.

- abdominal or back pain,
- abnormal skin sensations like tingling
- cough, sore throat, congested nose and sinus,
- diarrhea
- dry or itchy skin
- eczema
- headache,
- increased hair loss
- joint pain or inflamed
- leg cramps
- nausea (queasiness),
- vomiting,
- weight loss (usually mild),
- weakness

ARAVA can cause abnormal blood test results. Your healthcare professional will do blood tests during your treatment.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
COMMON			
Hypertension (high blood pressure): shortness of breath, fatigue, dizziness or fainting, chest pain or pressure, swelling in your ankles and legs, bluish colour to your lips and skin, racing pulse or heart palpitations		√	
Gastrointestinal problems: diarrhea, vomiting, dehydration, constipation, having gas, severe weight loss (anorexia), blood in stool, bloody vomit, black tarry stools		√	
Loss of appetite	√		
Mouth sores or ulcers: the appearance of round lesions that have red edges and are yellow, white, or gray in the middle, difficulty eating or drinking, fever		√	
Pain and swelling of the tendon	√		
Skin rash: as painful blister, red rash spreading and skin peeling			√
UNCOMMON			
Blood problems (low white or red blood cells or platelets): shortness of breath, weakness, frequent infections, cold sores, pale skin, rapid heart rate, fatigue, fever, bruising easily, heavy bleeding or bleeding for longer than usual if you hurt yourself		√	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Eye disorders: lazy eye, dimness of vision, eye infection, cataract, pink eye		√	
Urinary tract infection (infection in urinary system including kidneys, ureters, bladder and urethra): Pain or burning sensation while urinating, frequent urination, blood in urine, pain in the pelvis, strong smelling urine, cloudy urine		√	
Diabetes (condition where the body does not produce enough insulin): excessive eating, thirst, and urination; unexplained weight loss, poor wound healing, infections		√	
Heart related problems: chest pain, irregular, fast heart beat, widening of blood vessels, varicose veins (enlarged twisted veins)		√	
Infection (including infection of the blood that can be fatal): fever and chills, nausea, vomiting, diarrhea, little or no urine, low blood pressure, palpitations, rapid breathing, rapid heartbeat, generally feeling unwell		√	
Liver problems including Hepatotoxicity and hepatic necrosis: yellowing of your skin and eyes (jaundice), right upper stomach area pain or swelling, nausea or vomiting, unusual dark urine, light-colored stool,			√

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
fever, unusual tiredness			
Lung problems including Interstitial lung disease and Pneumonia (diseases that infect, inflame or scar lung tissue): shortness of breath when rest that gets worse with exertion, dry cough, cough which may produce phlegm, fatigue, fever, sweating and shaking chills, chest pain when you breath or cough		√	
Severe allergic reactions: sudden wheeziness, drop in blood pressure, and chest pain or tightness; or swelling of eyelids, face, lips, tongue or throat			√
Skin problems: Toxic Epidermal Necrolysis (TEN), Stevens-Johnson syndrome (SJS), Erythema multiforme (severe skin reactions): redness, blistering and/or peeling of large areas of the skin, raised red or purple skin patches, possibly with blister or crust in the center; possibly swollen lips, mild itching or burning			√
Pancreatitis (inflammation of the pancreas): upper abdominal pain, fever, rapid heart beat, nausea, vomiting, tenderness when touching the abdomen			√
UNKNOWN			
Peripheral neuropathy (nerve			√

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
damage): weakness, numbness and pain, usually in the hands and feet			
Colitis (inflammation of colon): abdominal pain, bloody stools, diarrhea, fever, rectal pain, bloating, weight loss		√	
Shortness of breath, fatigue, dizziness, chest pain		√	
Skin ulcer: round, open sore in the skin through which the underlying tissues can be seen			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Do not expose ARAVA tablets to light. Store this medicine at temperatures between 15 °C and 30 °C, in a dry place. As with all medicines, you should keep ARAVA tablets out of the reach of children. Do not use the tablets in this package after the expiry date shown on the container label.

Keep out of reach and sight of children.

If you want more information about ARAVA:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website www.sanofi.ca, or by calling 1-800-265-7927.

This leaflet was prepared by sanofi-aventis Canada Inc.

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