Patient Information Leaflet

Scheduling Status: S4

KYPROLIS® 60 mg powder for solution for infusion

Carfilzomib

Read all of this leaflet carefully before you start using KYPROLIS®

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- KYPROLIS® has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What KYPROLIS® is and what it is used for

KYPROLIS® is a medicine that contains the active substance carfilzomib.

KYPROLIS® is a protease inhibitor. It is a type of medicine used to treat adult patients with multiple myeloma who have received at least one previous treatment for multiple myeloma.

KYPROLIS® may be given to you:

- on its own;
- in combination with lenalidomide and dexamethasone;

- in combination with dexamethasone and daratumumab;
- only with dexamethasone.

Lenalidomide, dexamethasone and daratumumab are other medicines used to treat multiple myeloma.

2. What you need to know before you use KYPROLIS®

Do not use KYPROLIS®:

- If you are allergic to carfilzomib or any of the other ingredients of this medicine (listed in section 6).
- If you are pregnant or breastfeeding.

Tell your doctor or healthcare professional before being given the injection if:

- You have heart problems, including a history of chest pain (angina pectoris), heart attack, irregular heartbeat, high blood pressure or if you have ever taken a medicine for your heart.
- You have lung problems, including a history of shortness of breath at rest or with activity (dyspnoea).
- You have kidney problems, including kidney failure or if you have ever received dialysis.
- You have liver problems, including a history of hepatitis, fatty liver, or if you have ever been told your liver is not working properly.
- You have 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.
- You have blood clots in your veins or lungs.
- You have any other major medical disease for which you were hospitalized or received medication.

You may need extra tests to check that your heart, kidneys and liver are working properly.

Using other medicines with KYPROLIS®:

Always tell your healthcare professional the name of all the medications you are currently taking, have recently taken, or might take in the future. This includes any medicines obtained without a prescription, such as vitamins or herbal remedies (This includes complementary or traditional medicines).

Tell your doctor or nurse if you are taking medicines used to prevent pregnancy such as oral contraceptives or other hormonal contraceptives since these may not be suitable for use with KYPROLIS®.

Pregnancy and Breastfeeding:

For women receiving KYPROLIS®

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

KYPROLIS® should not be used if you are trying to become pregnant or are pregnant. Treatment with KYPROLIS® has not been evaluated in pregnant women. While receiving KYPROLIS® and for 30 days after stopping treatment, you should use a reliable method of birth control to ensure you do not become pregnant. You should talk to your doctor ~~or~~ or nurse about reliable methods of birth control. It is important that you tell your doctor if you are pregnant, think you may be pregnant, or plan on becoming pregnant. If you become pregnant while receiving KYPROLIS®, notify your doctor immediately.

If you are breastfeeding, you should not receive KYPROLIS®. It is not known if KYPROLIS® passes into breast milk in humans. It is important to tell your healthcare professional if you are breastfeeding or plan to do so.

For men receiving KYPROLIS®

While receiving KYPROLIS® and for 90 days after stopping treatment, you should use a reliable method of birth control, such as a condom, to ensure your partner does not become pregnant. You should talk to your doctor or nurse about reliable methods of birth control.

If your partner becomes pregnant while you are receiving KYPROLIS® or within 90 days after stopping treatment, notify your doctor or nurse immediately.

Driving and using machinery:

Patients being treated with KYPROLIS® may experience fatigue, dizziness, fainting, and/or a drop in blood pressure. This may impair your ability to drive or operate machinery. If you have these symptoms; you should not drive a car or operate machinery.

KYPROLIS® contains sodium

The medicine contains 216 mg sodium (main component of cooking/table salt) in 60 ml vial this is equivalent to 11 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Kyprolis contains cyclodextrin

This medicine contains 3,000 mg cyclodextrin (betadex sulfobutyl ether sodium) per 60 mg vial. This is equivalent to 88 mg/kg for a 70 kg adult.

3. How to use KYPROLIS®

You will not be expected to give yourself KYPROLIS®, it will be given to you by a healthcare professional. KYPROLIS® once weekly will be infused into your vein each week for 3 weeks, followed by one week without dosing.

KYPROLIS® twice weekly will be infused into your vein 2 days in a row, each week for 3 weeks, followed by one week without dosing. Each 28 day period is considered one treatment cycle. This means that KYPROLIS® will be given on Days 1, 8, and 15 for once weekly dosing and Days 1, 2, 8, 9, 15, and 16 for twice weekly dosing of each 28 day cycle.

When KYPROLIS® is given alone or with lenalidomide and dexamethasone, the doses on Day 8 and 9 of each cycle will not be given from Cycle 13 onwards. The dose will be calculated based on your height and weight (body surface area). Your healthcare professional will determine the dose of KYPROLIS® that you receive. Most patients will receive treatment until their disease progresses (gets worse).

However, KYPROLIS® treatment may also be stopped if you experience side effects that cannot be managed. If you have any further questions on the use of KYPROLIS®, ask your doctor or nurse.

If you receive more KYPROLIS® than you should:

As KYPROLIS® is being given by a doctor or nurse, it is unlikely that you will be given too much. However, if you are given too much KYPROLIS® your doctor will monitor you for side effects.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. POSSIBLE SIDE EFFECTS

KYPROLIS® may have side effects.

Not all side effects reported for KYPROLIS® are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving KYPROLIS®, please consult your doctor, pharmacist or other health care professional for advice.

KYPROLIS® can make some conditions worse or cause serious side effects, including life-threatening complications.

Tell your doctor immediately if you get any of the following:

- Chest pains, shortness of breath, or if there is swelling of your ankles and feet, which may be symptoms of heart problems.
- Difficulty breathing, including shortness of breath at rest or with activity or a cough (dyspnoea), rapid breathing, feeling like you can't breathe in enough air, wheezing, or cough, which can be signs of lung toxicities.
- Extremely high blood pressure, severe chest pain, severe headache, confusion, blurred vision, nausea and vomiting, or severe anxiety, which may be signs of a condition known as hypertensive crisis.
- Shortness of breath with everyday activities or at rest, irregular heartbeat, racing pulse, tiredness, dizziness, and fainting spells, which can be signs of a condition

known as pulmonary hypertension.

- Swollen ankles, feet, or hands, loss of appetite, passing less urine, or abnormal blood tests, which may be symptoms of kidney problems or kidney failure.
- A side effect called Tumour Lysis Syndrome, which may be caused by the rapid breakdown of tumour cells which results in abnormal blood tests and may cause irregular heartbeat or kidney failure.
- A reaction to KYPROLIS® infusion, which can include the following symptoms: fever, chills or shaking, joint pain, muscle pain, facial flushing or swelling, swelling of the throat, weakness, shortness of breath, low blood pressure, fainting, slow heartbeat, chest tightness, or chest pain.
- Unusual bruising or bleeding, such as a cut that does not stop bleeding in a normal amount of time or internal bleeding such as coughing up blood, vomiting up blood, dark tarry stools, or bright red blood in your stools
- Leg pain (which could be a symptom of blood clots in the deep veins of the leg), chest pain or shortness of breath (which may be a symptom of blood clots in the lungs)
- Liver problems, including liver failure, which may cause yellowing of your skin and eyes (jaundice), abdominal pain or swelling, nausea or vomiting. If you have ever had hepatitis B infection, treatment with KYPROLIS® may cause the hepatitis B infection to become active again.
- Bleeding, bruising, weakness, confusion, fever, nausea, vomiting and diarrhoea, and acute kidney failure, which may be signs of a blood condition known as thrombotic microangiopathy.
- Headaches, confusion, seizures, visual loss, and high blood pressure (hypertension), which may be symptoms of a neurologic condition known as Posterior Reversible Encephalopathy Syndrome (PRES).
- 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 which may be symptoms of a central nervous system

infection known as Progressive Multifocal Leukoencephalopathy (PML)

Frequent side effects:

- Heart disease including heart attack and heart failure
- Irregular heartbeat (palpitations)
- Pacing pulse
- Chest pain
- Shortness of breath/difficulty breathing
- Blood clots in the veins (deep vein thrombosis)
- Liver problems including yellowing of skin or eyes (jaundice), an increase in your liver enzymes, bilirubin, or bile acids in the blood
- Fainting spells
- Confusion
- Facial flushing or swelling
- Fluid in the lungs
- Blood clot in the lungs
- Sepsis (systemic infection including infection in the blood) and/or septic shock (life-threatening form of sepsis)
- Pneumonia
- Acute renal failure
- Swelling of the hands, feet or ankles
- Dry cough
- Cough with phlegm
- Wheezing
- High blood pressure (hypertension)
- Headache
- Blurred vision
- Nausea
- Vomiting

- Anxiety
- Dizziness
- Decreased appetite
- Passing less urine
- Infusion site reaction (pain, redness, irritation, or swelling where you received the injection into your vein)
- Pain, swelling, irritation or discomfort at the infusion site
- Fever
- Chills
- Joint pain
- Muscle pain
- Feeling too hot
- Muscle weakness
- Low platelets, which may cause easy bruising or bleeding
- Low red blood cell count (anaemia), which may cause tiredness (fatigue)
- Low white blood cell count, which may decrease your ability to fight infection and may be associated with fever
- Nosebleed
- Change in voice or hoarseness
- Pain in the throat
- Cataract
- Diarrhoea
- Constipation
- Indigestion
- Stomach pain
- Toothache
- Runny nose or nasal congestion
- Sore throat
- Inflammation of the nose and throat

- Bronchitis
- Respiratory tract infection
- Urinary tract infection
- Flu like symptoms (influenza)
- Viral infection
- Low blood pressure (hypotension)
- Increased blood levels of c-reactive protein, sugar, calcium, uric acid, or potassium
- Decreased blood levels of protein, potassium, magnesium, calcium, sodium, or phosphate
- Dehydration
- Pain
- Back pain
- Pain in limbs, hands, or feet
- Bone pain
- Muscle spasms
- Aching muscles
- Numbness, tingling or decreased sensation in hands and/or feet
- Insomnia (difficulty sleeping)
- Rash
- Itchy skin
- Redness of the skin
- Increased sweating
- General feeling of illness or discomfort
- Infection of the stomach and intestine
- Ringing in the ears (tinnitus)

Less frequent side effects:

- Tumour lysis syndrome, which may be caused by rapid breakdown of tumour cells and increase the levels of potassium, uric acid, phosphate in your blood, and may

lead to acute kidney failure

- Extremely high blood pressure (hypertensive crisis)
- Thrombotic microangiopathy including Thrombotic Thrombocytopenic
- Purpura/Haemolytic Uraemic Syndrome (TTP/HUS), which may cause the following symptoms: bleeding, bruising, weakness, confusion, fever, nausea, vomiting, diarrhoea and acute kidney failure
- Posterior Reversible Encephalopathy Syndrome (PRES), with symptoms of headaches, confusion, seizures, visual loss, and high blood pressure
- (hypertension)
- Bleeding in the brain
- Stroke
- Multi-organ failure
- Liver failure
- Perforation in stomach, small intestine, or large bowel (GI perforation)
- Bleeding in the stomach and bowels
- Abnormal amount of fluid between the heart and the lining around the heart (pericardial effusion)
- Swelling and irritation of the lining around the heart (pericarditis)
- Allergic reaction
- Rapid breathing
- Bleeding in the lungs
- Inflammation of the colon caused by a bacteria called Clostridium difficile
- Infection of the back of the eye (cytomegalovirus)
- Intestinal blockage

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online

under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of KYPROLIS®.

Alternatively, you can report side effects to:

Amgen South Africa (Pty) Ltd.

Tel: +27 (0)11 100 5300

Email: safety-south-africa@amgen.com

5. STORING AND DISPOSING OF KYPROLIS®

Store all medicines out of the reach of children.

Unopened vials should be stored in a refrigerator (between 2 °C and 8 °C).

Keep the vial in the original package to protect it from light.

KYPROLIS® is for single use only. Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

Do not use KYPROLIS® after the expiry date printed on the vial and the carton.

6. Contents of the pack and other information

What KYPROLIS® contains:

The active substance is carfilzomib.

The other ingredients are anhydrous citric acid; sulfobutylether beta-cyclodextrin and water for injection.

What KYPROLIS® looks like and contents of the pack

KYPROLIS® is a white to off-white powder supplied in a sterile vial packed in a carton.

The single-use vial (closed with a grey rubber stopper and a grey aluminium seal with a purple plastic flip off cap) is distributed individually in a carton and contains a dose of 60 mg of carfilzomib.

Holder of Certificate of Registration

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