PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrKyprolis®

carfilzomib for injection

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

Your cancer will be treated with KYPROLIS in combination with other medicines. Read the leaflets for the other drugs as well as this one. This will help you understand the information related to those medicines.

Serious Warnings and Precautions

KYPROLIS should be prescribed and managed by a healthcare professional experienced in the use of anticancer drugs.

If you are given the 56 mg/m^2 or 70 mg/m^2 dose of KYPROLIS, it must be given over 30 minutes. If you are given the 27 mg/m^2 dose of KYPROLIS, it must be given over at least 10 minutes.

KYPROLIS may cause serious side effects, which can cause death. These include:

- Heart problems
- Breathing problems
- Liver problems
- Blood clots in the veins (deep vein thrombosis) and lungs (pulmonary embolism)
- Blood clots in small blood vessels (thrombotic microangiopathies)
- Swelling in the back of the brain (Posterior Reversible Encephalopathy Syndrome [PRES])
- Bleeding into your organs, eg, the brain, lungs or gastrointestinal tract (stomach or bowel)

What is KYPROLIS used for?

KYPROLIS is used to treat patients with multiple myeloma who have received 1 to 3 previous treatments. Multiple myeloma is a cancer of plasma cells (a type of white blood cell in the bone marrow that produces antibodies).

KYPROLIS can be used together with the following medicines:

- dexamethasone alone,
- lenalidomide plus dexamethasone,
- daratumumab plus dexamethasone,
- isatuximab plus dexamethasone

How does KYPROLIS work?

KYPROLIS is a proteasome inhibitor. Proteasomes play an important role in cells by breaking down proteins that are damaged or no longer needed. KYPROLIS blocks proteasomes, which can lead to a build-up of proteins within cells. KYPROLIS can cause cell death, especially in multiple myeloma cells because they contain a higher amount of abnormal proteins.

What are the ingredients in KYPROLIS?

Medicinal ingredient: carfilzomib

Non-medicinal ingredients: anhydrous citric acid, sodium hydroxide (for pH adjustment), and sulfobutylether beta-cyclodextrin

KYPROLIS comes in the following dosage forms:

Powder for solution: 10, 30, or 60 mg/vial

Do not use KYPROLIS if:

- You are allergic to carfilzomib or any other ingredients in KYPROLIS.

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

- have or have had heart problems, including a history of chest pain (angina), heart attack, irregular heartbeat, high blood pressure or if you have ever taken a medicine for your heart
- have or have had lung problems, including a history of shortness of breath at rest or with activity (dyspnea)
- have or have had kidney problems, including kidney failure or if you have ever received dialysis
- have or had liver problems, including a history of hepatitis, fatty liver, or if you have ever been told your liver is not working properly
- have or had unusual bleeding, including easy bruising, bleeding from an injury, such as a cut that does not stop bleeding in a normal amount of time, or internal bleeding, which can indicate you have low platelets
- have or had blood clots in your veins
- have or have had any other major medical problem for which you were hospitalized or received medication
- are pregnant or plan to become pregnant
- are male and are considering fathering a child
- are breast-feeding or plan to breast-feed
- are on a controlled sodium diet

Other warnings you should know about:

- **Check-ups and testing**

  Your healthcare professional will examine you and review your full medical history before starting treatment with KYPROLIS. You will be followed closely during treatment.

  Your healthcare professional may:

  - Do blood and/or urine tests before and during treatment with KYPROLIS. This is to make sure you have enough blood cells and your liver and kidneys are working properly.
  - Check your blood pressure. If your blood pressure is too high, it may need to be lowered before you begin treatment with KYPROLIS.
  - Check if you are getting enough fluids before starting treatment with KYPROLIS.

- **Infections**

  - Infections have occurred in patients treated with KYPROLIS. In some cases, these infections have been serious and some people have died from them.
  - Your healthcare professional will monitor you for signs and symptoms of an infection. If you develop an infection, your healthcare professional will treat your infection right away.

- **Hepatitis B Reactivation**
  - Cases of Hepatitis B reactivation have been reported in patients receiving KYPROLIS. This is when a previous viral infection of the liver becomes active again. It is a serious condition and can cause death.
  - Before you start KYPROLIS, your healthcare professional will do tests to find out if you have Hepatitis B. If you do have this virus, you may need to take antiviral medications before initiating KYPROLIS treatments and continue during your treatment and for at least 6 months after your last dose.
  - During treatment with KYPROLIS, your healthcare professional will monitor you for signs of Hepatitis B reactivation. If this virus becomes active during your treatment, you may need to stop taking KYPROLIS. If this happens, your healthcare professional will decide if you can restart KYPROLIS once your infection is under control.
- **Progressive Multifocal Leukoencephalopathy (PML)**
  - Cases of PML have been reported in patients treated with KYPROLIS who have had or are currently taking other medicines that weakens your immune system (immunosuppressive medicines). PML is a rare brain disorder caused by an infection. PML can cause death.
  - Your healthcare professional will monitor you for any signs and symptoms of PML. If PML is suspected, your healthcare professional will interrupt your treatment and refer you to a specialist for additional tests. If PML is confirmed, your healthcare professional will stop your treatment with KYPROLIS.

- **Pregnancy, breast-feeding and birth control**

  For women taking KYPROLIS:

  - KYPROLIS should not be taken if you are pregnant, think you may be pregnant or if you are trying to become pregnant.
  - During KYPROLIS treatment and for 30 days after stopping treatment, you should use an effective method of birth control to ensure you do not become pregnant. You should talk to your healthcare professional about effective methods of birth control.
  - Tell your healthcare professional right away if you become pregnant while taking KYPROLIS, or within 30 days after stopping KYPROLIS.
  - If you are breast-feeding, you should not take KYPROLIS. It is not known if KYPROLIS passes into breast milk in humans. Talk to your healthcare professional on the best way to feed your baby during treatment.

  For men taking KYPROLIS:

  - While taking KYPROLIS and for 90 days after stopping treatment, you should use an effective method of birth control to ensure your partner does not become pregnant. You should talk to your healthcare professional about effective methods of birth control.
  - Tell your healthcare professional right away if your partner becomes pregnant while you are taking KYPROLIS or within 90 days after stopping treatment.

- **Asian Population**

  Heart failure occurs more often in Asian patients who take KYPROLIS.

- **Children and adolescents**

  KYPROLIS is NOT recommended for use in patients under the age of 18 years.

- **Driving and Using Machines**

  Treatment with KYPROLIS may cause fatigue, dizziness and a drop in blood pressure that could affect your ability to drive or operate machines. Do not drive or perform tasks which may require special attention until you know how KYPROLIS affects you.

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 KYPROLIS:

- Certain types of birth control methods
  - KYPROLIS may stop certain types of birth control methods (eg, oral hormonal methods) from working.
  - There may be a higher risk of blood clots when KYPROLIS is used together with certain types of birth control methods (eg, hormonal methods).

How to take KYPROLIS:

- KYPROLIS will be given to you by a healthcare professional. The KYPROLIS powder will first be mixed into a solution. This solution will then be given through a tube placed in your vein. This is called an intravenous (IV) infusion. KYPROLIS will be infused over 10 or 30 minutes.
- KYPROLIS is given in treatment cycles that each last 28 days. For each treatment cycle, KYPROLIS is given once or twice each week for the first three weeks. This is followed by one week without treatment.
- KYPROLIS will be given with other medicines. These medicines will be given to you according to one of the following schedules:

1. KYPROLIS with lenalidomide and dexamethasone:

- KYPROLIS:
  - Cycles 1-12: KYPROLIS will be given on Days 1, 2, 8, 9, 15, and 16.
  - Cycle 13 and onwards: KYPROLIS will only be given on Days 1, 2, 15 and 16.
- Lenalidomide: you will take daily on Days 1-21 of each cycle.
- Dexamethasone: you will take on Days 1, 8, 15 and 22 of each cycle.

Or

2. KYPROLIS and dexamethasone (<u>twice</u> a week treatment):

- KYPROLIS: will be given on Days 1, 2, 8, 9, 15, and 16 of each cycle.
- Dexamethasone: you will take on Days 1, 2, 8, 9, 15, 16, 22 and 23 of each cycle.

Or

3. KYPROLIS and dexamethasone (<u>once</u> a week treatment):

- KYPROLIS: will be given on Days 1, 8, and 15 of each cycle.
- Dexamethasone:
  - Cycles 1-9: you will take dexamethasone on Days 1, 8, 15, and 22.
  - Cycle 10 and onwards: you will only take dexamethasone on Days 1, 8 and 15.

Or

4. KYPROLIS with dexamethasone and daratumumab:

- KYPROLIS: will be given on Days 1, 2, 8, 9, 15 and 16 of each cycle.
- Dexamethasone: you will take on Days 1, 2, 8, 9, 15, 16 and 22 of each cycle.
- Daratumumab:
  - Cycle 1: daratumumab will be given on Days 1, 2, 8, 15 and 22.
  - Cycle 2: daratumumab will be given on Days 1, 8, 15 and 22.
  - Cycles 3-6: daratumumab will be given on Days 1 and 15.
  - Cycle 7 and onwards: daratumumab will only be given on Day 1 of each cycle.

Or

5. **KYPROLIS with isatuximab and dexamethasone:**
    - KYPROLIS: will be given on Days 1, 2, 8, 9, 15 and 16 of each cycle.
    - Isatuximab:
        - Cycle 1: you will take isatuximab on Days 1, 8, 15 and 22.
        - Cycle 2 and onwards: you will only take isatuximab on Days 1 and 15.
    - Dexamethasone: you will take on Days 1, 2, 8, 9, 15, 16, 22 and 23 of each cycle.

You and your healthcare professional will decide the schedule that is right for you. Your healthcare professional will also decide for how long you should receive KYPROLIS.

Most patients will receive treatment until their disease gets worse. Your healthcare professional may stop your KYPROLIS treatment if you experience side effects that cannot be managed.

Usual Dose:

- Your healthcare professional will decide how much KYPROLIS you should receive. This will be based on your height and weight.
- The starting dose of KYPROLIS is 20 mg/m^2. The dose may be increased to either 27 mg/m^2, 56 mg/m^2 or 70 mg/m^2. This will depend on how well you tolerated the starting dose and the dosing schedule you are following.

Overdose:

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

Missed Dose:

It is important for you to keep all your appointments to receive KYPROLIS. If you miss an appointment, ask your healthcare professional when you should schedule your next dose.

What are possible side effects from using KYPROLIS?

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

- Fatigue, weakness, general feeling of illness or discomfort
- Diarrhea, nausea, constipation, vomiting, digestion problems, stomach pain, decreased appetite, dehydration
- Pain, redness, irritation or swelling where you received the injection into your vein (infusion site reaction)
- Fever, chills, common cold, the flu, bronchitis
- Headache, dizziness
- Numbness, tingling, or decreased sensation in hands and/or feet
- Nose bleed
- Change in voice or hoarseness, pain in the throat

- Blurred vision
- Ringing in the ears (tinnitus)
- Toothache
- Trouble sleeping, anxiety
- Rash, itchy skin
- Reddening of the skin on neck, upper chest or face
- Increased sweating, feeling too hot
- Back pain, joint pain, pain in legs, arms, hands, or feet, bone pain, muscle pain, muscle spasms, muscle weakness, aching muscles

KYPROLIS may alter your blood test results. Your healthcare professional will decide when to perform blood tests and will interpret the results.

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			
Thrombocytopenia (decreased platelets): bruising or bleeding	X		
Pneumonia, pneumonitis (lung infection/inflammation): cough, bloody or coloured mucus, fever, shortness of breath		X	
Dyspnea, interstitial lung disease (breathing problems): difficulty breathing, including shortness of breath at rest or with activity, rapid breathing, wheezing or cough		X	
COMMON			
Deep vein thrombosis (blood clot in the leg): leg swelling or pain			X
Pulmonary embolism (blood clot in the lungs): chest pain or shortness of breath			X
Heart failure/heart attack, atrial fibrillation, palpitations, tachycardia, pericardial effusion, cardiomyopathy (heart problems): chest pain (angina), shortness of breath, rapid, strong or irregular heartbeat or if there is swelling of your ankles and feet			X
Bleeding events: coughing up blood, vomiting up blood, dark tarry stools, or bright red blood in your stools			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**	
Kidney problems/kidney failure: swollen ankles, feet or hands, loss of appetite, passing less urine, or abnormal blood test results			X
Infusion reactions/drug hypersensitivity: fever, chills or shaking, joint pain, flushing or swelling, swelling of the throat, shortness of breath, low blood pressure	X		
Pulmonary hypertension (high blood pressure in the arteries of the lungs): shortness of breath with everyday activities or at rest, irregular heartbeat, fast pulse, tiredness, dizziness, and fainting spells			X
Urinary tract infection: pain or burning sensation while urinating, frequent urination	X		
Sepsis (infection of the blood) and/or septic shock (a life-threatening form of sepsis): fever or dizziness	X		
Infection of the stomach and intestine: severe and persistent diarrhea and/or pain in the abdomen	X		
Peripheral edema: leg or arm swelling		X	
Acute Respiratory Distress Syndrome, acute respiratory failure (lung failure): severe difficulty breathing, including shortness of breath at rest or with activity, rapid breathing, wheezing or coughing			X
UNCOMMON			
Tumour lysis syndrome (symptoms caused by the sudden, rapid death of cancer cells due to the treatment): irregular heartbeat, muscle spasms or twitching, passing less urine and abnormal blood tests due to rapid breakdown of cancer cells			X
Liver problems (including reactivation of Hepatitis B infection): yellowing of your skin and eyes, stomach pain or swelling, nausea or vomiting			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**	
Hypertensive crisis: very high blood pressure, severe chest pain, severe headache, confusion, blurred vision, nausea and vomiting, or severe anxiety			X
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			X
Posterior reversible encephalopathy syndrome (PRES) (a rare neurological disorder): headaches, confusion, seizures, speech and visual loss, and high blood pressure due to swelling in the back of the brain			X
Thrombotic microangiopathies (damage to the smallest blood vessels inside your body's main organs causing clots): bleeding, bruising, weakness, confusion, fever, nausea, vomiting, diarrhea, and acute kidney failure due to blood clots in small vessels			X
Inflammation of the colon: diarrhea resulting from inflammation of the colon caused by bacteria called *Clostridium difficile*	X		
Multi-organ dysfunction syndrome (failure of multiple organs): failure of multiple organs (eg, lung, kidney, heart) at the same time including passing less urine, difficulty breathing (including shortness of breath at rest or with activity), rapid breathing, wheezing or cough; yellowing of your skin and eyes, stomach pain or swelling, nausea or vomiting; chest pain (angina), shortness of breath, rapid, strong or irregular heartbeat, or if there is swelling of your ankles and feet			X
Intestinal obstruction (blockage that stop or impairs passage of contents of the intestines): nausea, vomiting, bloating, inability to pass gas, severe abdominal pain, pain that comes and goes, loss of appetite, constipation or diarrhea			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**	
Pancreatitis (inflammation of the pancreas): upper abdominal pain, fever, rapid pulse, nausea, vomiting, and tenderness when touching the abdomen			X
RARE			
Cytomegalovirus (infection in the back of the eye): floaters in the eye, flashes in the eye, blurred vision, blind spot in vision, and loss of peripheral vision		X	
VERY RARE			
Progressive Multifocal Leukoencephalopathy (PML) (central nervous system infection): blurred or double vision, vision loss, difficulty speaking, weakness in an arm or a leg, a change in the way you walk, problems with your balance, persistent numbness, decreased sensation or loss of sensation, memory loss or confusion		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, 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 healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

KYPROLIS will be stored and managed by healthcare professionals. The information below on how to store KYPROLIS is meant for your healthcare professional.

Unopened vials:

- Store refrigerated (2°C to 8°C).
- Keep in the original carton to protect from light. Protection from light is not necessary during administration.

Reconstituted solution:

- Reconstituted solutions in the vial, syringe or IV bag can be stored refrigerated (2°C to 8°C) for up to 24 hours, or at room temperature (15°C to 30°C) for up to 4 hours.

Keep out of reach and sight of children.

If you want more information about KYPROLIS:

- 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.amgen.ca, or by calling 1-866-50-AMGEN (1-866-502-6436).

This leaflet was prepared by Amgen Canada Inc.

Last Revised: July 25, 2023