PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr CYRAMZA®

Ramucirumab intravenous injection

Read this carefully before you start taking **CYRAMZA** 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 **CYRAMZA**.

Serious Warnings and Precautions

- Increases risk of severe bleeding, including severe bleeding in your stomach or bowel.
- Increases risk of developing a hole in your stomach or bowel. In some cases this could result in death.
- Talk to your healthcare professional before you plan to have surgery and treatment should be stopped if you have a wound that is not healing properly.

What is CYRAMZA used for?

CYRAMZA is a targeted cancer medicine used to treat advanced stomach cancer (also known as gastric cancer) and cancer of the gastro-esophageal junction (part of the food tube just as it joins the stomach), either by itself or in combination with paclitaxel (another anticancer medicine), in adults whose disease has progressed despite prior treatment with chemotherapy.

How does CYRAMZA work?

CYRAMZA is a vascular endothelial growth factor (VEGF) Receptor 2 antagonist that belongs to a group of biologic substances called monoclonal antibodies. In order to grow, tumours require oxygen and nutrients which are delivered through the blood. As tumours grow, they require larger amounts of oxygen and nutrients. Tumours get this supply by inducing the growth of new blood vessels. This process is called angiogenesis (an´-gee-o-jen´-i-sis). CYRAMZA works by blocking angiogenesis and helps starve the tumour of oxygen and other nutrients. CYRAMZA is not chemotherapy; it is considered a biologic antiangiogenic therapy.

What are the ingredients in CYRAMZA?

Medicinal ingredients: ramucirumab

Non-medicinal ingredients: glycine (E640), histidine, histidine monohydrochloride, polysorbate 80 (E433), sodium chloride and water for injection

CYRAMZA comes in the following dosage forms:

CYRAMZA is available as a solution in 10 mL or 50 mL single-use vials. Each vial contains either 100 mg ramucirumab in 10 mL (10 mg/mL) or 500 mg ramucirumab in 50 mL (10 mg/mL). After dilution and preparation, CYRAMZA is administered as an intravenous infusion.

Do not use CYRAMZA if:

- you are allergic to this drug or to any ingredient in the formulation

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

- have any condition which increases the risk of bleeding;
- have high blood pressure;
- are going to have planned surgery, had recent surgery or have a poorly healing wound after surgery;
- have severe liver disease (‘cirrhosis’) and associated conditions, such as excessive accumulation of fluid in your abdomen (‘ascites’);
- have had blood clots in your arteries (‘arterial thromboembolic events’);
- have ever had a heart attack or stroke;
- have had a hole in your stomach or bowel (‘gastrointestinal perforation’);
- have a weakened heart muscle (‘heart failure’);
- have had an allergic reaction to the infusion;
- are pregnant or plan to become pregnant;
- are breastfeeding;
- have any allergies to this drug or its ingredients

Other warnings you should know about:

Pregnancy, breast-feeding and fertility

Avoid getting pregnant while receiving this medicine and for at least 3 months after the last dose of CYRAMZA as this medicine may potentially cause harm to your unborn child. As CYRAMZA inhibits the development of new blood vessels, it may decrease the likelihood of you becoming pregnant or maintaining a pregnancy. Talk to your doctor about the best contraception for you.

Discontinue nursing or discontinue CYRAMZA. Do not breast-feed your baby during treatment with CYRAMZA and for at least 3 months after you receive the last dose, as this medicine may have harmful effects on the growth and development of your baby.

Children and adolescents

CYRAMZA should **not** be given to patients under the age of 18 years because there is no information about the safety nor how it works in this age group.

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 CYRAMZA

- There are no known relevant Drug-Drug, Drug-Food or Drug-Herb interactions

How to take CYRAMZA:

CYRAMZA will be given to you by a healthcare professional.

CYRAMZA is given by intravenous infusion (through a needle placed in a vein in the arm, hand, or through a central line). The infusion lasts about 60 minutes. You will receive an infusion once every 2 weeks.

You may receive CYRAMZA alone or in combination with paclitaxel, another anticancer agent. Your doctor will determine your treatment plan. If you receive CYRAMZA in combination with paclitaxel, you should read the patient information for paclitaxel as well. Ask your doctor or health care team if you have any questions.

Usual dose:

The recommended dose of CYRAMZA for the treatment of gastric cancer is 8 mg per kg of your body weight once every 2 weeks.

If your doctor has prescribed paclitaxel, you will receive it once every week for 3 weeks followed by 1 week without treatment. It will be given by intravenous infusion for about 60 minutes. If you receive paclitaxel on the same day as CYRAMZA, it will be given after the CYRAMZA infusion has finished.

The number of infusions you will receive depends on how you are responding to treatment. Your doctor will discuss this with you.

Premedication:

You may be given medication to reduce the risk of an infusion-related reaction to the infusion before you receive CYRAMZA. If you experience an infusion-related reaction during CYRAMZA therapy, you will be given premedication for all future infusions. Symptoms of infusion-related reactions may include increased muscle tension, back pain, chest pain and/or tightness, chills, flushing, difficulty in breathing, wheezing, and feeling of tingling or numbness in hands or feet. In severe cases, symptoms may include breathing distress caused by narrowing of the airways, faster heartbeat, and feeling weak.

Dose adjustments:

During each infusion, your doctor or nurse will check for side effects. The time over which your infusion is given may lengthen if you experience an infusion-related reaction during treatment.

The amount of protein in your urine will be checked regularly during treatment. Depending on the protein level measured, CYRAMZA may be temporarily discontinued. Once the urine protein level has decreased to a certain level, treatment may be restarted with a lower dose.

CYRAMZA treatment will be temporarily stopped if you:

- develop high blood pressure, until it is controlled with antihypertensive medication
- develop wound healing problems, until the wound is healed or prior to planned surgery
- have significantly increased protein in your urine

CYRAMZA treatment will be permanently stopped if you:

- develop a blood clot in your arteries (‘arterial thromboembolic events’)
- develop a hole in your stomach or bowel (‘gastrointestinal perforation’)
- experience severe bleeding
- experience a severe infusion-related reaction
- develop high blood pressure that cannot be controlled with medication
- are passing more than a certain amount of protein with your urine or if you develop a severe kidney disease (‘nephrotic syndrome’)

Overdose:

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

Missed Dose:

If you miss an infusion, contact your doctor immediately for further instructions.

What are possible side effects from using CYRAMZA?

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

Tell your doctor **immediately** if you experience any of the following **serious side effects** during CYRAMZA treatment:

- **vomit bright red blood or coffee ground material, blood in the stool or black, tarry stools, pain, severe fatigue, shortness of breath or a sense you may pass out when you get up from lying or sitting** which could be due to bleeding from your stomach or bowel
- **chest pain (may or may not feel like pressure or tightness in your chest) or loss of strength in an arm or leg, change in speech or change in vision** which could be due to blood clots in the arteries (can lead to a heart attack or stroke)
- **sudden onset of severe abdominal pain** which could be a symptom of a hole in the stomach or bowel
- **sudden onset of shivers and shakes often with a fever** which could be the result of a serious infection (sepsis)
- new or worsening **weakness and tiredness, swelling of the feet and ankles, and/or shortness of breath,** which could be symptoms of weakened heart muscle (heart failure)

Tell your doctor if you experience any of the following other side effects:

Very common: may affect more than 1 in 10 people

- high blood pressure
- protein in the urine
- feeling tired or weak
- low white blood cell count (may increase risk of infection) which on its own may not cause any symptoms and is commonly only discovered as a result of routine blood tests
- diarrhea
- nose bleed
- abdominal pain
- swelling of hands, feet and legs due to fluid retention
- inflammation of the mouth
- low platelet count (cells that help the blood to clot). This does not usually cause any

problems and is commonly found in routine blood tests.

- low blood levels of albumin

Common: may affect up to 1 in 10 people

- intestinal blockage; symptoms may include constipation and abdominal pain
- rash
- headache
- low blood levels of potassium (hypokalemia) which can cause muscle weakness, twitching or abnormal heart rhythm
- low blood levels of sodium (hyponatremia) which can cause tiredness and confusion or muscle twitching
- thyroid dysfunction
- abnormal growth of blood vessels usually on the surface of the skin; this may appear as a red, raised lesion and may grow larger and/or bleed (hemangioma)
- altered voice such as hoarseness

Uncommon: may affect up to 1 in 100 people

- fistula (an abnormal tube like connection between internal parts of the body that are not normally connected)

Rare: may affect up to 1 in 1000 people

A brain condition called Posterior Reversible Encephalopathy Syndrome (PRES). Symptoms may include seizure, headache, nausea/vomiting, blindness, or loss of alertness.

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			
Holes in the gut wall (gastrointestinal perforation): a hole in the stomach, gut or bowel [symptoms include severe stomach pain, vomiting, fever or chills]		✓	
Severe bleeding in your gut [symptoms may include extreme tiredness, weakness, dizziness or change in the colour of your stools]		✓	
Blood clots in the arteries: can lead to a heart attack or stroke [symptoms of a heart attack may include chest pain or heaviness in the chest; symptoms of a stroke may include sudden numbness or weakness of the arm, leg and face, feeling confused, difficulty speaking or		✓	

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**	
understanding others, sudden difficulty in walking or loss of balance or coordination or sudden dizziness]			
RARE			
Damage to small blood vessels in various organs of the body. This occurs most commonly in the kidney. Red blood cells and platelets may be destroyed because of this blood vessel damage (thrombotic microangiopathy). Red blood cells carry oxygen and platelet are cells that help the blood to clot. Blood flow to organs may be reduced. [Symptoms include bruising/bleeding, tiredness, shortness of breath, decreased urine output, swollen legs, headache, confusion, and symptoms of stroke. Protein in the urine and high blood pressure may occur.]		✓	
A brain condition called Posterior Reversible Encephalopathy Syndrome (PRES). [Symptoms may include seizure, headache, nausea/vomiting, blindness, or loss of alertness.]		✓	✓

Tell your doctor if you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities. These are not all the possible side effects you may feel when taking CYRAMZA. If you experience any side effects not listed here, contact 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 CYRAMZA in a refrigerator at 2°C to 8°C (36°F to 46°F) until time of use. Keep the vial in the outer carton in order to protect from light.

Do not freeze or shake the vial.

Keep out of reach and sight of children.

If you want more information about CYRAMZA:

- 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.lilly.ca, or by calling 1-888-545-5972.
- The information in this document is current as of the last revision date shown below. For the most current information please visit our website or contact us directly.
- You may need to read this package insert again. Please do not throw it away until you have finished your medicine

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