Package leaflet: Information for the patient

Kyprolis 60 mg powder for solution for infusion

(carfilzomib)

1000163382-xxx-xx

Read all of this leaflet carefully before you start using this medicine because it contains
important information for you.
– Keep this leaflet. You may need to read it again.
– If you have any further questions, ask your doctor or nurse.
– If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

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.

Carfilzomib works by blocking the proteasome. The proteasome is a system within the cells that breaks down proteins when they are damaged or no longer needed. By preventing the breakdown of proteins in cancer cells, which are more likely to contain more abnormal proteins, Kyprolis causes the death of cancer cells.

Kyprolis is used to treat adult patients with multiple myeloma who have had at least one previous treatment for this disease. Multiple myeloma is a cancer of plasma cells (a type of white blood cell).

Kyprolis will be given to you together with daratumumab and dexamethasone, with lenalidomide and dexamethasone, or only with dexamethasone. Daratumumab, lenalidomide and dexamethasone are other medicines used to treat multiple myeloma.

2. What you need to know before you use Kyprolis

Your doctor will examine you and review your full medical history. You will be monitored closely during treatment. Before starting Kyprolis, and during treatment, you will undergo blood testing. This is to check that you have enough blood cells and your liver and kidneys are working properly. Your doctor or nurse will check if you are getting enough fluids.

You must read the package leaflet of all medicines that you take in combination with Kyprolis so that you understand the information related to those medicines.

Do not use Kyprolis if you are allergic to carfilzomib or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or nurse before using Kyprolis if you have any of the conditions listed below.
You may need extra tests to check that your heart, kidneys and liver are working properly.

- 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
- Lung problems, including a history of shortness of breath at rest or with activity (dyspnoea)
- Kidney problems, including kidney failure or if you have ever received dialysis
- Liver problems, including a history of hepatitis, fatty liver, or if you have ever been told your liver is not working properly
- Unusual bleeding, including easy bruising, bleeding from an injury, such as a cut, that takes longer than expected to stop, or internal bleeding such as coughing up blood, vomiting up blood, dark tarry stools, or bright red blood in your stools; or bleeding in the brain leading to sudden numbness or paralysis on one side of the face, legs or arms, sudden severe headache or trouble seeing or difficulty speaking or swallowing. This can indicate you have low numbers of platelets (cells that help the blood to clot)
- A history of blood clots in your veins
- Leg or arm pain or swelling (which could be a symptom of blood clots in the deep veins of the leg or arm), chest pain or shortness of breath (which may be a symptom of blood clots in the lungs)
- Any other major disease for which you were hospitalised or received any medicine.

Conditions you need to look out for

You must look out for certain symptoms while you are taking Kyprolis to reduce the risk of any problems. Kyprolis can make some conditions worse or cause serious side effects, which may be fatal, such as heart problems, lung problems, kidney problems, tumour lysis syndrome (a life-threatening condition that occurs when cancer cells break and release their content to the bloodstream), reactions to the Kyprolis infusion, unusual bruising or bleeding, (including internal bleeding), blood clots in your veins, liver problems, certain blood conditions, or a neurological condition known as PRES. See 'Conditions you need to look out for' in section 4.

Tell your doctor if you have ever had or might now have a hepatitis B infection. This is because this medicine could cause hepatitis B virus to become active again. Your doctor will check you for signs of this infection before, during and for some time after treatment with this medicine. Tell your doctor right away if you get worsening tiredness, or yellowing of your skin or white part of your eyes.

At any time during or after your treatment, tell your doctor or nurse immediately if you: experience blurred, loss of or double vision, difficulty speaking, weakness in an arm or a leg, a change in the way you walk or problems with your balance, persistent numbness, decreased sensation or loss of sensation, memory loss or confusion. These may all be symptoms of a serious and potentially fatal brain condition known as Progressive Multifocal Leukoencephalopathy (PML). If you had these symptoms prior to treatment with carfilzomib, tell your doctor about any change in these symptoms.

Other medicines and Kyprolis

Tell your doctor if you are taking, have recently taken or might take any other medicines. This includes any medicines obtained without a prescription, such as vitamins or herbal remedies.

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

Pregnancy and breast-feeding

For women taking Kyprolis

Do not take Kyprolis if you are pregnant, think you may be pregnant or are planning to have a baby. Treatment with Kyprolis has not been evaluated in pregnant women. While taking Kyprolis, and for 30 days after stopping treatment you should use a suitable method of contraception to ensure you do not become pregnant. You should talk to your doctor or nurse about suitable methods of contraception.

If you become pregnant while taking Kyprolis, notify your doctor or nurse immediately.

Do not take Kyprolis if you are breast-feeding. It is not known if Kyprolis passes into breast milk in humans.

Lenalidomide is expected to be harmful to the unborn child. As Kyprolis is given in combination with lenalidomide, you must follow the Pregnancy Prevention Programme (see package leaflet for lenalidomide for information on pregnancy prevention and discuss with your doctor, pharmacist or nurse).

For men taking Kyprolis

While taking Kyprolis and for 90 days after stopping treatment, you should use a condom even if your partner is pregnant.

If your partner becomes pregnant whilst you are taking Kyprolis or within 90 days after stopping treatment, notify your doctor or nurse immediately.

Driving and using machines
While you are being treated with Kyprolis you may experience fatigue, dizziness, fainting, and/or a drop in blood pressure. This may impair your ability to drive or operate machines. Do not drive a car or operate machines if you have these symptoms.

Kyprolis contains sodium

This medicine contains 37 mg sodium per 10 mg vial. This is equivalent to 1.9% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

This medicine contains 109 mg sodium per 30 mg vial. This is equivalent to 5.5% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

This medicine contains 216 mg sodium per 60 mg 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 500 mg cyclodextrin (betadex sulfobutyl ether sodium) per 10 mg vial. This is equivalent to 88 mg/kg for a 70 kg adult.

This medicine contains 1,500 mg cyclodextrin (betadex sulfobutyl ether sodium) per 30 mg vial. This is equivalent to 88 mg/kg for a 70 kg adult.

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

Kyprolis will be given to you by a doctor or nurse. The dose will be calculated based on your height and weight (body surface area). Your doctor or nurse will determine the dose of Kyprolis that you receive.

Kyprolis will be given as an infusion into a vein. The infusion may last up to 30 minutes. Kyprolis is given 2 days in a row each week, for 3 weeks, followed by one week without treatment.

Each 28-day period is one treatment cycle. This means that Kyprolis will be given to you on days 1, 2, 8, 9, 15, and 16 of each 28-day cycle. The doses on day 8 and 9 of each cycle will not be given from cycle 13 onwards if you are treated with Kyprolis in combination with lenalidomide and dexamethasone.

Most patients will receive treatment for as long as their disease improves or remains stable. However, Kyprolis treatment may also be stopped if you experience side effects that cannot be managed.

Together with Kyprolis you will also be given either lenalidomide and dexamethasone, daratumumab and dexamethasone, or only dexamethasone. You may also be given other medicines.

If you are given too much Kyprolis
As this medicine 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

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Conditions you need to look out for

Some side effects could be serious. Tell your doctor straight away if you get notice any of the following symptoms:

- Chest pains, shortness of breath, or if there is swelling of your 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 toxicity
- Very 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 test results, which may be symptoms of kidney problems or kidney failure
- A side effect called tumour lysis syndrome, which can be caused by the rapid breakdown of tumour cells and may cause irregular heartbeat, kidney failure or abnormal blood test results
- Fever, chills or shaking, joint pain, muscle pain, facial flushing, or swelling of the face, lips, tongue and/or throat which may cause difficulty breathing or swallowing (angioedema), weakness, shortness of breath, low blood pressure, fainting, slow heart rate, chest tightness, or chest pain can occur as a reaction to the infusion
- Unusual bruising or bleeding, such as a cut, that takes longer than usual to stop bleeding; or internal bleeding such as coughing up blood, vomiting up blood, dark tarry stools, or bright red blood in your stools; or bleeding in the brain leading to sudden numbness or paralysis on one side of the face, legs or arms, sudden severe headache or trouble seeing or difficulty speaking or swallowing
- Leg or arm pain or swelling (which could be a symptom of blood clots in the deep veins of the leg or arm), chest pain or shortness of breath (which may be a symptom of blood clots in the lungs)
- Yellowing of your skin and eyes (jaundice), abdominal pain or swelling, nausea or vomiting, which could be symptoms of liver problems including liver failure. If you have ever had hepatitis B infection, treatment with this medicine 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 (fits), visual loss, and high blood pressure (hypertension), which may be symptoms of a neurologic condition known as posterior reversible encephalopathy syndrome (PRES).

Other possible side effects

Very common side effects (may affect more than 1 in 10 people)
- Serious lung infection (pneumonia)
- Respiratory tract infection (infection of the airways)
- Low platelets, which may cause easy bruising or bleeding (thrombocytopenia)
- Low white blood cell count, which may decrease your ability to fight infection and may be associated with fever
- Low red blood cell count (anaemia) which may cause tiredness and fatigue
- Changes to blood tests (decreased blood levels of potassium, increased blood levels of creatinine)
- Decreased appetite
- Difficulty sleeping (insomnia)
- Headache
- Numbness, tingling, or decreased sensation in hands and/or feet
- Dizziness
- High blood pressure (hypertension)
- Shortness of breath
- Cough
- Diarrhoea
- Nausea
- Constipation
- Vomiting
- Stomach pain
- Back pain
- Joint pain
- Pain in limbs, hands or feet
- Muscle spasms
- Fever
- Chills
- Swelling of the hands, feet or ankles
- Feeling weak
- Tiredness (fatigue)

Common side effects (may affect up to 1 in 10 people)
- Infusion reaction
- Heart failure and heart problems including rapid, strong or irregular heartbeat
- Heart attack
- Kidney problems, including kidney failure
- Blood clots in the veins (deep vein thrombosis)
- Feeling too hot

- Blood clot in the lungs
- Fluid in the lungs
- Wheezing
- Serious infection including infection in the blood (sepsis)
- Lung infection
- Liver problems including an increase in liver enzymes in the blood
- Flu-like symptoms (influenza)
- Reactivation of the chicken pox virus (shingles) that can cause a skin rash and pain (herpes zoster)
- Urinary tract infection (infection of structures that carry urine)
- Cough which could include chest tightness or pain, nasal congestion (bronchitis)
- Sore throat
- Inflammation of the nose and throat
- Runny nose, nasal congestion or sneezing
- Viral infection
- Infection of the stomach and intestine (gastroenteritis)
- Bleeding in the stomach and bowels
- Changes to blood tests (decreased blood levels of sodium, magnesium, protein, calcium or phosphate, increased blood levels of calcium, uric acid, potassium, bilirubin, c-reactive protein or sugar)
- Dehydration
- Anxiety
- Feeling confused
- Blurred vision
- Cataract
- Low blood pressure (hypotension)
- Nose bleed
- Change in voice or hoarseness
- Indigestion
- Toothache
- Rash
- Bone pain, muscle pain, chest pain
- Muscle weakness
- Aching muscles
- Itchy skin
- Redness of the skin
- Increased sweating
- Pain
- Pain, swelling, irritation or discomfort where you received the injection into your vein
- Ringing in the ears (tinnitus)
- A general feeling of illness or discomfort

Uncommon side effects (may affect up to 1 in 100 people)
- Bleeding in the lungs
- Inflammation of the colon caused by a bacteria called Clostridium difficile
- Allergic reaction to Kyprolis
- Multi-organ failure
- Reduced blood flow to the heart
- Bleeding in the brain
- Stroke
- Difficulty breathing, rapid breathing and/or fingertips and lips looking slightly blue (acute respiratory distress syndrome)
- Swelling of the lining of the heart (pericarditis), symptoms include pain behind the breast bone, sometimes spreading across to the neck and shoulders, sometimes with a fever
- Fluid build-up in the lining of the heart (pericardial effusion), symptoms include chest pain or pressure and shortness of breath
- A blockage in the flow of bile from the liver (cholestasis), which can cause itchy skin, yellow skin, very dark urine and very pale stools
- Perforation of the digestive system
- Cytomegalovirus infection
- Hepatitis B infection activated again (viral inflammation of the liver)
- Inflammation of the pancreas

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

5. How to store Kyprolis

Kyprolis will be stored in the pharmacy.

Keep this medicine out of the sight and reach of children.

Do not use Kyprolis after the expiry date printed on the vial and the carton. The expiry date refers to the last day of that month.

Store refrigerated (2°C - 8°C).
Do not freeze.
Store in the original carton in order to protect from light.

If this medicine becomes discoloured or shows any other signs of deterioration, please contact your pharmacist who will advise you on what to do.

The reconstituted product should be a clear, colourless to slightly yellow solution and should not be administered if any discolouration or particulate matter is observed.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Kyprolis is for single use only. Any unused product or waste material should be disposed of in accordance with local requirements.

6. Contents of the pack and other information

What Kyprolis contains
– The active substance is carfilzomib. Each vial contains 60 mg of carfilzomib. After reconstitution, 1 mL of solution contains 2 mg of carfilzomib.
– The other ingredients are betadex sulfobutyl ether sodium, anhydrous citric acid (E330) and sodium hydroxide (see section 2 'Kyprolis contains sodium').

What Kyprolis looks like and contents of the pack
Kyprolis is supplied in a glass vial as a white to off-white powder for solution for infusion, which is reconstituted (dissolved) before use. The reconstituted solution is a clear, colourless or slightly yellow solution.

Each pack contains 1 vial.

Product Licence Holder and Manufacturer

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Is this leaflet hard to see or read?
Call +45 63 95 27 00
to obtain the leaflet in a format suitable for you.

The following information is intended for healthcare professionals only:

Instructions for reconstitution and preparation of Kyprolis powder for solution for infusion for intravenous administration

Carfilzomib is a cytotoxic agent. Therefore, caution should be used during handling and preparation of Kyprolis. Use of gloves and other protective equipment is recommended.

Kyprolis vials contain no antimicrobial preservatives and are intended for single use only. Proper aseptic technique must be observed.

The reconstituted solution contains carfilzomib at a concentration of 2 mg/mL. Read the complete preparation instructions prior to reconstitution:

1. Calculate the dose (mg/m2) and number of vials of Kyprolis required using the patient's BSA at baseline. Patients with a BSA greater than 2.2 m2 should receive a dose based upon a BSA of 2.2 m2. Dose adjustments do not need to be made for weight changes of ≤ 20%.

2. Remove vial from refrigerator just prior to use.

3. Use only a 21-gauge or larger gauge needle (0.8 mm or smaller external diameter needle) to aseptically reconstitute each vial by slowly injecting 5 mL (for 10 mg vial), 15 mL (for 30 mg vial) or 29 mL (for 60 mg vial) sterile water for injections through the stopper and directing the solution onto the INSIDE WALL OF THE VIAL to minimise foaming.

4. Gently swirl and/or invert the vial slowly for approximately 1 minute, or until complete dissolution. DO NOT SHAKE. If foaming occurs, allow the solution to settle in the vial until foaming subsides (approximately 5 minutes) and the solution is clear.

5. Visually inspect for particulate matter and discolouration prior to administration. The reconstituted product should be a clear, colourless to slightly yellow solution and should not be administered if any discolouration or particulate matter is observed.

6. Discard any unused portion left in the vial.

7. Kyprolis can be administered directly by intravenous infusion or optionally administered in an intravenous bag. Do not administer as an intravenous push or bolus.

8. When administering in an intravenous bag, use only a 21-gauge or larger gauge needle (0.8 mm or smaller external diameter needle) to withdraw the calculated dose from the vial and dilute into a 50 or 100 mL intravenous bag containing 5% glucose solution for injection.

From a microbiological point of view, the product should be used immediately. If not used
immediately, in-use storage times and conditions are the responsibility of the user and should not be longer than 24 hours at 2°C – 8°C.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.