

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrAFINITOR® Everolimus tablets

Read this carefully before you start taking **AFINITOR**® 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 **AFINITOR**.

Serious Warnings and Precautions

- AFINITOR should only be prescribed and managed by healthcare professionals who are experienced in:
 - Anticancer medicines.
 - Treating patients with Tuberous Sclerosis Complex (TSC).
- If you are taking AFINITOR for the treatment of Subependymal Giant Cell Astrocytoma (SEGA) associated with TSC:
 - Your healthcare professional will monitor the level of everolimus in your blood during treatment.
 - The ideal length of treatment is not known.
 - Your condition may reappear once you stop taking AFINITOR.
 - There is a risk for developmental delays and delayed puberty in patients taking everolimus.
 - AFINITOR is not to be used in children and adolescents (below 18 years of age) who have liver problems.
 - **Risk of Medication Errors:** AFINITOR and AFINITOR DISPERZ are not interchangeable. The doses and the way you should be taking these two drugs are not the same. Taking AFINITOR DISPERZ instead of AFINITOR could lead to the medicine not working properly or to more side effects.
- If you are taking AFINITOR for the treatment of angiomyolipoma of the kidney associated with TSC:
 - The ideal start and length of treatment is not known.
 - Female patients who were having periods may experience secondary amenorrhea when taking everolimus. This is when periods stop happening.
- AFINITOR can cause serious side effects including:
 - **Lung problems:** AFINITOR can cause:
 - **Non-infectious pneumonitis** (inflammation of the lungs)
 - **Interstitial lung disease** (inflammation or scarring of the lungs)These lung problems can lead to death. Tell your healthcare professional **right away** if you have any new or worsening lung problems.
 - **Infections:** AFINITOR can make you more likely to get an infection. Some cases have resulted in death in both adults and children. Any infections should

be treated and fully healed before starting therapy with AFINITOR. Tell your healthcare professional **right away** if you experience signs of infection when taking AFINITOR.

- **Kidney failure** (kidney problems): Cases of kidney failure (including severe kidney failure) have been reported in patients taking everolimus. Some have resulted in death. Your healthcare professional will monitor your kidney function before you start AFINITOR and regularly during treatment.

See the Serious side effects and what to do about them table, below, for more information on these and other serious side effects.

What is AFINITOR used for?

AFINITOR is used to treat:

- Adult women with hormone receptor-positive, HER2-negative advanced breast cancer:
 - Who are in menopause; and
 - In whom letrozole or anastrozole no longer keep their disease under control.For these patients, AFINITOR is given with a medicine called exemestane.
- Adults with a type of pancreatic cancer known as Pancreatic Neuroendocrine Tumour (PNET) in patients whose disease cannot be treated with surgery. For these patients their disease will:
 - Be advanced, or
 - Have spread outside the pancreas, or
 - Have worsened in the last 12 months.
- Adults with a type of cancer known as Neuroendocrine Tumour (NET) that originates from the gastrointestinal (GI) tract or lungs. For these patients, their disease:
 - Cannot be treated with surgery,
 - Will be advanced or spread outside the GI tract or lung, and
 - Will have progressed.
- Adults with metastatic kidney cancer. This means their disease has spread outside of the kidney to other parts of the body. These patients will have received previous treatment with sunitinib or sorafenib, which did not work.
- Adults with an angiomyolipoma of the kidney (a kidney tumour) that is linked to a genetic condition called Tuberous Sclerosis Complex (TSC). These patients will not need immediate surgery.
- Children (1 year of age or older) and adults with Subependymal Giant Cell Astrocytoma (SEGA), a brain tumour seen with a genetic condition called Tuberous Sclerosis Complex (TSC). For these patients, their disease will have progressed and cannot be treated with surgery. As well, they will not need immediate surgery.

How does AFINITOR work?

Everolimus, the active ingredient in AFINITOR, works by blocking a specific enzyme that is involved in tumour cell growth, division and survival. Taking AFINITOR may help to:

- Slow down the growth and spread of:

- Kidney cancer cells.
 - Pancreatic neuroendocrine cells.
 - Breast cancer cells when taken with exemestane.
- Reduce the size of brain tumours (SEGA) and kidney tumours (angiomyolipomas) that are associated with TSC.

What are the ingredients in AFINITOR?

Medicinal ingredients: Everolimus

Non-medicinal ingredients: Butylated hydroxytoluene (E321), crospovidone, hypromellose, lactose anhydrous, lactose monohydrate and magnesium stearate.

AFINITOR comes in the following dosage forms:

Tablets: 2.5 mg, 5 mg and 10 mg.

Do not use AFINITOR if:

- You are allergic to:
 - Everolimus or any other ingredients in AFINITOR.
 - Sirolimus.
 - Temsirolimus.
- You have seizures (of any type) other than those caused by TSC.

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

- Are taking other medicines.
- Have any problems with your liver or have previously had any liver disease.
- Have any infections. All infections must be treated and fully healed before starting AFINITOR.
- Have had hepatitis B, because it may be reactivated during your treatment with AFINITOR.
- Are going to have or have recently had surgery, or still have an unhealed wound following surgery. AFINITOR might affect the way your wound heals.
- Have received or are about to receive radiation treatment.
- Have kidney problems.
- Are pregnant, think you may be pregnant, or are planning to become pregnant.

Other warnings you should know about:

AFINITOR can cause serious side effects, including:

- **Diabetes, worsening of diabetes, or high blood sugar:** Everolimus, the active ingredient in AFINITOR, may cause a high level of sugar in the blood, including type II diabetes. Your healthcare professional will monitor your blood sugar level before you start AFINITOR and regularly during treatment. More monitoring may be required if you take other medicines. If you have diabetes, closely monitor your blood sugar while taking AFINITOR.
- **Stomatitis (mouth sores):** Mouth sores may appear in your mouth when taking AFINITOR. Stomatitis mostly occurs within the first 8 weeks of treatment. If you experience stomatitis, you might need treatment with a mouthwash or gel. Some

mouthwashes and gels can make your stomatitis worse. Do not try anything without checking with your healthcare professional first.

- **Bleeding problems:** Some patients taking everolimus have reported various types of bleeding problems, including:
 - **Hemoptysis** (coughing up blood)
 - **Hematuria** (blood in the urine)
 - **Gastrointestinal (GI) bleeding** (bleeding anywhere along the GI tract between mouth and anus)
 - **Intracerebral hemorrhage** (bleeding in the brain)

Some cases have resulted in death. Your risk of experiencing bleeding problems increases if you have a history of bleeding disorders, or are taking medications that:

- Have an effect on blood clotting.
- Increase the risk of bleeding.

Stop taking AFINITOR and tell your healthcare professional **right away** if you experience signs of bleeding during your treatment.

- **Rhabdomyolysis** (breakdown of damaged muscle): Some cases of rhabdomyolysis have been reported in patients taking everolimus. Your healthcare professional will monitor you for signs of rhabdomyolysis during therapy with AFINITOR. Stop taking AFINITOR and tell your healthcare professional **right away** if you experience symptoms of rhabdomyolysis.
- **Radiation sensitization and radiation recall** (severe reactions at sites of radiation): Severe radiation reactions have been observed in some patients taking everolimus. These reactions happened during or shortly after radiation therapy. Tell your healthcare professional if you:
 - Have received radiation therapy in the past.
 - Are receiving radiation therapy at the present time.
 - Will receive radiation therapy.

See the Serious side effects and what to do about them table, below, for more information on these and other serious side effects.

Vaccinations: Patients taking AFINITOR should avoid:

- Receiving live vaccines.
- Close contact with those who have received live vaccines.

Your child should complete the recommended childhood series of live vaccinations before starting therapy with AFINITOR.

Fertility: AFINITOR may affect your ability to become pregnant or father a child. Absence of menstrual periods in females who previously had periods was observed in some female patients taking everolimus. Some male patients taking everolimus were reported having:

- Unusual levels of reproductive hormones required for the development of sperm.
- Absence of sperm.

Talk to your healthcare professional if you wish to have children in the future.

Pregnancy:

- AFINITOR could harm an unborn baby.
- Use a highly effective birth control method during your treatment with AFINITOR and for

- at least 8 weeks after your last dose.
- Continue using this method of birth control even if your periods have stopped. Your periods may stop during your treatment with AFINITOR; however, it could still be possible for you to become pregnant.
- Patients who have not yet had their first period should also use effective birth control.
- Contact your healthcare professional if you:
 - Become pregnant.
 - Experience irregular or delayed periods.
 - Experience absence of periods.

Breastfeeding: It is possible that AFINITOR will pass into breastmilk and could harm a breastfed baby. Do not breastfeed:

- During treatment with AFINITOR.
- For two weeks after the last dose of AFINITOR.

Talk to your healthcare professional about ways to feed your baby during this time.

Check-ups and testing: You will have blood tests before you start AFINITOR and regularly during treatment. These tests will check:

- The amount of blood cells in your body.
- That your liver or kidneys are working properly.
- The level of electrolytes in your body.
- The amount of cholesterol or triglycerides (types of fat) in your blood.
- Your blood sugar level.

Depending on your blood test results, your healthcare professional may adjust your dose, stop or discontinue your therapy with AFINITOR.

If your child takes AFINITOR, your healthcare professional should monitor every 12 months their:

- Height and weight
- Reproductive development (puberty)

Your child's neurological development may also be monitored according to TSC guidelines.

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 AFINITOR:

- Ketoconazole, itraconazole, voriconazole, fluconazole – used to treat fungal infections.
- Clarithromycin, telithromycin, erythromycin – used to treat bacterial infections.
- Rifampicin, rifabutin – used to treat bacterial infections, primarily tuberculosis.
- St. John's Wort – an herbal remedy used mainly for depression.
- Phenytoin, carbamazepine, oxcarbazepine, phenobarbital, clobazam – used to treat seizures and epilepsy.
- Ritonavir, amprenavir, fosamprenavir, efavirenz, nevirapine, atazanavir, nelfinavir – used to treat viral infections, primarily HIV.
- Verapamil, diltiazem – used to treat heart conditions or high blood pressure.
- Angiotensin-converting enzyme (ACE) inhibitors – used to treat high blood pressure and other cardiovascular problems.
- Statins e.g. atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin – used to lower blood cholesterol levels.

- Cyclosporine – used to suppress the immune system.
- Aprepitant – used to prevent nausea and vomiting.
- Midazolam – used to produce sleepiness and drowsiness.
- Pimozide – used to treat mental disorders.
- Quinidine – used to treat certain types of irregular heartbeats.
- Ergotamine – used to treat migraines and headaches.

Do not take live vaccines or come in close contact with people who have received them while taking AFINITOR. AFINITOR can make you more likely to get an infection.

Do not eat or drink any product or juices containing grapefruit, start fruit or Seville oranges while taking AFINITOR. They can affect the way the medicine works.

How to take AFINITOR:

AFINITOR and AFINITOR DISPERZ are not interchangeable. Make sure you are using the correct tablets prescribed for you. Check with your healthcare professional if you are not sure. Do not switch use of the products without direction from your healthcare professional.

- Take AFINITOR exactly as your healthcare professional tells you.
- Take your tablets at about the same time each day (preferably in the morning).
- Take with or without food. Be consistent in how you take AFINITOR either always on an empty stomach or always with food.
- Place the tablet in your mouth and swallow whole with a glass of water. Do not chew or crush the tablets. This may affect how quickly the medicine gets into your body.

Usual dose:

The dose of AFINITOR prescribed to you will depend on:

- The type of disease you have.
- Any other condition you have.
- Any other medications you are taking.
- Blood test results.
- Your height and weight.

Your healthcare professional will tell you how many AFINITOR tablets to take each day.

Continue taking AFINITOR as long as your healthcare professional tells you.

Overdose:

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

Missed Dose:

If you forget to take AFINITOR,

- Take the missed dose as soon as you remember if it's only been up to 6 hours after the time you usually take your dose
- Skip the missed dose if it has been more than 6 hours after the time you usually take your dose. The next day, take AFINITOR at your usual time. Do not take a double dose to make up for the one that you missed.

What are possible side effects from using AFINITOR?

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

Like all medicines, AFINITOR can cause side effects.

Side effects include:

- Dry mouth
- Swollen or bleeding gums
- Jaw pain
- Vomiting
- Difficulty swallowing
- Heartburn
- Pain in the abdomen
- Inflammation of the stomach or intestines
- Gas
- Constipation
- Diarrhea
- Fever
- Chills
- Common cold
- Sore throat
- Feeling sick
- Loss of appetite
- Slow healing of cuts and wounds
- Feeling weak or tired
- Toothache
- Problems with sinuses
- Weight loss
- Dehydration
- Back pain
- Joint pain
- Arm or leg pain
- Muscle pain or spasms
- Migraine
- Dizziness
- Change in tastes

- Headache
- Loss of taste
- Difficulty sleeping
- Changes in behaviour
- Cough
- Nose bleeds
- Runny nose
- Mouth or throat pain
- Shortness of breath
- Swelling of arms, hands, feet, ankles, face or other parts of the body
- Dry skin
- Skin redness
- Itchy skin
- Skin rash
- Acne
- Tingling or numbness of the skin
- Nail problems
- Hair loss
- Chest pain
- High blood pressure
- Hemorrhoids
- Cysts that become scaly, crusty or hard on your skin
- Abnormal or new patches of pigmented skin, lumps, bumps, sores or moles
- Hot flashes
- Hearing loss
- Pink eye
- Swelling of eyelids
- Cyst on the ovaries

If any of these affects you severely, **tell your healthcare professional.**

AFINITOR can cause abnormal blood test results. Your healthcare professional will perform blood tests before you take AFINITOR and regularly during treatment. They will tell you if your test results are abnormal and if you need treatment to correct these side effects.

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	
VERY COMMON			
Anemia, Pure Red Cell Aplasia (decreased number of red blood cells): fatigue, loss of energy, irregular heartbeats, pale skin, shortness of breath, weakness, headache, dizziness		√	
Leukopenia, lymphopenia, neutropenia (decreased white blood cells): infections, fatigue, fever, aches, pains and flu-like symptoms		√	
Non-infectious Pneumonitis (inflammation of the lung tissue): shortness of breath, cough, fatigue, loss of appetite, unintentional weight loss			√
Stomatitis (mouth sores, redness and swelling of the lining of the mouth)		√	
COMMON			
Acute respiratory failure: blue color on skin, lips, and fingernails; feel sleepy; irregular heartbeats; loss of consciousness; sudden worsening of shortness of breath			√
Allergic Reaction: difficulty swallowing or breathing, wheezing; drop in blood pressure; feeling sick to your stomach and throwing up; hives or rash; swelling of the face, lips, tongue or throat.			√
Bronchospasm (when there is a sudden narrowing of the airway): difficulty breathing with wheezing or coughing			√
Cellulitis (skin infection): pain, tenderness, swelling, redness of the skin		√	
Convulsion: seizure, spasms, shaking or fits			√

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	
Depression (sad mood that won't go away): difficulty sleeping or sleeping too much, changes in appetite or weight, feelings of worthlessness, guilt, regret, helplessness or hopelessness, withdrawal from social situations, family, gatherings and activities with friends, reduced libido (sex drive) and thoughts of death or suicide. If you have a history of depression, your depression may become worse			√
Diabetes, worsening of diabetes, or high blood sugar: increased thirst, frequent urination, extreme fatigue or lack of energy, dry skin, headache, blurred vision, tingling or numbness in the hands or feet			√
Lymphoedema (build-up of lymph in tissues): Swelling of part or all of your arm (including fingers) or leg (including toes), feeling of heaviness, restricted movement, discomfort		√	
Ear infection: ear pain, tugging or pulling at your ear, trouble sleeping, trouble hearing, loss of balance, fever, fluid draining from the ear, headache, loss of appetite		√	
Heart Failure (heart does not pump blood as well as it should): shortness of breath, fatigue and weakness, swelling in ankles, legs and feet, cough, fluid retention, lack of appetite, nausea, rapid or irregular heartbeat, reduced ability to exercise			√

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	
Hemoptysis: coughing up blood			√
Herpes Zoster virus (shingles): a painful skin rash of fluid-filled blisters, blisters appear along a strip of skin, itching		√	
Infection: fever and chills, nausea, vomiting, diarrhea, generally feeling unwell		√	
Interstitial lung disease (diseases that inflame or scar lung tissue): shortness of breath when rest that gets worse with exertion, dry cough			√
Kidney failure (kidney problems): confusion; itchiness or rashes; puffiness in your face and hands; swelling in your feet or ankles; urinating less or not at all; weight gain		√	
Palmar-plantar erythrodysesthesia syndrome (also called Hand-Foot syndrome): red or swollen palms, thick calluses and blisters of the hands and soles of the feet, tingling or burning, tightness of the skin		√	
Pleural effusion (fluid around the lungs): chest pain, difficult or painful breathing, cough			√
Pneumonitis, pulmonary embolism, acute respiratory syndrome (lung or breathing problems): cough, chest pain, shortness of breath		√	
Tachycardia (abnormally fast heartbeat)			√
Thrombocytopenia (low blood platelets): bruising or bleeding for longer than usual if you hurt yourself, fatigue and weakness			√
Urinary tract infection (infection in urinary system including kidneys, ureters,		√	

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	
bladder and urethra): Pain or burning sensation while urinating, frequent urination, blood in urine, pain in the pelvis, strong smelling urine, cloudy urine			
UNCOMMON			
Intestinal obstruction (partial or complete blockage of the small intestine): abdominal cramps or pain, loss of appetite, constipation, vomiting, inability to have a bowel movement or pass gas, swelling of the abdomen		√	
RARE			
Angioedema (swelling of tissue under the skin): difficulty breathing; swollen face, hands and feet, genitals, tongue, throat; Swelling of the digestive tract causing diarrhea, nausea or vomiting		√	
Deep vein thrombosis (blood clot in the deep veins of the leg or arm): swelling, pain, arm or leg may be warm to the touch and may appear red		√	
Gastrointestinal (GI) bleeding (bleeding anywhere along the GI tract between mouth and anus): blood in vomit, black tarry stool, bright red blood in your stool or coming from rectum, rapid pulse, low blood pressure, low urine flow, confusion, weakness, dizziness			√
Hematuria (blood in the urine): pink, red or very dark urine			√
Hepatitis B reactivation (a previous viral infection of the liver becomes active again): fever, skin rash, joint pain and inflammation as well as tiredness, loss of appetite,		√	

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	
nausea, jaundice (yellowing of the skin or whites of eyes), pain in the upper right abdomen, pale stools and dark urine. Hepatitis B reactivation can be fatal in some cases			
Intracerebral hemorrhage (bleeding in the brain): sudden, severe headache; confusion; nausea and vomiting; seizures; loss of consciousness			√
Liver failure (serious disturbance of liver function, hepatic failure): yellow colour to skin, whites of the eyes (jaundice), bleeding easily, swollen abdomen, mental disorientation or confusion, sleepiness, coma			√
Rhabdomyolysis (breakdown of damaged muscle): muscle tenderness, weakness, red-brown (tea-coloured) urine			√
Sepsis and septic shock (infection of the blood): fever or dizziness, chills, high or very low body temperature, little or no urine, low blood pressure, palpitations, rapid breathing, rapid heartbeat		√	
Vaginal bleeding changes: increased or decreased menstrual bleeding, spotting, infrequent periods or absence of bleeding			√
VERY RARE			
Radiation sensitization and radiation recall (severe reactions at sites of radiation) including: - Severe skin reactions: skin rash, blistering, peeling or discoloration of the skin			√

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	
<ul style="list-style-type: none"> - Pneumonitis (inflammation of lung tissue): shortness of breath, which may be accompanied by a cough, fever or chills - Esophagitis (inflammation of the esophagus): difficulty or pain when swallowing, chest pain, heartburn or acid reflux 			
<p>Stroke (bleeding or blood clot in the brain): sudden numbness, weakness or tingling of the face, arm, or leg, particularly on one side of the body, sudden headache, blurry vision, difficulty swallowing or speaking, or lethargy, dizziness, fainting, vomiting, trouble understanding, trouble with walking and loss of balance</p>			√

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:

- Store between 15 – 30°C.
- Store in the original package to protect from light and moisture.
- Do not use after the expiry date shown on the box.
- Keep out of reach and sight of children.

If you want more information about AFINITOR:

- 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.novartis.ca, or by calling 1-800-363-8883.

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