A QUICK START GUIDE

WHICH KYPROLIS® REGIMEN

IS RIGHT FOR MY PATIENT WITH RELAPSED MULTIPLE MYELOMA?

KYPROLIS® is offered in 3 single-dose vial sizes: 10 mg, 30 mg, and 60 mg.[1]

INDICATION

- KYPROLIS® (carfilzomib) is indicated in combination with dexamethasone or with lenalidomide plus dexamethasone or with daratumumab and dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.

IMPORTANT SAFETY INFORMATION FOR KYPROLIS

Cardiac Toxicities

- New onset or worsening of pre-existing cardiac failure (e.g., congestive heart failure, pulmonary edema, decreased ejection fraction), 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 administration.
- Monitor patients for signs or symptoms of cardiac failure or ischemia. Evaluate promptly if cardiac toxicity is suspected. Withhold KYPROLIS for Grade 3 or 4 cardiac adverse reactions until recovery, and consider whether to restart at 1 dose level reduction based on a benefit/risk assessment.

Kyprolis® (carfilzomib) for Injection

Please see additional Important Safety Information throughout.

DKd ONCE WEEKLY

Patients that may benefit from DKd:

- Refractory to, or progressed on, lenalidomide
- Need a powerful triplet
- High-risk cytogenetics*
- Want a once-weekly dosing option

Key clinical trial information

Phase 3 DKd vs Kd study (CANDOR) design (N = 466)[1,2]

- Randomized 2:1, open-label, multicenter study in patients with RRMM[1]
- KYPROLIS® dosing: DKd 56 mg/m^2 twice weekly vs Kd 56 mg/m^2 twice-weekly for 28-day cycles until disease progression or unacceptable toxicity[1]
- Eligible patients had 1 to 3 prior lines of therapy[1,2,†]
  - Median prior lines of therapy: 2
  - Median age (min, max): 64 (29-84)
  - ECOG PS scores of 0-2: 99%

Prior therapies (N = 466)[1,2,‡]

- Bortezomib: 90%
- Lenalidomide: 42%
- Refractory to lenalidomide: 33%

Study endpoints[2,3]

- Primary: PFS
- Select secondary: ORR, CR, MRD-negative CR at 12 months, OS, and safety[§]

Dosing[1,4,5]

DKd 70 mg/m^2 | **2nd-generation PI + mAb + dex**
DKd once weekly**

Infusion time
30 minutes

KYPROLIS® priming dose
20 mg/m^2 on Day 1 of Cycle 1 to evaluate tolerability

Target KYPROLIS® therapeutic dose
70 mg/m^2 starting Day 8 of Cycle 1

Treatment schedule

- Administer KYPROLIS® 70 mg/m^2 1 day each week for 3 weeks
- Follow with a 13-day rest period, as part of a 28-day treatment cycle
- Continue until disease progression or unacceptable toxicity occurs

Calculating the priming & therapeutic dose[1]

Patient's body surface area (BSA; m^2) **x dose** (mg/m^2)

Examples:

Calculate the correct DKd once-weekly mg/m^2 dose for a patient with a BSA of 1.8 m^2

Priming dose: 1.8 m^2 x 20 mg/m^2 = 36 mg

Therapeutic dose: 1.8 m^2 x 70 mg/m^2 = 126 mg

In patients with a BSA > 2.2 m^2, calculate the dose based upon a BSA of 2.2 m^2.

- DKd also offers a twice-weekly, 56-mg/m^2 dosing option with a 20-mg/m^2 priming dose[1,††]

Refer to Darzalex® (daratumumab) and dexamethasone Prescribing Information for additional dosage information on that product.

Please refer to Important Hydration Information at the end.

Key efficacy

Primary endpoint: *Median progression-free survival*[1,2]
With a median follow-up of nearly 17 months in the DKd arm, the majority of patients on DKd had not progressed, so median PFS was not yet reached, vs 15.8 months with Kd (HR = 0.63; 95% CI: 0.46-0.85; *P* = 0.0014, one-sided)

Select secondary endpoint: *Overall response rate*[1,2]
84% with DKd vs 75% with Kd
(*P* = 0.0040, one-sided)[§]

*High-risk defined as a patient with cytogenetic abnormalities that are considered high-risk, including t(4; 14), t(14; 16), or del17p.[2]
†Subjects with > 3 prior regimens was 0 in the DKd arm and 1 in the Kd arm.[1]
‡Prior treatment subgroups were balanced across treatment arms.[1,2]
§ORR was defined as proportion of patients with PR or better.[2]
**Once-weekly dosing was demonstrated in the EQUULEUS study, a phase 1b, open-label, multicohort study (N = 85) which evaluated the combination of once-weekly KYPROLIS® with IV daratumumab and dexamethasone in patients with relapsed or refractory multiple myeloma who received 1 to 3 prior lines of therapy. KYPROLIS® was administered weekly on Days 1, 8, and 15 of each 28-day cycle at a dose of 70 mg/m^2 with a priming dose of 20 mg/m^2 on Day 1 of Cycle 1. Safety and tolerability of DKd were evaluated as primary endpoints. Results from the EQUULEUS study set a precedent of DKd regimen safety and efficacy for the phase 3 CANDOR study and provided the rationale for the once-weekly dosing of DKd.[1,6]
††Demonstrated in the phase 3 CANDOR study.[1,2]

DKd = KYPROLIS®+Darzalex® (daratumumab) and dexamethasone; Kd = KYPROLIS®+dexamethasone; RRMM = relapsed or refractory multiple myeloma; ECOG PS = Eastern Cooperative Oncology Group Performance Status; PFS = progression-free survival; ORR = overall response rate; CR = complete response; MRD = minimal residual disease; OS = overall survival; PI = proteasome inhibitor; mAb = monoclonal antibody; dex = dexamethasone; HR = hazard ratio; CI = confidence interval; PR = partial response; IV = intravenous.

IMPORTANT SAFETY INFORMATION FOR KYPROLIS

Cardiac Toxicities (cont'd)

- 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.

Please see additional Important Safety Information throughout.

Kyprolis® (carfilzomib) for Injection

KRd TWICE WEEKLY

Patients that may benefit from KRd:

- Eligible for lenalidomide
- Want a powerful triplet therapy at first relapse
- Standard-risk or high-risk cytogenetics*

Key clinical trial information

Phase 3 KRd vs Rd study (ASPIRE) design (N = 792)[1]

- Randomized 1:1, open-label superiority study in patients with RRMM[1]
- KYPROLIS® dosing: KRd 27 mg/m^2 twice weekly vs Rd 25 mg for 28-day cycles[1]
- Eligible patients had 1 to 3 prior lines of therapy[1,7,†]
  - Median prior lines of therapy: 2
  - Median age (min, max): 64 (31-91)
  - ECOG PS scores of 0-2: 100%

Prior therapies (N = 792)[7]

- Bortezomib: 66%
- Lenalidomide: 20%

Study endpoints[7]

- Primary: PFS
- Select secondary: OS

Dosing[1,4,8]

KRd | 27 mg/m^2

2nd-generation PI + IMiD + dex
KRd twice weekly

Infusion time
10 minutes

KYPROLIS® priming dose
20 mg/m^2 on Days 1 and 2 of Cycle 1 to evaluate tolerability

Target KYPROLIS® therapeutic dose
27 mg/m^2 starting Day 8 of Cycle 1

Treatment schedule

- Administer KYPROLIS® 27 mg/m^2 2 consecutive days each week for 3 weeks
- Follow with a 12-day rest period, as part of a 28-day treatment cycle
- From Cycle 13, omit Day 8 and 9 doses
- Discontinue KYPROLIS® after Cycle 18

Calculating the priming & therapeutic dose[1]

Patient's body surface area (BSA; m^2) **x dose** (mg/m^2)

Examples:

Calculate the correct KRd twice-weekly mg/m^2 dose for a patient with a BSA of 1.8 m^2

Priming dose: 1.8 m^2 x 20 mg/m^2 = 36 mg

Therapeutic dose: 1.8 m^2 x 27 mg/m^2 = 49 mg

In patients with a BSA > 2.2 m^2, calculate the dose based upon a BSA of 2.2 m^2.

Please refer to Important Hydration Information at the end.

Key efficacy

Primary endpoint: *Median progression-free survival*[1,7]
26.3 months KRd vs 17.6 months Rd
(HR = 0.69; 95% CI: 0.57-0.83; *P* = 0.0001, two-sided)

Secondary endpoint: *Median overall survival*[1,7]
48.3 months KRd vs 40.4 months Rd
(HR = 0.79; 95% CI: 0.67-0.95; *P* = 0.0091, two-sided)

*Standard risk is defined as cytogenetic abnormalities absent or that are not considered high risk (trisomies, t(11;14), t(6;14)), and/or R-ISS stage I. High risk is defined as relapse within 12 months from transplant or progression within the first year of diagnosis, high cytogenetic risk (from FISH) with chromosomal abnormalities (ie, t(14;16), t(14;20), del(17p)), R-ISS III, and/or high risk gene expression profiling.[9,10]

†Including 2 patients with 4 prior regimens.[1]

KRd = KYPROLIS®+lenalidomide and dexamethasone; Rd = lenalidomide+dexamethasone; IMiD = immunomodulatory drug; R-ISS = Revised International Staging System; FISH = fluorescence in situ hybridization.

IMPORTANT SAFETY INFORMATION FOR KYPROLIS

Cardiac Toxicities (cont'd)

- For 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 prior to starting treatment with KYPROLIS and remain under close follow-up with fluid management.

Please see additional Important Safety Information throughout.

Kyprolis® (carfilzomib) for Injection

Kd TWICE WEEKLY

Patients that may benefit from Kd twice weekly:

- Not eligible for lenalidomide
- Better suited for doublet therapy
- Appropriate for those exposed to a PI or naïve in prior therapy
- Standard-risk or high-risk cytogenetics*
- Have concerns about peripheral neuropathy

Key clinical trial information

Phase 3 Kd vs Vd study (ENDEAVOR) design (N = 929)[1]

- Randomized 1:1, open-label superiority study in patients with RRMM[1,11]
- KYPROLIS® dosing: Kd 56 mg/m^2 twice weekly vs Vd 1.3 mg/m^2 twice weekly for 28-day cycles for Kd and 21-day cycles for Vd until disease progression or unacceptable toxicity[1]
- Eligible patients had 1 to 3 prior lines of therapy[1,11,†]
  - Median prior lines of therapy: 2
  - Median age (min, max): 65 (30-89)
  - ECOG PS scores of 0-2: 100%

Prior therapies (N = 929)[1]

- Bortezomib: 54%
- Lenalidomide: 38%

Study endpoints[11]

- Primary: PFS
- Select secondary: OS

Dosing[1,4]

Kd | 56 mg/m^2

2nd-generation PI doublet
Kd twice weekly

Infusion time
30 minutes

KYPROLIS® priming dose
20 mg/m^2 on Days 1 and 2 of Cycle 1 to evaluate tolerability

Target KYPROLIS® therapeutic dose
56 mg/m^2 starting Day 8 of Cycle 1

Treatment schedule

- Administer KYPROLIS® 56 mg/m^2 2 consecutive days each week for 3 weeks
- Follow with a 12-day rest period, as part of a 28-day treatment cycle
- Continue until disease progression or unacceptable toxicity occurs

Calculating the priming & therapeutic dose[1]

Patient's body surface area (BSA; m^2) **x dose** (mg/m^2)

Examples:

Calculate the correct Kd twice-weekly mg/m^2 dose for a patient with a BSA of 1.8 m^2

Priming dose: 1.8 m^2 x 20 mg/m^2 = 36 mg

Therapeutic dose: 1.8 m^2 x 56 mg/m^2 = 101 mg

In patients with a BSA > 2.2 m^2, calculate the dose based upon a BSA of 2.2 m^2.

Please refer to Important Hydration Information at the end.

Key efficacy

Primary endpoint: *Median progression-free survival*[1,11]
18.7 months Kd vs 9.4 months Vd
(HR = 0.53; 95% CI: 0.44-0.65; *P* < 0.0001, one-sided)

Secondary endpoint: *Median overall survival*[1,11]
47.6 months Kd vs 40.0 months Vd
(HR = 0.79; 95% CI: 0.65-0.96; *P* = 0.01, one-sided)

*Standard risk is defined as cytogenetic abnormalities absent or that are not considered high risk (trisomies, t(11;14), t(6;14)), and/or R-ISS stage I. High risk is defined as relapse within 12 months from transplant or progression within the first year of diagnosis, high cytogenetic risk (from FISH) with chromosomal abnormalities (ie, t(14;16), t(14;20), del(17p)), R-ISS III, and/or high risk gene expression profiling.[9,10]

†Subjects with 4 prior regimens was 0 in the Kd arm and 2 in the Vd arm.[1]

Vd = bortezomib+dexamethasone.

IMPORTANT SAFETY INFORMATION FOR KYPROLIS

Acute Renal Failure

- Cases of acute renal failure, including some fatal renal failure events, and renal insufficiency (including renal failure) have occurred. 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.

Please see additional Important Safety Information throughout.

Kyprolis® (carfilzomib) for Injection

Kd ONCE WEEKLY

Patients that may benefit from Kd once weekly:

- Not eligible for lenalidomide
- Better suited for doublet therapy
- Standard-risk or high-risk cytogenetics*
- Want a once-weekly dosing option

Key clinical trial information

Phase 3 Kd 70 mg/m² once weekly vs Kd 27 mg/m² twice weekly study (A.R.R.O.W.) design (N = 478)[1,12]

- Randomized 1:1, multicenter, open-label study in patients with RRMM[12]
- KYPROLIS® dosing: Kd 70 mg/m² once weekly vs Kd 27 mg/m² twice weekly for 28-day cycles until disease progression or unacceptable toxicity[1]
- Eligible patients had 2 to 3 prior lines of therapy[1,†]
  - 2 prior lines of therapy: Kd 70 (48%) vs Kd 27 (53%)
  - Median age (min, max): 66 (35-85)
  - ECOG PS scores of 0-2: 100%
  - Refractory to most recent prior therapy

Prior therapies (N = 478)[1]

- Bortezomib: 99%
- Lenalidomide: 84%

Study endpoint[12]

- Primary: PFS

Dosing[1,4]

Kd 70 mg/m²

2nd-generation PI doublet
Kd once weekly

Infusion time
30 minutes

KYPROLIS® priming dose
20 mg/m² on Day 1 of Cycle 1 to evaluate tolerability

Target KYPROLIS® therapeutic dose
70 mg/m² starting Day 8 of Cycle 1

Treatment schedule

- Administer KYPROLIS® 70 mg/m² 1 day each week for 3 weeks
- Follow with a 13-day rest period, as part of a 28-day treatment cycle
- For Cycles 10 and beyond, dexamethasone is not given on Day 22
- Continue until disease progression or unacceptable toxicity occurs

Calculating the priming & therapeutic dose[1]

Patient's body surface area (BSA; m²) **x dose** (mg/m²)

Examples:

Calculate the correct Kd once-weekly mg/m² dose for a patient with a BSA of 1.8 m²

Priming dose: 1.8 m² x 20 mg/m² = 36 mg

Therapeutic dose: 1.8 m² x 70 mg/m² = 126 mg

In patients with a BSA > 2.2 m², calculate the dose based upon a BSA of 2.2 m².

Please refer to Important Hydration Information at the end.

Key efficacy

Primary endpoint: *Median progression-free survival[1,12]*
11.2 months Kd 70 mg/m² once weekly vs 7.6 months Kd 27 mg/m² twice weekly
(HR = 0.69; 95% CI: 0.54-0.88; *P* = 0.0014, one-sided)
Kd 27 mg/m² is not an FDA-approved dose for KYPROLIS®.[1]

*Standard risk is defined as cytogenetic abnormalities absent or that are not considered high risk (trisomies, t(11;14), t(6;14)), and/or R-ISS stage I. High risk is defined as relapse within 12 months from transplant or progression within the first year of diagnosis, high cytogenetic risk (from FISH) with chromosomal abnormalities (ie, t(14;16), t(14;20), del(17p)), R-ISS III, and/or high risk gene expression profiling.[9,10]

†Subjects with > 3 prior regimens was 0 in the Kd 70 mg/m² once weekly arm and 1 in the Kd 27 mg/m² twice weekly arm.[1]

IMPORTANT SAFETY INFORMATION FOR KYPROLIS

Tumor Lysis Syndrome

- Cases of Tumor Lysis Syndrome (TLS), including fatal outcomes, have occurred. Patients with 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, and withhold until resolved.

Please see additional Important Safety Information throughout.

Kyprolis® (carfilzomib) for Injection

Kyprolis® (carfilzomib) for Injection

IMPORTANT SAFETY INFORMATION FOR KYPROLIS (cont'd)

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. Some events have been fatal. In the event of drug-induced pulmonary toxicity, discontinue KYPROLIS.

Pulmonary Hypertension

- Pulmonary arterial hypertension (PAH) was reported. 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 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 based on a benefit/risk assessment.

Hypertension

- Hypertension, including hypertensive crisis and hypertensive emergency, has been observed, some fatal. Control hypertension prior to starting KYPROLIS. Monitor blood pressure regularly in all patients. If hypertension cannot be adequately controlled, withhold KYPROLIS and evaluate. Consider whether to restart based on a benefit/risk assessment.

Venous Thrombosis

- Venous thromboembolic events (including deep venous thrombosis and pulmonary embolism) have been observed. Provide thromboprophylaxis for patients being treated with the combination of KYPROLIS with dexamethasone or with lenalidomide plus dexamethasone or with daratumumab and dexamethasone. The thromboprophylaxis regimen should be based on an assessment of the patient's underlying risks.
- For patients using hormonal contraception associated with a risk of thrombosis, consider an alternative method of effective contraception during treatment.

Infusion-Related Reactions

- Infusion-related reactions, including life-threatening reactions, have occurred. Signs and symptoms include fever, chills, arthralgia, myalgia, facial flushing, facial edema, laryngeal 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. Premedicate with dexamethasone to reduce the incidence and severity of infusion-related reactions.

Hemorrhage

- Fatal or serious cases of hemorrhage have been reported. Hemorrhagic events have included gastrointestinal, pulmonary, and intracranial hemorrhage and epistaxis. Promptly evaluate signs and symptoms of blood loss. Reduce or withhold dose as appropriate.

Thrombocytopenia

- KYPROLIS causes thrombocytopenia with recovery to baseline platelet count usually by the start of the next cycle. Monitor platelet counts frequently during treatment. Reduce or withhold dose as appropriate.

Hepatic Toxicity and Hepatic Failure

- Cases of hepatic failure, including fatal cases, have occurred. 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. Monitor for signs and symptoms of TTP/HUS. Discontinue if diagnosis is suspected. If the diagnosis of TTP/HUS is excluded, KYPROLIS may be restarted. The safety of reinitiating KYPROLIS is not known.

Please see additional Important Safety Information on the next page.

IMPORTANT SAFETY INFORMATION FOR KYPROLIS (cont'd)

Posterior Reversible Encephalopathy Syndrome (PRES)

- Cases of PRES have occurred in patients receiving KYPROLIS. If PRES is suspected, discontinue and evaluate with appropriate imaging. The safety of reinitiating KYPROLIS is not known.

Progressive Multifocal Leukoencephalopathy (PML)

- Cases of PML, including fatal cases, have occurred. In addition to KYPROLIS, other contributary factors may include prior or concurrent use of immunosuppressive therapy. Consider PML in any patient with new onset of or changes in pre-existing neurological signs or symptoms. If PML is suspected, discontinue and initiate evaluation for PML including neurology consultation.

Increased Fatal and Serious Toxicities in Combination with Melphalan and Prednisone in Newly Diagnosed Transplant-ineligible Patients

- In a clinical trial of transplant-ineligible patients with newly diagnosed multiple myeloma comparing KYPROLIS, melphalan, and prednisone (KMP) vs bortezomib, melphalan, and prednisone (VMP), a higher incidence of serious and fatal adverse reactions was observed in patients in the KMP arm. KMP is not indicated for transplant-ineligible patients with newly diagnosed multiple myeloma.

Embryo-fetal Toxicity

- KYPROLIS can cause fetal harm when administered to a pregnant woman.
- Advise pregnant women of the potential risk to a fetus. Females of reproductive potential should use effective contraception during treatment with KYPROLIS and for 6 months following the final dose. Males of reproductive potential should use effective contraception during treatment with KYPROLIS and for 3 months following the final dose.

Adverse Reactions

- The most common adverse reactions in the combination therapy trials: anemia, diarrhea, fatigue, hypertension, pyrexia, upper respiratory tract infection, thrombocytopenia, cough, dyspnea, and insomnia.

Please click here for the full Prescribing Information.

REFERENCES: 1. KYPROLIS® (carfilzomib) prescribing information, Onyx Pharmaceuticals Inc., an Amgen Inc. subsidiary. **2.** Dimopoulos M, Quach H, Mateos MV, et al. Carfilzomib, dexamethasone, and daratumumab versus carfilzomib and dexamethasone for patients with relapsed or refractory multiple myeloma (CANDOR): results from a randomised, multicentre, open-label, phase 3 study. *Lancet.* 2020;396:186-197. **3.** Dimopoulos M, Quach H, Mateos MV, et al. Carfilzomib, dexamethasone, and daratumumab versus carfilzomib and dexamethasone for patients with relapsed or refractory multiple myeloma (CANDOR): results from a randomised, multicentre, open-label, phase 3 study [supplementary appendix]. *Lancet.* 2020;396:186-197. **4.** Orlowski RZ, Kuhn DJ. Proteasome inhibitors in cancer therapy: lessons from the first decade. *Clin Cancer Res.* 2008;14:1649-1657. **5.** DARZALEX® (daratumumab) prescribing information, Janssen Biotech Inc. **6.** Chari A, Martinez-Lopez J, Mateos M, et al. Daratumumab plus carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma. *Blood.* 2019;134:421-431. **7.** Stewart AK, Rajkumar SV, Dimopoulos MA, et al. Carfilzomib, lenalidomide, and dexamethasone for relapsed multiple myeloma. *N Engl J Med.* 2015;372:142-152. **8.** REVLIMID® (lenalidomide) prescribing information, Celgene Corporation. **9.** Dingli D, Ailawadhi S, Bergsagel PL, et al. Therapy for relapsed multiple myeloma: guidelines from the Mayo Stratification for Myeloma and Risk-Adapted Therapy. *Mayo Clin Proc.* 2017;92:578-598. **10.** Palumbo A, Avet-Loiseau H, Oliva S, et al. Revised International Staging System for multiple myeloma: a report from International Myeloma Working Group. *J Clin Oncol.* 2015;33:2863-2869. **11.** Dimopoulos MA, Moreau P, Palumbo A, et al. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study. *Lancet Oncol.* 2016;17:27-38. **12.** Moreau P, Mateos MV, Berenson JR, et al. Once weekly versus twice weekly carfilzomib dosing in patients with relapsed and refractory multiple myeloma (A.R.R.O.W.): interim analysis results of a randomized, phase 3 study. *Lancet Oncol.* 2018;19:953-964.

Kyprolis® (carfilzomib) for Injection

MANAGE HYDRATION THROUGHOUT TREATMENT

Adequate hydration is required prior to dosing in Cycle 1, especially in patients at high risk of tumor lysis syndrome or renal toxicity[1]

- Consider hydration with both oral fluids (30 mL per kg at least 48 hours before Cycle 1, Day 1) and IV fluids (250 mL to 500 mL of appropriate IV fluid prior to each dose in Cycle 1)
- If needed, give an additional 250 mL to 500 mL of IV fluids following KYPROLIS® administration
- Continue oral and/or IV hydration, as needed, in subsequent cycles
- Monitor patients for evidence of volume overload and adjust hydration to individual patient needs, especially in patients with or at risk for cardiac failure

Please see the full Prescribing Information for KYPROLIS® for dosing and administration.

Please see Important Safety Information throughout.

For additional information, contact your KYPROLIS® Sales Rep or visit www.kyprolis-hcp.com.

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Oncology

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