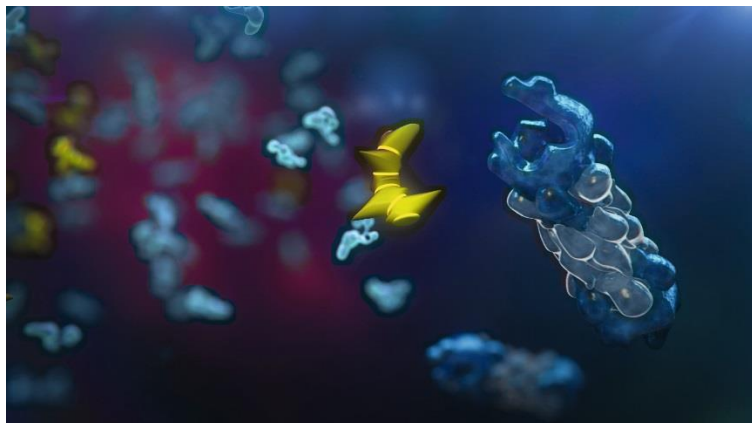


Kyprolis® (carfilzomib) MOA Image



Kyprolis (carfilzomib) (yellow, center) specifically and irreversibly binds to the proteasome (blue, right). This inhibition leads to a build-up of proteins and in some cells, signals for cell death.

Kyprolis® For EU

Kyprolis (carfilzomib) in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

Important EU Product Safety Information

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Kyprolis treatment should be supervised by a physician experienced in the use of anti-cancer therapy. The most serious side effects that may occur during Kyprolis treatment include: cardiac toxicity, pulmonary toxicities, pulmonary hypertension, dyspnoea, hypertension including hypertensive crises, acute renal failure, tumour lysis syndrome, infusion reactions, thrombocytopenia, hepatic toxicity, posterior reversible encephalopathy syndrome (PRES) and thrombotic thrombocytopenic purpura/haemolytic uremic syndrome (TTP/HUS). The most common side effects are anaemia, fatigue, diarrhoea, thrombocytopenia, nausea, pyrexia, dyspnoea, respiratory tract infection, cough and peripheral oedema.

Please refer to the Summary of Product Characteristics for full European prescribing information.

Important U.S. Product Safety Information

Cardiac Toxicities

New onset or worsening of pre-existing cardiac failure (e.g., congestive heart failure, pulmonary edema, decreased ejection fraction), restrictive cardiomyopathy, myocardial ischemia, and myocardial infarction including fatalities have occurred following administration of Kyprolis. Death due to cardiac arrest has occurred within a day of Kyprolis administration.

Withhold Kyprolis for Grade 3 or 4 cardiac adverse events until recovery, and consider whether to restart Kyprolis based on a benefit/risk assessment.

Adequate hydration is required prior to each dose in Cycle 1. Monitor all patients for evidence of volume overload, especially patients at risk for cardiac failure. Adjust total fluid intake as clinically appropriate in patients with baseline cardiac failure or who are at risk for cardiac failure.

Patients ≥ 75 years, the risk of cardiac failure is increased. Patients with New York Heart Association Class III and IV heart failure, recent myocardial infarction, and conduction abnormalities may be at greater risk for cardiac complications.

Acute Renal Failure

Cases of acute renal failure and renal insufficiency adverse events (renal impairment, acute renal failure, renal failure) have occurred in patients receiving Kyprolis. Acute renal failure was reported more frequently in patients with advanced relapsed and refractory multiple myeloma who received Kyprolis monotherapy. This risk was greater in patients with a baseline reduced estimated creatinine clearance. Monitor renal function with regular measurement of the serum creatinine and/or estimated creatinine clearance. Reduce or withhold dose as appropriate.

Tumor Lysis Syndrome

Cases of Tumor Lysis Syndrome (TLS), including fatal outcomes, have occurred in patients receiving Kyprolis. Patients with multiple myeloma and a high tumor burden should be considered at greater risk for TLS. Adequate hydration is required prior to each dose in Cycle 1, and in subsequent cycles as needed. Consider uric acid lowering drugs in patients at risk for TLS. Monitor for evidence of TLS during treatment and manage promptly. Withhold Kyprolis until TLS is resolved.

Pulmonary Toxicity

Acute Respiratory Distress Syndrome (ARDS), acute respiratory failure, and acute diffuse infiltrative pulmonary disease such as pneumonitis and interstitial lung disease have occurred in patients receiving Kyprolis. Some events have been fatal. In the event of drug-induced pulmonary toxicity, discontinue Kyprolis.

Pulmonary Hypertension

Pulmonary arterial hypertension (PAH) was reported in patients treated with Kyprolis. Evaluate with cardiac imaging and/or other tests as indicated. Withhold Kyprolis for PAH until resolved or returned to baseline and consider whether to restart Kyprolis based on a benefit/risk assessment.

Dyspnea

Dyspnea was reported in patients treated with Kyprolis. Evaluate dyspnea to exclude cardiopulmonary conditions including cardiac failure and pulmonary syndromes. Stop Kyprolis for Grade 3 or 4 dyspnea until resolved or returned to baseline. Consider whether to restart Kyprolis based on a benefit/risk assessment.

Hypertension

Hypertension, including hypertensive crisis and hypertensive emergency, has been observed with Kyprolis. Some of these events have been fatal. Monitor blood pressure regularly in all patients. If hypertension cannot be adequately controlled, withhold Kyprolis and evaluate. Consider whether to restart Kyprolis based on a benefit/risk assessment.

Venous Thrombosis

Venous thromboembolic events (including deep venous thrombosis and pulmonary embolism) have been observed with Kyprolis. Thromboprophylaxis is recommended and should be based on an assessment of the patient's underlying risks, treatment regimen, and clinical status.

Infusion Reactions

Infusion reactions, including life-threatening reactions, have occurred in patients receiving Kyprolis. Symptoms include fever, chills, arthralgia, myalgia, facial flushing, facial edema, vomiting, weakness, shortness of breath, hypotension, syncope, chest tightness, or angina. These reactions can occur immediately following or up to 24 hours after administration of Kyprolis. Premedicate with dexamethasone to reduce the incidence and severity of infusion reactions. Inform patients of the risk and of symptoms of an infusion reaction and to contact a physician immediately if they occur.

Thrombocytopenia

Kyprolis causes thrombocytopenia with recovery to baseline platelet count usually by the start of the next cycle. Thrombocytopenia was reported in patients receiving Kyprolis. Monitor platelet counts frequently during treatment with Kyprolis. Reduce or withhold dose as appropriate.

Hepatic Toxicity and Hepatic Failure

Cases of hepatic failure, including fatal cases, have been reported during treatment with Kyprolis. Kyprolis can cause increased serum transaminases. Monitor liver enzymes regularly. Reduce or withhold dose as appropriate.

Thrombotic Thrombocytopenic Purpura /Hemolytic Uremic Syndrome (TTP/HUS)

Cases of TTP/HUS including fatal outcome have occurred in patients receiving Kyprolis. Monitor for signs and symptoms of TTP/HUS. Discontinue Kyprolis if diagnosis is suspected. If the diagnosis of TTP/HUS is excluded, Kyprolis may be restarted. The safety of reinitiating Kyprolis therapy in patients previously experiencing TTP/HUS is not known.

Posterior Reversible Encephalopathy Syndrome (PRES)

Cases of PRES have occurred in patients receiving Kyprolis. PRES was formerly known as Reversible Posterior Leukoencephalopathy Syndrome. Consider a neuro-radiological imaging (MRI) for onset of visual or neurological symptoms, such as seizure, headache, lethargy, confusion, blindness, and altered consciousness, along with hypertension.. Discontinue Kyprolis if PRES is suspected and evaluate. The safety of reinitiating Kyprolis therapy in patients previously experiencing PRES is not known.

Embryo-fetal Toxicity

Kyprolis can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals.

Females of reproductive potential should be advised to avoid becoming pregnant while being treated with Kyprolis and the potential hazard to the fetus if Kyprolis is used during pregnancy.

ADVERSE REACTIONS

The most common adverse events of all grades occurring in at least 20 percent of patients treated with Kyprolis in monotherapy trials: anemia, fatigue, thrombocytopenia, nausea, pyrexia, decreased platelets, dyspnea, diarrhea, decreased lymphocyte, headache, decreased hemoglobin, cough, edema peripheral.

The most common adverse events of all grades occurring in at least 20 percent of patients treated with Kyprolis in the combination therapy trial: decreased lymphocytes, decreased absolute neutrophil count, decreased phosphorus, anemia, neutropenia, decreased total white blood cell count, decreased platelets, diarrhea, fatigue, thrombocytopenia, pyrexia, muscle spasm, cough, upper respiratory tract infection, decreased hemoglobin, hypokalemia.

Full prescribing information for the U.S. is available at www.kyprolis.com.

About Amgen

Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its biologics manufacturing expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be one of the world's leading independent biotechnology companies, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.