KYPROLIS® (CARFILZOMIB) FOR INJECTION
U.S. FACT SHEET

INDICATION

KYPROLIS is indicated in combination with dexamethasone or lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.[1] KYPROLIS as a single agent is indicated for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.[1]

MECHANISM OF ACTION

Proteasomes play an important role in cell function and growth by breaking down proteins that are damaged or no longer needed.[2] KYPROLIS has been shown to block proteasomes, leading to an excessive buildup of proteins within cells.[3] In some cells, KYPROLIS can cause cell death, especially in myeloma cells because they are more likely to contain a higher amount of abnormal proteins.[2] The irreversibility of KYPROLIS' binding has also been shown to offer a sustained inhibition of the targeted enzymes.[4]

STUDY RESULTS OF INTEREST

ENDEAVOR

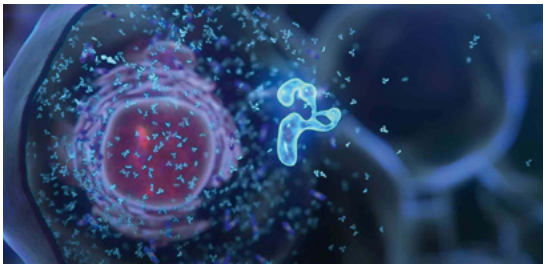
The U.S. Food and Drug Administration (FDA) approved use of KYPROLIS in combination with dexamethasone based on results from the Phase 3 head-to-head ENDEAVOR (Randomiz**E**d, Ope**N** Label, Phase 3 Study of Carfilzomib Plus **DE**xameth**A**sone **V**s Bortezomib Plus Dexamethas**O**ne in Patients With **R**elapsed Multiple Myeloma) trial.[1] ENDEAVOR was a randomized study of 929 patients which evaluated KYPROLIS in combination with low-dose dexamethasone vs. Velcade (bortezomib) and low-dose dexamethasone in patients whose multiple myeloma had relapsed after at least one, but not more than three, prior therapeutic regimens.[1] In the study:

- **Patients with relapsed multiple myeloma treated with KYPROLIS and dexamethasone achieved superior progression-free survival (PFS) of 18.7 months** compared to 9.4 months in those receiving bortezomib and dexamethasone (HR=0.53; 95 percent CI: 044,0.65 p<0.0001).[1]
- **Treatment with the KYPROLIS combination resulted in a two-fold increase in the median duration of response (21.3 months)** compared to the bortezomib combination (10.4 months).[1]

FAST FACTS: MULTIPLE MYELOMA

- ✓ Multiple myeloma is an orphan disease that accounts for approximately **1% OF ALL CANCERS**.[5]
- ✓ In 2015, **26,850 INDIVIDUALS IN THE U.S.** were diagnosed with multiple myeloma and **11,240 LOST THEIR LIFE** to the disease.[6]
- ✓ Multiple myeloma is **MORE COMMON IN MEN** than in women, and is most frequently diagnosed in **PATIENTS AGED 65-74**.[6]

ASPIRE



The U.S. FDA approved KYPROLIS in combination with lenalidomide and dexamethasone based on data from the pivotal Phase 3 ASPIRE (C**A**rfilzomib, Lenalidomide, and Dexameth**S**one versus Lenalidomide and Dexamethasone for the treatment of **P**at**I**ents with **R**elapsed Multiple My**E**loma) trial.[1] ASPIRE was an international, randomized trial which evaluated KYPROLIS in combination with lenalidomide and dexamethasone (regimen referred to as KRd) versus lenalidomide and dexamethasone (regimen referred to as Rd) in patients who had previously received treatment with one to three prior regimens.[3] In the study:

- **In the KYPROLIS arm, patients lived significantly longer without their disease worsening** compared to those in the control arm (median PFS, 26.3 months vs. 17.6 months [HR: 0.69; 95 percent CI: 0.57 to 0.83; P=0.0001]).[3]
- **Patients treated with the KYPROLIS combination were three times more likely to receive a complete response (CR)** compared to those in the control arm (31.8 vs. 9.4 percent of patients, respectively).[3]
- The data for overall survival, a secondary endpoint, are not yet mature.[3]

SAFETY

In ENDEAVOR, the most common adverse reactions (greater than or equal to 20 percent) in the KYPROLIS arm were anemia, diarrhea, dyspnea, fatigue, insomnia, pyrexia, and thrombocytopenia.[1] Treatment discontinuation due to adverse events and on-study deaths were comparable between the two arms.[1] A number of known adverse reactions were reported at a higher rate in the KYPROLIS group compared with the bortezomib group, including any-grade dyspnea, hypertension, pyrexia, and cough as were any-grade cardiac failure (grouped term; 8 percent vs. 3 percent) and acute renal failure (grouped term; 8 percent vs. 5 percent).[1] Rates of grade 3 or higher adverse events were 73 percent in the KYPROLIS group and 67 percent in the bortezomib group.[1] Grade 3 or higher adverse events of interest in the KYPROLIS and bortezomib groups included hypertension (preferred term; 9 percent vs. 3 percent), dyspnea (preferred term; 5 percent vs. 2 percent), cardiac failure (grouped term; 5 percent vs. 2 percent), acute renal failure (grouped term; 4 percent vs. 3 percent), ischemic heart disease (grouped term; 2 percent vs. 2 percent) and pulmonary hypertension (grouped term; 0.6 percent vs. 0.2 percent).[1]

In ASPIRE, the most common adverse reactions (greater than or equal to 20 percent) in the KYPROLIS arm were anemia, cough, diarrhea, fatigue, hypokalemia, muscle spasms, neutropenia, pyrexia, thrombocytopenia and upper respiratory tract infection.[1] Discontinuation of treatment due to adverse events (AEs) occurred in 15 percent of patients in the KRd arm versus 17.7 percent of patients in the Rd arm.[3] The rate of death due to AEs within 30 days of the last dose was balanced between the KRd arm and the Rd arm.[1] The most common causes of death not due to progressive disease occurring in patients in the KRd arm compared to the Rd arm included cardiac disorders (3 percent versus 2 percent), infection (2 percent versus 3 percent), renal (0 percent versus less than 1 percent) and other AEs (2 percent versus 3 percent).[1] Serious AEs (SAEs) were reported in 60 percent of the patients in the KRd arm and 54 percent of the patients in the Rd arm.[1] The most common SAEs reported in the KRd arm compared to the Rd arm were pneumonia (14 percent versus 11 percent), respiratory tract infection (4 percent versus 2 percent), pyrexia (4 percent versus 2 percent) and pulmonary embolism (3 percent versus 2 percent).[1] AEs leading to discontinuation of KYPROLIS occurred in 12 percent of patients and the most common events included pneumonia (1 percent), myocardial infarction (1 percent) and upper respiratory tract infection (1 percent).[1]

DOSING AND ADMINISTRATION

With Dexamethasone

KYPROLIS is administered intravenously as a 30-minute infusion on two consecutive days, each week for three weeks followed by a 12-day rest period.[1] Each 28-day period is considered one treatment cycle.[1] The recommended starting dose of KYPROLIS is 20 mg/m^2 in Cycle 1 on Days 1 and 2.[1] If tolerated, dosing should be escalated to a target dose of 56 mg/m^2 on Day 8 of Cycle 1.[1]

With Lenalidomide and Dexamethasone

KYPROLIS is administered intravenously as a 10-minute infusion on two consecutive days, each week for three weeks followed by a 12-day rest period.[1] Each 28-day period is considered one treatment cycle.[1] The recommended starting dose of KYPROLIS is 20 mg/m^2 in Cycle 1 on Days 1 and 2. If tolerated, dosing should be escalated to a target dose of 27 mg/m^2 on Day 8 of Cycle 1.[1] Treatment may be continued until disease progression or until unacceptable toxicity occurs.[1]

KYPROLIS may be administered through Cycle 18. Treatment with lenalidomide and dexamethasone may continue thereafter. From Cycle 13, the day 8 and 9 doses of KYPROLIS are omitted.[1]

As a Monotherapy

Physicians have two options for dosing and administration of KYPROLIS as a single agent:

- KYPROLIS can be administered intravenously as a 30-minute infusion on two consecutive days, each week for three weeks followed by a 12-day rest period.[1] Each 28-day period is considered one treatment cycle.[1] The recommended starting dose of KYPROLIS is 20 mg/m2 in Cycle 1 on Days 1 and 2.[1] If tolerated, dosing should be escalated to a target dose of 56 mg/m^2 on Day 8 of Cycle 1.[1]
- KYPROLIS can be administered intravenously as a 10-minute infusion on two consecutive days, each week for three weeks followed by a 12-day rest period.[1] Each 28-day period is considered one treatment cycle.[1] The recommended starting dose of KYPROLIS is 20 mg/m^2 in Cycle 1 on Days 1 and 2.[1] If tolerated, dosing should be escalated to a target dose of 27 mg/m^2 on Day 8 of Cycle 1.[1] Treatment may be continued until disease progression or until unacceptable toxicity occurs.[1]

IMPORTANT SAFETY INFORMATION REGARDING KYPROLIS® (CARFILZOMIB) FOR INJECTION

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. Some events occurred in patients with normal baseline ventricular function. Death due to cardiac arrest has occurred within one day of KYPROLIS administration.
- Monitor patients for clinical signs or symptoms of cardiac failure or cardiac ischemia. Evaluate promptly if cardiac toxicity is suspected. Withhold KYPROLIS for Grade 3 or 4 cardiac adverse events until recovery, and consider whether to restart KYPROLIS at 1 dose level reduction based on a benefit/risk assessment.
- While 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, conduction abnormalities, angina, or arrhythmias may be at greater risk for cardiac complications and should have a comprehensive medical assessment (including blood pressure and fluid management) prior to starting treatment with KYPROLIS and remain under close follow-up.

Acute Renal Failure

- Cases of acute renal failure and renal insufficiency adverse events (including 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. 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 for patients being treated with the combination of KYPROLIS with dexamethasone or with lenalidomide plus dexamethasone. The thromboprophylaxis regimen should be based on an assessment of the patient's underlying risks.

- Patients using oral contraceptives or a hormonal method of contraception associated with a risk of thrombosis should consider an alternative method of effective contraception during treatment with KYPROLIS in combination with dexamethasone or lenalidomide plus dexamethasone.

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 regardless of baseline values. Reduce or withhold dose as appropriate.

Thrombotic Microangiopathy

- Cases of thrombotic microangiopathy, including thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (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. 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. Males of reproductive potential should be advised to avoid fathering a child while being treated with KYPROLIS. If this drug is used during pregnancy, or if pregnancy occurs while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Adverse Reactions

- The most common adverse events occurring in at least 20% of patients treated with KYPROLIS in the combination therapy trials: anemia, cough, diarrhea, dyspnea, fatigue, hypokalemia, insomnia, muscle spasm, neutropenia, pyrexia, thrombocytopenia, upper respiratory tract infection.

- The most common adverse events occurring in at least 20% of patients treated with KYPROLIS in monotherapy trials: anemia, cough, dyspnea, diarrhea, edema peripheral, fatigue, headache, nausea, pyrexia, thrombocytopenia.

Please see full Prescribing Information at www.kyprolis.com.

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

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FORWARD LOOKING STATEMENTS

This fact sheet contains forward-looking statements that are based on the current expectations and beliefs of Amgen Inc. and its subsidiaries (Amgen) and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Amgen Inc., including Amgen Inc.'s most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen Inc.'s most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to Amgen's business. Unless otherwise noted, Amgen is providing this information as of Jan. 21, 2016, and expressly disclaims any duty to update information contained in this fact sheet.

No forward-looking statement can be guaranteed and actual results may differ materially from those Amgen projects. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly, or sometimes, even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for Amgen and its partners to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and Amgen expects similar variability in the future. Amgen develops product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as Amgen may have believed at the time of entering into such relationship. Also, Amgen or others could identify safety, side effects or manufacturing problems with Amgen's products after they are on the market. Amgen's business may be impacted by government investigations, litigation and product liability claims. If Amgen fails to meet the compliance obligations in the corporate integrity agreement between Amgen and the U.S. government, Amgen could become subject to significant sanctions. Amgen depends on third parties for a significant portion of its manufacturing capacity for the supply of certain of its current and future products and limits on supply may constrain sales of certain of its current products and product candidate development.

In addition, sales of Amgen's products (including products of Amgen's wholly-owned subsidiaries) are affected by the reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government and others' regulations and reimbursement policies may affect the development, usage and pricing of Amgen's products. In addition, Amgen competes with other companies with respect to some of its marketed products as well as for the discovery and development of new products. Amgen believes that some of its newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Amgen's products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with its products. In addition, while Amgen and its partners routinely obtain patents for their products and technology, the protection of Amgen's products offered by patents and patent applications may be challenged, invalidated or circumvented by its competitors and there can be no guarantee of Amgen's or its partners' ability to obtain or maintain patent protection for Amgen's products or product candidates. Amgen cannot guarantee that it will be able to produce commercially successful products or maintain the commercial success of its existing products. Amgen's stock price may be affected by actual or perceived market opportunity, competitive position and success or failure of its products or product candidates. Further, the discovery of significant problems with a product similar to one of Amgen's products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on Amgen's business and results of operations. Amgen's efforts to integrate the operations of companies it has acquired may not be successful. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our ongoing restructuring plan. Our business performance could affect or limit the ability of Amgen's Board of Directors to declare a dividend or their ability to pay a dividend or repurchase Amgen common stock.

References

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