PHYSICIAN OFFICE CODING AND BILLING INFORMATION SHEET FOR KYPROLIS® (CARFILZOMIB) FOR INJECTION

INDICATIONS

- KYPROLIS® (carfilzomib) is indicated in combination with dexamethasone, or with lenalidomide plus dexamethasone, or with daratumumab plus dexamethasone, or with daratumumab plus hyaluronidase-fihj plus dexamethasone, or with isatuximab plus dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.
- KYPROLIS® is indicated as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more 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.
- 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.
- 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 for KYPROLIS on pages 6-7.

Kyprolis® (carfilzomib) for injection

PHYSICIAN OFFICE CODING AND BILLING INFORMATION SHEET FOR KYPROLIS® (CARFILZOMIB) FOR INJECTION

Item	Coding Information (HCPCS/CPT/ICD)	Notes
KYPROLIS	J9047, injection, carfilzomib, 1 mg [1]	**KYPROLIS VIALS:** KYPROLIS is supplied in single-dose vials containing 60 mg, 30 mg, or 10 mg of carfilzomib. [3] The NDC numbers for KYPROLIS, in the 11-digit format, are as follows[3]: - 60-mg vial: 76075-0101-01 - 30-mg vial: 76075-0102-01 - 10-mg vial: 76075-0103-01 **MEDICARE MUE FOR KYPROLIS[3-6]:** Under Medicare fee-for-service, J9047 has a Medically Unlikely Edit (MUE). Based on the approved dosing range, Medicare will deny KYPROLIS claims billed for more than 160 units per date of service. - For example, at the BSA of up to 2.2 m^2, the calculated dose for Kd70 is up to 154 mg **JW MODIFIER[7]:** For unused drug from single-use vials, some payers (eg, Medicare fee-for-service) require providers to report the JW modifier on a claim and to document the discarded amount in the patient's medical record.
Administration	96413, chemotherapy administration, IV infusion technique; up to 1 hour, single or initial substance/drug [2] OR 96409, chemotherapy administration, intravenous push technique (including infusions less than 15 minutes), single or initial substance/drug [2]	KYPROLIS® can be administered as a 10-minute or 30-minute IV infusion, depending on the selected regimen[1]: - At the priming dose of 20 mg/m^2 and at the therapeutic dose of 70 mg/m^2 once-weekly (DKd or Kd): KYPROLIS® is administered as a 30-minute IV infusion. - At the priming dose of 20 mg/m^2 and at the therapeutic dose of 56 mg/m^2 twice-weekly (DKd, Kd, or K): KYPROLIS® is administered as a 30-minute IV infusion. - At the priming dose of 20 mg/m^2 and at the therapeutic dose of 27 mg/m^2 twice-weekly (KRd or K): KYPROLIS® is administered as a 10-minute IV infusion.
Office visit	Relevant Evaluation and Management (E&M) code *,†	See payer guidelines.
Diagnosis/ Condition	Appropriate diagnosis code(s) for patient condition	**ICD-10-CM Example:** C90.00, multiple myeloma not having achieved remission C90.02, multiple myeloma in relapse [8]

* Bill relevant E&M code only if a separately identifiable E&M service is performed. Document accordingly.

† Some payers, including Medicare, will not allow a Level 1 office visit to be billed with an injection/infusion code for the same date of service, and only allow for other levels when Modifier 25 is billed.

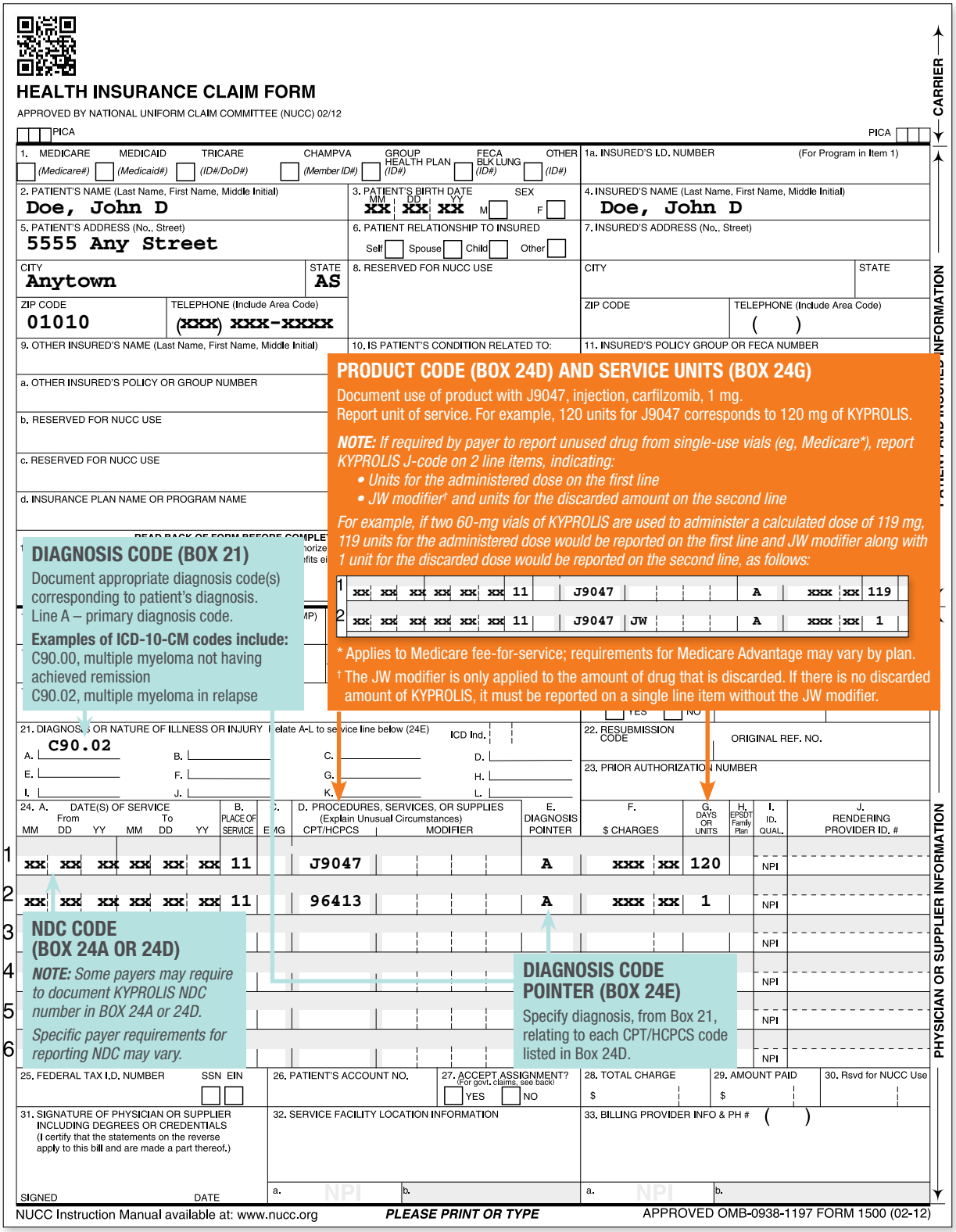
The information provided in this Coding and Billing Information document is of a general nature and for informational purposes only and is not intended to be a comprehensive list nor instructive. Coding and coverage policies change periodically and often without warning. The responsibility to determine coverage and reimbursement parameters, and appropriate coding for a particular patient and/or procedure, is always the responsibility of the provider or physician. Healthcare providers should consult the payer or Medicare contractor to determine which CPT® code(s) are most appropriate for administration of Kyprolis®. The codes provided here are not an exhaustive list of drug administration services. Please refer to the CPT® manual for a complete list of drug administration codes. The information provided in this section should in no way be considered a guarantee of coverage or reimbursement for any product or service.

BSA = body surface area; IV = intravenous; Kd = KYPROLIS® (carfilzomib) and dexamethasone; KRd = KYPROLIS®+lenalidomide and dexamethasone; DKd = KYPROLIS®+daratumumab and dexamethasone

Please see Important Safety Information for KYPROLIS on pages 6-7.

THE SAMPLE CMS 1500 FOR PHYSICIAN OFFICE — KYPROLIS AT 70 mg/m^2 OR 56 mg/m^2

Physician Office Administration of KYPROLIS at the Therapeutic Dose of 70 mg/m^2 or 56 mg/m^2



HEALTH INSURANCE CLAIM FORM

APPROVED BY NATIONAL UNIFORM CLAIM COMMITTEE (NUCC) 02/12

PICA

1. MEDICARE (Medicare#) MEDICAID (Medicaid#) TRICARE (ID#/DoD#) CHAMPVA (Member ID#) GROUP HEALTH PLAN (ID#) FECA BLK LUNG (ID#) OTHER (ID#)

1a. INSURED'S I.D. NUMBER (For Program in Item 1)

2. PATIENT'S NAME (Last Name, First Name, Middle Initial): Doe, John D

3. PATIENT'S BIRTH DATE MM DD YY: xx xx xx SEX M F

4. INSURED'S NAME (Last Name, First Name, Middle Initial): Doe, John D

5. PATIENT'S ADDRESS (No., Street): 5555 Any Street

6. PATIENT RELATIONSHIP TO INSURED: Self Spouse Child Other

7. INSURED'S ADDRESS (No., Street)

CITY: Anytown STATE: AS

8. RESERVED FOR NUCC USE

CITY STATE

ZIP CODE: 01010 TELEPHONE (Include Area Code): (xxx) xxx-xxxx

ZIP CODE TELEPHONE (Include Area Code): ( )

9. OTHER INSURED'S NAME (Last Name, First Name, Middle Initial)

10. IS PATIENT'S CONDITION RELATED TO:

11. INSURED'S POLICY GROUP OR FECA NUMBER

a. OTHER INSURED'S POLICY OR GROUP NUMBER

b. RESERVED FOR NUCC USE

c. RESERVED FOR NUCC USE

d. INSURANCE PLAN NAME OR PROGRAM NAME

PRODUCT CODE (BOX 24D) AND SERVICE UNITS (BOX 24G)

Document use of product with J9047, injection, carfilzomib, 1 mg.
Report unit of service. For example, 120 units for J9047 corresponds to 120 mg of KYPROLIS.

NOTE: *If required by payer to report unused drug from single-use vials (eg, Medicare*), report KYPROLIS J-code on 2 line items, indicating:*

- *Units for the administered dose on the first line*
- *JW modifier† and units for the discarded amount on the second line*

For example, if two 60-mg vials of KYPROLIS are used to administer a calculated dose of 119 mg, 119 units for the administered dose would be reported on the first line and JW modifier along with 1 unit for the discarded dose would be reported on the second line, as follows:

1	xx	xx	xx	xx	xx	xx	11		J9047			A	xxx	xx	119
2	xx	xx	xx	xx	xx	xx	11		J9047	JW		A	xxx	xx	1

* Applies to Medicare fee-for-service; requirements for Medicare Advantage may vary by plan.

† The JW modifier is only applied to the amount of drug that is discarded. If there is no discarded amount of KYPROLIS, it must be reported on a single line item without the JW modifier.

DIAGNOSIS CODE (BOX 21)

Document appropriate diagnosis code(s) corresponding to patient's diagnosis.
Line A – primary diagnosis code.

Examples of ICD-10-CM codes include:
C90.00, multiple myeloma not having achieved remission
C90.02, multiple myeloma in relapse

21. DIAGNOSIS OR NATURE OF ILLNESS OR INJURY Relate A-L to service line below (24E) ICD Ind.

A. C90.02 B. C. D.
E. F. G. H.
I. J. K. L.

22. RESUBMISSION CODE ORIGINAL REF. NO.

23. PRIOR AUTHORIZATION NUMBER

24. A. DATE(S) OF SERVICE From MM	DD	YY	To MM	DD	YY	B. PLACE OF SERVICE	C. EMG	D. PROCEDURES, SERVICES, OR SUPPLIES (Explain Unusual Circumstances) CPT/HCPCS	MODIFIER	E. DIAGNOSIS POINTER	F. $ CHARGES	G. DAYS OR UNITS	H. EPSDT Family Plan	I. ID. QUAL.	J. RENDERING PROVIDER ID. #
1 xx	xx	xx	xx	xx	xx	11		J9047		A	xxx	xx 120		NPI	
2 xx	xx	xx	xx	xx	xx	11		96413		A	xxx	xx 1		NPI	
3														NPI	
4														NPI	
5														NPI	
6														NPI	

NDC CODE (BOX 24A OR 24D)

NOTE: *Some payers may require to document KYPROLIS NDC number in BOX 24A or 24D.*

Specific payer requirements for reporting NDC may vary.

DIAGNOSIS CODE POINTER (BOX 24E)

Specify diagnosis, from Box 21, relating to each CPT/HCPCS code listed in Box 24D.

25. FEDERAL TAX I.D. NUMBER SSN EIN

26. PATIENT'S ACCOUNT NO.

27. ACCEPT ASSIGNMENT? (For govt. claims, see back) YES NO

28. TOTAL CHARGE $

29. AMOUNT PAID $

30. Rsvd for NUCC Use

31. SIGNATURE OF PHYSICIAN OR SUPPLIER INCLUDING DEGREES OR CREDENTIALS (I certify that the statements on the reverse apply to this bill and are made a part thereof.)

SIGNED DATE

32. SERVICE FACILITY LOCATION INFORMATION

a. NPI b.

33. BILLING PROVIDER INFO & PH # ( )

a. NPI b.

NUCC Instruction Manual available at: www.nucc.org **PLEASE PRINT OR TYPE** APPROVED OMB-0938-1197 FORM 1500 (02-12)

PATIENT AND INSURED INFORMATION

PHYSICIAN OR SUPPLIER INFORMATION

CARRIER

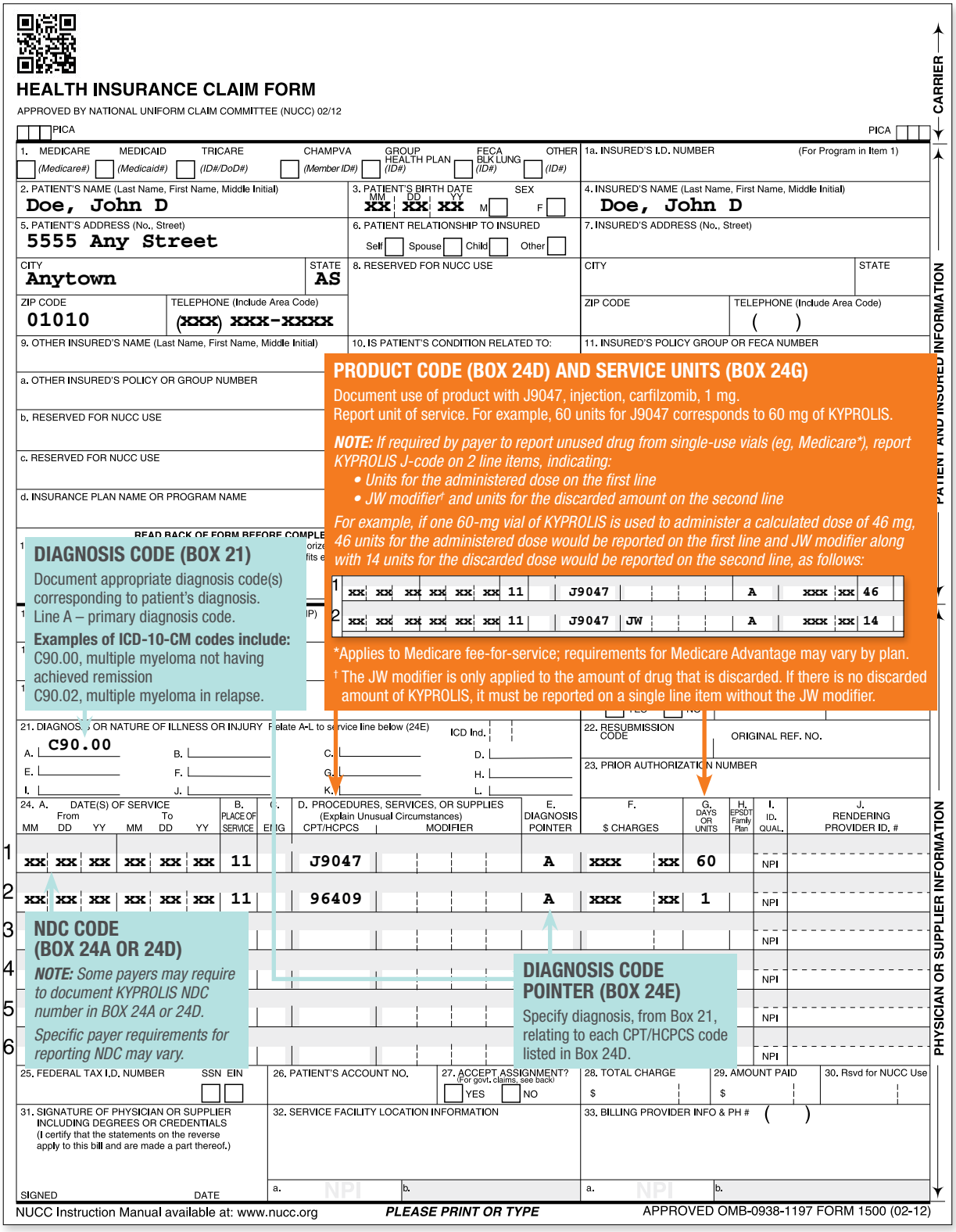
These sample forms are intended as a reference for coding and billing for product and associated services. They are not intended to be directive; the use of the recommended codes does not guarantee reimbursement. Healthcare providers may deem other codes or policies more appropriate and should select the coding options that most accurately reflect their internal system guidelines, payer requirements, practice patterns, and the services rendered. Healthcare providers are responsible for ensuring the accuracy and validity of all billing and claims for appropriate reimbursement.

Please see Important Safety Information for KYPROLIS on pages 6-7.

Kyprolis® (carfilzomib) for injection

THE SAMPLE CMS 1500 FOR PHYSICIAN OFFICE — KYPROLIS AT 27 mg/m^2

Physician Office Administration of KYPROLIS at the Therapeutic Dose of 27 mg/m^2



HEALTH INSURANCE CLAIM FORM

APPROVED BY NATIONAL UNIFORM CLAIM COMMITTEE (NUCC) 02/12

PICA

1. MEDICARE (Medicare#) MEDICAID (Medicaid#) TRICARE (ID#/DoD#) CHAMPVA (Member ID#) GROUP HEALTH PLAN (ID#) FECA BLK LUNG (ID#) OTHER (ID#)

1a. INSURED'S I.D. NUMBER (For Program in Item 1)

2. PATIENT'S NAME (Last Name, First Name, Middle Initial): Doe, John D

3. PATIENT'S BIRTH DATE MM DD YY: xx xx xx SEX M F

4. INSURED'S NAME (Last Name, First Name, Middle Initial): Doe, John D

5. PATIENT'S ADDRESS (No., Street): 5555 Any Street

6. PATIENT RELATIONSHIP TO INSURED: Self Spouse Child Other

7. INSURED'S ADDRESS (No., Street)

CITY: Anytown STATE: AS

8. RESERVED FOR NUCC USE

CITY STATE

ZIP CODE: 01010 TELEPHONE (Include Area Code): (xxx) xxx-xxxx

ZIP CODE TELEPHONE (Include Area Code): ( )

9. OTHER INSURED'S NAME (Last Name, First Name, Middle Initial)

10. IS PATIENT'S CONDITION RELATED TO:

11. INSURED'S POLICY GROUP OR FECA NUMBER

a. OTHER INSURED'S POLICY OR GROUP NUMBER

b. RESERVED FOR NUCC USE

c. RESERVED FOR NUCC USE

d. INSURANCE PLAN NAME OR PROGRAM NAME

READ BACK OF FORM BEFORE COMPLE

21. DIAGNOSIS OR NATURE OF ILLNESS OR INJURY Relate A-L to service line below (24E) ICD Ind.

A. C90.00 B. C. D.

E. F. G. H.

I. J. K. L.

22. RESUBMISSION CODE ORIGINAL REF. NO.

23. PRIOR AUTHORIZATION NUMBER

24. A. DATE(S) OF SERVICE From MM	DD	YY	To MM	DD	YY	B. PLACE OF SERVICE	C. EMG	D. PROCEDURES, SERVICES, OR SUPPLIES (Explain Unusual Circumstances) CPT/HCPCS	MODIFIER	E. DIAGNOSIS POINTER	F. $ CHARGES	G. DAYS OR UNITS	H. EPSDT Family Plan	I. ID. QUAL.	J. RENDERING PROVIDER ID. #
1	xx xx xx	xx xx xx	11		J9047		A	xxx xx	60		NPI	
2	xx xx xx	xx xx xx	11		96409		A	xxx xx	1		NPI	
3											NPI	
4											NPI	
5											NPI	
6											NPI	

25. FEDERAL TAX I.D. NUMBER SSN EIN

26. PATIENT'S ACCOUNT NO.

27. ACCEPT ASSIGNMENT? (For govt. claims, see back) YES NO

28. TOTAL CHARGE $

29. AMOUNT PAID $

30. Rsvd for NUCC Use

31. SIGNATURE OF PHYSICIAN OR SUPPLIER INCLUDING DEGREES OR CREDENTIALS (I certify that the statements on the reverse apply to this bill and are made a part thereof.)

SIGNED DATE

32. SERVICE FACILITY LOCATION INFORMATION

a. NPI b.

33. BILLING PROVIDER INFO & PH # ( )

a. NPI b.

NUCC Instruction Manual available at: www.nucc.org **PLEASE PRINT OR TYPE** APPROVED OMB-0938-1197 FORM 1500 (02-12)

CARRIER

PATIENT AND INSURED INFORMATION

PHYSICIAN OR SUPPLIER INFORMATION

PRODUCT CODE (BOX 24D) AND SERVICE UNITS (BOX 24G)

Document use of product with J9047, injection, carfilzomib, 1 mg.
Report unit of service. For example, 60 units for J9047 corresponds to 60 mg of KYPROLIS.

NOTE: *If required by payer to report unused drug from single-use vials (eg, Medicare*), report KYPROLIS J-code on 2 line items, indicating:*

- *Units for the administered dose on the first line*
- *JW modifier† and units for the discarded amount on the second line*

For example, if one 60-mg vial of KYPROLIS is used to administer a calculated dose of 46 mg, 46 units for the administered dose would be reported on the first line and JW modifier along with 14 units for the discarded dose would be reported on the second line, as follows:

1	xx	xx	xx	xx	xx	xx	11		J9047			A	xxx	xx	46
2	xx	xx	xx	xx	xx	xx	11		J9047	JW		A	xxx	xx	14

*Applies to Medicare fee-for-service; requirements for Medicare Advantage may vary by plan.

† The JW modifier is only applied to the amount of drug that is discarded. If there is no discarded amount of KYPROLIS, it must be reported on a single line item without the JW modifier.

DIAGNOSIS CODE (BOX 21)

Document appropriate diagnosis code(s) corresponding to patient's diagnosis.
Line A – primary diagnosis code.

Examples of ICD-10-CM codes include:
C90.00, multiple myeloma not having achieved remission
C90.02, multiple myeloma in relapse.

NDC CODE (BOX 24A OR 24D)

NOTE: *Some payers may require to document KYPROLIS NDC number in BOX 24A or 24D.*

Specific payer requirements for reporting NDC may vary.

DIAGNOSIS CODE POINTER (BOX 24E)

Specify diagnosis, from Box 21, relating to each CPT/HCPCS code listed in Box 24D.

These sample forms are intended as a reference for coding and billing for product and associated services. They are not intended to be directive; the use of the recommended codes does not guarantee reimbursement. Healthcare providers may deem other codes or policies more appropriate and should select the coding options that most accurately reflect their internal system guidelines, payer requirements, practice patterns, and the services rendered. Healthcare providers are responsible for ensuring the accuracy and validity of all billing and claims for appropriate reimbursement.

Please see Important Safety Information for KYPROLIS on pages 6-7.

Kyprolis® (carfilzomib) for injection

AMGEN ASSIST 360™
Support, Simplified

FINANCIAL SUPPORT OPTIONS FOR ANY INSURANCE TYPE

Whatever type of insurance your patients have—even if they have none—we can help you understand how their Amgen medicine may be covered, and refer them to programs that may be able to help them afford their medication, such as Amgen FIRST STEP™. *

For Eligible† Commercially Insured Patients

The Amgen FIRST STEP™ program can help patients cover their out-of-pocket prescription costs, including deductible, co-insurance, or co-payment.

- **$0** out-of-pocket for first dose or cycle
- **As little as $5‡** out-of-pocket for subsequent doses or cycles, up to the brand program benefit maximum
- No income eligibility requirement

For Patients On Government Insurance Like Medicare

Amgen Assist 360™ can refer patients to independent nonprofit patient assistance programs that may be able to help them afford the co-pay costs for their prescribed medicine. §

For Uninsured Patients

Amgen Safety Net Foundation, a nonprofit patient assistance program sponsored by Amgen, helps qualified patients access Amgen medicines at no cost.

Call **1-888-4ASSIST (1-888-427-7478)** Monday–Friday, 9 AM to 8 PM ET
or visit **WWW.AMGENASSIST360.COM/ENROLL**

* Resources include referrals to independent nonprofit patient assistance programs. Eligibility for resources provided by independent nonprofit patient assistance programs is based on the nonprofits' criteria. Amgen has no control over these programs and provides referrals as a courtesy only.

† Terms, conditions, and program maximums apply. This program is not open to patients receiving prescription reimbursement under any federal, state, or government-funded healthcare program. Not valid where prohibited by law. Other restrictions may apply. Please see full Terms and Conditions at www.AmgenFirstStep.com.

‡ As little as $5 out-of-pocket cost for subsequent dose or cycle of KYPROLIS® through Amgen FIRST STEP™.

§ Amgen Assist 360™ can refer patients to independent nonprofit patient assistance programs that may be able to help them afford the co-pay costs for their prescribed medicine.

References: 1. CMS. 2020 Alpha-Numeric HCPCS File. https://www.cms.gov/Medicare/Coding/HCPCSReleaseCodeSets/Alpha-Numeric-HCPCS-Items/2020-Alpha-Numeric-HCPCS-File. Accessed July 25, 2021. **2.** American Medical Association. Current Procedural Terminology (CPT®) copyright 2020 American Medical Association. 2021. All rights reserved. **3.** KYPROLIS® (carfilzomib) prescribing information. Onyx Pharmaceuticals, Inc., an Amgen Inc. subsidiary. **4.** CMS. Medically Unlikely Edits - Facility Outpatient Hospital Services MUE Table – Effective 07-01-2021. https://www.cms.gov/Medicare/Coding/NationalCorrectCodInitEd/MUE.html. Accessed July 25, 2021. **5.** CMS. Medically Unlikely Edits – Practitioner Services MUE Table – Effective 07-01-2021. https://www.cms.gov/Medicare/Coding/NationalCorrectCodInitEd/MUE.html. Accessed July 25, 2021. **6.** CMS. Medicare NCCI 2021 Coding Policy Manual. Chapter 1. https://www.cms.gov/Medicare/Coding/NationalCorrectCodInitEd. Accessed July 25, 2021. **7.** CMS. MLN Matters MM9603. https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/MM9603.pdf. Accessed July 25, 2021. **8.** CMS. ICD-10-CM. 2021.

Please see Important Safety Information for KYPROLIS on pages 6-7.

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), 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.
- 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.
- 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.

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.

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.

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.

Please see additional Important Safety Information for KYPROLIS on page 7.

Kyprolis® (carfilzomib) for injection

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.

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 occurring in at least 20% of patients taking KYPROLIS in the combination therapy trials: anemia, diarrhea, hypertension, fatigue, upper respiratory tract infection, thrombocytopenia, pyrexia, cough, dyspnea, and insomnia.
- The most common adverse reactions occurring in at least 20% of patients taking KYPROLIS in monotherapy trials: anemia, fatigue, thrombocytopenia, nausea, pyrexia, dyspnea, diarrhea, headache, cough, edema peripheral.

Please click here to see full Prescribing Information for KYPROLIS.

Kyprolis® (carfilzomib) for injection