

**READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION**

PrRYDAPT™

Midostaurin capsules

Read this carefully before you start taking **RYDAPT™** 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 **RYDAPT**.

What is RYDAPT used for?

RYDAPT is used in combination with other chemotherapy treatments to treat acute myeloid leukemia (AML) in adults who have a new diagnosis of a defect in a gene called FLT3. A test will confirm if you have the FLT3 kind of AML. AML is a type of cancer of white blood cells.

RYDAPT is also used on its own in adults to treat diseases called aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL). These are disorders in which the body produces too many mast cells, a type of white blood cell. Symptoms are caused when too many mast cells infiltrate organs like the liver, bone marrow and spleen, or release substances like histamine into the blood.

How does RYDAPT work?

Midostaurin blocks the action of some enzymes (kinases) of cells that are not normal. This stops their division and growth.

What are the ingredients in RYDAPT?

Medicinal ingredients: midostaurin (from a benzyl alcohol and ethanol solvate form of midostaurin).

Non-medicinal ingredients: all-rac- α -tocopherol (vitamin E), corn oil mono-di-triglycerides, ethanol anhydrous, gelatin, glycerol, iron oxide red, iron oxide yellow, macrogol 400, macrogolglycerol hydroxystearate, purified water, red pharmaceutical ink, titanium dioxide.

RYDAPT comes in the following dosage forms:

Capsules, 25 mg

Do not use RYDAPT if:

- You are allergic to midostaurin or any of the other ingredients of RYDAPT.
- You are under 18 years old.

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

- have any infections.
- have heart disorders.

- have problems with your lungs or problems breathing.

Other warnings you should know about:

Breast-feeding, pregnancy, females of child-bearing potential and male patients

Tell your doctor if you:

- are breast-feeding.
- are pregnant.
- think you might be pregnant.
- are planning to have a baby.

Your doctor will talk to you about the risks of taking RYDAPT if you are breast-feeding or pregnant. Breast-feeding should be stopped during treatment and for at least 4 months after stopping RYDAPT.

Do not take RYDAPT if you are pregnant. RYDAPT may harm your unborn baby. If you could get pregnant, take a pregnancy test 7 days before taking RYDAPT. You must use effective birth control while you are taking RYDAPT and for 4 months after you stop taking it. It is not known if RYDAPT will reduce the effectiveness of hormonal contraceptives. If you are on hormonal contraceptives, such as the pill, you should add a barrier method of birth control to be sure to prevent pregnancy, such as a condom. Ask your doctor about options of effective birth control.

Male patients should use condoms during sex during treatment and for 4 months after stopping RYDAPT.

Fertility problems

RYDAPT may impair fertility in men and women. It is unknown whether these effects are reversible. You should discuss this with your doctor before starting treatment.

RYDAPT can interact with many drugs. This includes over the counter and herbal drugs. 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 RYDAPT:

- some medicines used to treat infections, such as ketoconazole or clarithromycin,
- some medicines used to treat epilepsy, such as carbamazepine,
- medicines used to treat tuberculosis, such as rifampicin,
- some medicines used to treat depression such as the herbal medicine St. John's Wort. It is also known as hypericum perforatum,
- medicines used to treat HIV, such as ritonavir,
- medicines that may cause a heart rhythm disorder called prolongation of the QT interval.

If you are taking any of these, your doctor might prescribe other alternative medicines.

If you are already taking RYDAPT, tell your doctor if you are prescribed a new drug.

Do not eat or drink anything that contains grapefruit while taking RYDAPT.

How to take RYDAPT:

RYDAPT should only be started by a physician experienced in anti-cancer drugs.

Take RYDAPT exactly as your doctor or pharmacist has told you. Check with them if you are not sure. Do NOT exceed or stop taking the dose unless your doctor tells you to. Stopping your treatment with RYDAPT may cause your condition to become worse. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

Take RYDAPT:

- by mouth.
- whole with a glass of water. Do NOT open, crush or chew.
- twice a day at about 12 hour intervals. For example take it at breakfast and dinner time.
- with food to help to prevent nausea.

Your doctor will give you medications to help prevent the nausea and vomiting during treatment with RYDAPT.

Recommended dose:

Patients with AML:

On days 8 to 21 of each cycle, take 50 mg (2 capsules) twice a day. This is a total of 4 capsules per day.

The doctor will decide how long each cycle will last.

Patients with ASM, SM-AHN, or MCL:

Take 100 mg (4 capsules) twice a day. This is a total of 8 capsules per day.

Depending on how you react to RYDAPT, your doctor may adjust your treatment. Your doctor may also stop your treatment for a period of time or entirely.

Overdose:

If you think you have taken too much RYDAPT, or if someone else accidentally takes your medicine, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms. Show the pack of RYDAPT. Medical treatment may be necessary.

Missed Dose:

If you miss a dose, skip the missed dose and continue as usual. Do not take a double dose to make up for forgotten capsules. Instead, wait until it is time for your next dose.

If vomiting occurs you should not take an additional dose of RYDAPT, but should take the next usual prescribed dose.

What are possible side effects from using RYDAPT?

These are not all the possible side effects you may feel when taking RYDAPT. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:

- Red or purple, flat, pinhead spots under the skin. They are called petechiae.
- Dry skin
- Excessive sweating, which is called hyperhidrosis.
- Swelling of the eyelid. It is called eyelid edema
- Eye pain, blurred vision, abnormal intolerance to light. This is called keratitis.
- Problem to fall asleep. This is called insomnia
- Throat pain, which is called laryngeal pain and mouth-throat pain, which is called oropharyngeal pain
- Sore throat combined with runny nose. This is called nasopharyngitis.
- Involuntary shaking of the body, which is called a tremor
- Headache
- Dizziness including dizziness with spinning sensation which is called vertigo
- Disturbance in attention
- Upper abdominal pain
- Diarrhea
- Constipation
- Upset stomach, indigestion. This is called dyspepsia.
- Pain in back, joints, neck, bones and arm and legs
- Cold sores in the mouth due to viral infection. This is called oral herpes.
- Feeling of pressure or pain in the cheeks and forehead. This is called sinusitis.
- Generalized swelling. This is called edema.
- Swelling of the lower limbs (calves, ankles). This is called edema peripheral.
- Tiredness. This is called fatigue.
- Weakness. This is called asthenia.
- Chills
- Bruise. This is called hematoma or contusion.
- Fall.

During RYDAPT treatment, you may also have side effects of abnormal blood test results (very common), which can give your doctor information on the functioning of some parts of your body, for example:

- High levels of the following enzymes:
 - Enzymes related to liver

Your heart and lung function will also be checked regularly.

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			
Allergic Reaction: difficulty breathing or swallowing, dizziness, swelling of the face, lips, tongue or throat, severe itching, with a red rash or raised bumps			X
Decreased Blood Clotting Activity: spontaneous bleeding or bruising		X	

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	
Lymphopenia/Neutropenia: weakness, fever, sore throat or mouth ulcers due to infections		X	
Infection at catheter site: redness of the skin, pain, tenderness, swelling at the site of the flexible tube	X		
Dermatitis exfoliative: skin rash with flaking or peeling	X		
Epistaxis: nose bleeding	X		
Dyspnea: shortness of breath, labored breathing	X		
Hypotension: dizziness, light headedness	X		
Stomatitis: mouth sores	X		
Nausea	X		
Vomiting	X		
Pyrexia: fever	X		
Low level of potassium in the blood (hypokalemia): irregular heartbeats, muscle weakness and spasm, generally feeling unwell.	X		
Increased blood sugar (hyperglycemia): frequent hunger, frequent thirst, increased volume of urination.	X		
High level of sodium in the blood (hypernatremia): thirst, weakness, cramps, headaches, confusion, convulsions, impaired consciousness	X		
Pleural effusion (fluid collection on the lungs/chest cavity): chest pain, difficult or painful breathing, cough		X	
Hemorrhoids: itching, irritation or pain around the anus, painful bowel movements	X		
Upper respiratory tract infection: cough, sore throat, stuffy or runny nose, sneezing	X		
Urinary tract infection or cystitis: painful and frequent urination due to a urinary bladder inflammation		X	

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			
High level of uric acid in the blood (hyperuricemia): repeated pain to the side and the abdomen which may spread to your groin area	X		
High level of calcium in the blood (hypercalcemia): periodic pain in upper right abdomen (accompanied by nausea and vomiting), repeated pain to the side and the abdomen which may spread to your groin area , bone pain, nausea, vomiting, constipation, stomach pain, frequent urination, thirst, and muscle weakness	X		
Acute Respiratory Distress Syndrome: Severe shortness of breath, labored and unusually rapid breathing, low blood pressure, confusion and extreme tiredness		X	
Blood clot in catheter (flexible tube)		X	
Weight increased	X		
Hypertension: headache, dizziness	X		
Fainting		X	
Anorectal discomfort	X		
Sinus tachycardia: fast heart beat	X		
Pericardial effusion (fluid collection in the sac around the heart): chest pain that feels better when you sit up rather than lie down. Feel light-headed or pass out. Irregular, fast, or forceful heartbeat. Difficult or painful breathing, cough		X	
Pneumonia: fever, cough, difficult or painful breathing, wheezing, chest in pain when breathing		X	
Gastrointestinal hemorrhage: vomiting of blood, black or bloody stools		X	
Erysipelas: red, swollen painful rash on any part of the skin	X		
Bronchitis: cough with phlegm,	X		

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	
chest pain, and fever			
Shingles: pain, burning, numbness or tingling, rash, fluid-filled blisters		X	
UNCOMMON			
Sepsis or Neutropenic Sepsis: Infections, fever, low blood pressure, decreased urination, rapid pulse, rapid breathing		X	
UNKNOWN FREQUENCY			
Infections or Lung Problems: new or worsening fever, cough with or without mucous, chest pain, trouble breathing or shortness of breath.			X
Heart Problems: chest pain or discomfort. Lightheadedness, fainting, dizziness. Blue colour of your lips, fingers or toes. Shortness of breath. Swelling of your legs of feet.			X

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to 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/adverse-reaction-reporting.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 store above 30°C. Store in the original package to protect from moisture.
- Keep out of reach and sight of children.
- Do not take this medicine after the expiry date, which is stated on the box.

Ask your pharmacist how to dispose of medicines you no longer use.

If you want more information about RYDAPT:

- 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](http://www.hc-sc.gc.ca) (www.hc-sc.gc.ca); the manufacturer's website (www.novartis.ca), or by calling 1-800-363-8883.

This leaflet was prepared by Novartis Pharmaceuticals Canada Inc.

Last Revised: October 2, 2018

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