Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 11/01/2022**
Policy Number: PA.CP.PHAR.309	**Effective Date: 10/2018** **Revision Date: 10/2022**
Policy Name: Carfilzomib (Kyprolis)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

4Q 2022 annual review: RT4 – added new indication in combination with Sarclisa plus dexamethasone and Darzalex Faspro plus dexamethasone for MM after one to three lines of therapy; per NCCN Compendium added additional MM uses as primary therapy in combination with dexamethasone, lenalidomide, and Darzalex, added previously treated MM combination regimens, added criteria set for systemic light chain amyloidosis; references reviewed and updated.

Name of Authorized Individual (Please type or print): **Venkateswara R. Davuluri, MD**	**Signature of Authorized Individual:**

Clinical Policy: Carfilzomib (Kyprolis)

Reference Number: PA.CP.PHAR.309
Effective Date: 10/2018
Last Review Date: 10/2022

Coding Implications
Revision Log

Description
Carfilzomib (Kyprolis®) is a proteasome inhibitor.

FDA Approved Indication(s)
Kyprolis is indicated

- For the treatment of adult patients with relapsed or refractory multiple myeloma (MM) who have received one to three lines of therapy in combination with:
  - Lenalidomide and dexamethasone or
  - Dexamethasone or
  - Daratumumab and dexamethasone or
  - Daratumumab and hyaluronidase-fihj and dexamethasone or
  - Isatuximab and dexamethasone

- As a single agent for the treatment of adult patients with relapsed or refractory MM who have received one or more lines of therapy.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Kyprolis is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all)**:**

1. Diagnosis of MM;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For primary therapy, Kyprolis is prescribed in one of the following ways (a, b, or c):*
   a. In combination with dexamethasone and Revlimid® (lenalidomide)
   b. In combination with dexamethasone and cyclophosphamide;
   c. In combination with dexamethasone, lenalidomide, and Darzalex® (daratumumab);
5. For previously treated multiple myeloma for relapsed or refractory disease, Kyprolis is prescribed in one of the following ways (a-h):*
   a. In combination with dexamethasone or with Revlimid® (lenalidomide) plus dexamethasone in patients who have received one to three lines of therapy *(see Appendix B for examples of prior therapy)*;
   b. As a single agent in patients who have received one or more lines of therapy;

c. In combination with Darzalex® (daratumumab) or Darzalex Faspro™ (daratumumab/hyaluronidase-fihj) and dexamethasone in patients who have received one or three lines of therapy;
d. In combination with Sarclisa (isatuximab-irfc) and dexamethasone in patients who have received one or three lines of therapy;
e. In combination with Xpovio (Selinexor) and dexamethasone for relapse or progressive disease;
f. In combination with dexamethasone and cyclophosphamide, with or without thalidomide, for relapse or progressive disease;
g. In combination with pomalidomide and dexamethasone for patients who have received at least two prior therapies, including an immunomodulatory agent and a proteasome inhibitor and who have demonstrated disease progression on or within 60 days of completion of the last therapy;
h. In combination with Bendeka (bendamustine) and dexamethasone in patients with late relapse or progressive disease (>3 prior therapies);

**Prior authorization may be required..*

6. For maintenance therapy for symptomatic multiple myeloma in combination with lenalidomide for transplant candidates who meets one of the following (a, b or c):
   a. Has had a previous response to primary myeloma therapy;
   b. Has had a response or has stable disease following an autologous hematopoietic cell transplant (HCT);
   c. Has had a response or has stable disease following a tandem autologous or allogeneic HCT for high risk patients with renal insufficiency and/or peripheral neuropathy;
7. Request meets one of the following (a, b, c, d, or e):
   a. Monotherapy: dose does not exceed 56 mg/m^2 twice weekly each 28-day cycle;
   b. With dexamethasone and Revlimid: dose does not exceed 27 mg/m^2 twice weekly 3 out of 4 weeks for twelve 28-day cycles, then 27 mg/m^2 twice weekly 2 out of 4 weeks for the next six 28-day cycles for up to a total of 18 cycles;
   c. With dexamethasone ± Darzalex: dose does not exceed (i or ii):
      i. 70 mg/m^2 once weekly each 28-day cycle;
      ii. 56 mg/m^2 twice weekly each 28-day cycle;
   d. With dexamethasone and Sarclisa: 56 mg/m^2 twice weekly each 28-day cycle;
   e. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   Approval duration: 6 months

B. Waldenstrom's Macroglobulinemia (Lymphoplasmacytic Lymphoma) (off-label) (must meet all)**:**

1. Diagnosis of Waldenstrom's macroglobulinemia (i.e., lymphoplasmacytic lymphoma) (WM/LPL);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Prescribed as a component of CaRD (carfilzomib, rituximab, and dexamethasone) regimen as primary or Kyprolis-relapsed therapy;

   **Prior authorization may be required.*

5. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

C. Systemic Light Chain Amyloidosis (off-label) (must meet all)**:**
1. Diagnosis of Systemic Light Chain Amyloidosis;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request is for relapsed/refractory non-cardiac disease;
5. Prescribed in one of the following ways (a or b):
   a. As a single agent;
   b. In combination with dexamethasone;
6. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*)..

Approval duration: 6 months

D. Other diagnoses/indications
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. Multiple Myeloma (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, c, d or e):
   a. Monotherapy: new dose does not exceed 56 mg/m^2 twice weekly each 28-day cycle;
   b. With Revlimid plus dexamethasone: new dose does not exceed 27 mg/m^2 twice weekly 3 out of 4 weeks for twelve 28-day cycles, then 27 mg/m^2 twice weekly 2 out of 4 weeks for the next six 28-day cycles for up to a total of 18 cycles;
   c. With dexamethasone ± Darzalex: new does not exceed (i or ii):
      i. 70 mg/m^2 once weekly each 28-day cycle;
      ii. 56 mg/m^2 twice weekly each 28-day cycle;
   d. With dexamethasone and Sarclisa: 56 mg/m^2 twice weekly each 28-day cycle;
   e. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 12 months

B. Waldenstrom's Macroglobulinemia (Lymphoplasmacytic Lymphoma) (off-label) (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;

3. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 12 months

C. Systemic Light Chain Amyloidosis (off-label) (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Kyprolis for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence)

Approval duration: 12 months

D. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CaRD: carfilzomib, rituximab, dexamethasone
FDA: Food and Drug Administration
MM: multiple myeloma
NCCN: National Comprehensive Cancer Network
WM/LPL: Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Kyprolis (carfilzomib), Velcade® (bortezomib), Revlimid (lenalidomide), cyclophosphamide, dexamethasone	MM: Examples of primary therapy • Bortezomib/lenalidomide/dexamethasone • Bortezomib/cyclophosphamide/dexamethasone • Carfilzomib/lenalidomide/dexamethasone • Daratumumab/lenalidomide/dexamethasone • Daratumumab/lenalidomide/bortezomib/dexamethasone • Carfilzomib/cyclophosphamide/dexamethasone • Carfilzomib/lenalidomide/dexamethasone	Varies
Kyprolis (carfilzomib), Velcade® (bortezomib), Revlimid (lenalidomide), Darzalex® (daratumumab), Ninlaro® (ixazomib), Pomalyst (pomalidomide), Empliciti® (elotuzumab), Farydak (panobinostat), Thalomid® (thalidomide), bendamustine, cyclophosphamide, dexamethasone	MM: Examples of therapy for previously treated for relapsed or refractory disease: • Bendamustine • Bortezomib/dexamethasone • Carfilzomib/lenalidomide/dexamethasone • Daratumumab/bortezomib/dexamethasone • Daratumumab/carfilzomib/dexamethasone • Daratumumab/lenalidomide/dexamethasone • Ixazomib/lenalidomide/dexamethasone • Pomalidomide/bortezomib/dexamethasone • Elotuzumab/lenalidomide/dexamethasone • Panobinostat/bortezomib/dexamethasone • Carfilzomib/cyclophosphamide/dexamethasone • Carfilzomib/dexamethasone • Pomalidomide/carfilzomib/dexamethasone • Carfilzomib/cyclophosphamide/thalidomide/dexamethasone •	Varies
Rituxan (rituximab) Kyprolis (carfilzomib) dexamethasone	WM/LPL: CaRD (carfilzomib, rituximab, and dexamethasone)	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Black Box Warnings
None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MM	Kyprolis + Dexamethasone: • Cycles: Kyprolis IV as a 30-minute infusion (28-day cycles). o Cycle 1: administer Kyprolis 20 mg/m^2 on Day 1 and 70 mg/m^2 on Days 8 and 15 o Cycle 2 and later: 70 mg/m^2 on Day 1, 8, and 15 • Dose (once weekly 20/70 mg/m^2 regimen): o Starting dose of Kyprolis 20 mg/m^2 on Cycle 1, Day 1 o If tolerated, escalate Kyprolis to 70 mg/m^2 on Day 8 of Cycle 1. o Dexamethasone: 40 mg PO or IV on Days 1, 8, 15 of all 28-day cycles and on Day 22 of Cycles 1-9. Kyprolis + Dexamethasone, OR **Monotherapy**: • Cycles: Kyprolis IV as a 30-minute infusion (28-day cycles). o Cycle 1: administer Kyprolis 20 mg/m^2 on Days 1 and 2, and 56 mg/m^2 on Day 8, 9, 15, and 16 o Cycle 2 and later: administer Kyprolis 56 mg/m^2 on Days 1, 2, 8, 9, 15 and 16 o For monotherapy: Cycle 13 and later: administer Kyprolis 56 mg/m^2 on Days 1, 2, 15 and 16 • Dose (twice weekly 20/56 mg/m^2 regimen): o Starting dose of Kyprolis 20 mg/m^2 on Cycle 1, Days 1 and 2 o If tolerated, escalate Kyprolis to 56 mg/m^2 on Day 8 of Cycle 1. *Do not include if Monotherapy:* o Dexamethasone: 20 mg PO or IV on Days 1, 2, 8, 9, 15, 16, 22 and 23 of each 28-day cycle. Kyprolis + Revlimid + Dexamethasone, OR **Monotherapy**: • Cycles: Kyprolis IV as a 10-minute infusion for 28-day cycles. o Cycle 1: administer Kyprolis 20 mg/m^2 on Days 1 and 2, and 27 mg/m^2 on Days 8, 9, 15 and 16 o Cycle 2 to 12: administer Kyprolis 27 mg/m^2 on Days 1, 2, 8, 9, 15 and 16 o Cycle 13 and later, administer Kyprolis 27mg/m^2 on Day 1, 2, 15 and 16	70 mg/m^2

Indication	Dosing Regimen	Maximum Dose
	○ Discontinue Kyprolis after Cycle 18 and continue Revlimid and dexamethasone thereafter. • Dose (twice weekly 20/27 mg/m^2 regimen): ○ Starting dose of Kyprolis: 20 mg/m^2 on Cycle 1, Days 1 and 2 ○ If tolerated, escalate Kyprolis to 27 mg/m^2 on Day 8 of Cycle 1. *Do not include if Monotherapy:* ○ Revlimid: 25 mg PO QD on Days 1–21 of each cycle. ○ Dexamethasone: 40 mg PO or IV on Days 1, 8, 15, and 22 of each 28-day cycle. Kyprolis + Darzalex + Dexamethasone: Twice weekly 20/56 mg/m^2 regimen: • Cycles: Kyprolis IV as a 30-minute infusion (28-day cycles). ○ Cycle 1: administer Kyprolis 20 mg/m^2 on Days 1 and 2 and 56 mg/m^2 on Days 8, 9, 15 and 16 ○ Cycle 2 and later: administer Kyprolis 56 mg/m^2 on Days 1, 2, 8, 9, 15 and 16 • Dose: ○ Starting dose of Kyprolis: 20 mg/m^2 on Cycle 1, Days 1 and 2 ○ If tolerated, escalate Kyprolis to 56 mg/m^2 on Day 8 of Cycle 1 ○ See prescribing information for Darzalex, Darzalex Faspro, and dexamethasone dosing. Once weekly 20/70 mg/m^2 regimen: • Cycles: Kyprolis IV as a 30-minute infusion (28-day cycles). ○ Cycle 1: administer Kyprolis 20 mg/m^2 on Day 1 and 70 mg/m^2 on Days 8 and 15 ○ Cycle 2 and later: administer Kyprolis 70 mg/m^2 on Days 1, 8 and 15 • Dose: ○ Starting dose of Kyprolis: 20 mg/m^2 on Cycle 1, Days 1 and 2 ○ If tolerated, escalate Kyprolis to 70 mg/m^2 on Day 8 of Cycle 1 ○ See prescribing information for Darzalex, Darzalex Faspro, and dexamethasone dosing. Kyprolis + Sarclisa + Dexamethasone: Twice weekly 20/56 mg/m^2 regimen:	

Indication	Dosing Regimen	Maximum Dose
	• Cycles: Kyprolis IV as a 30-minute infusion (28-day cycles). o Cycle 1: administer Kyprolis 20 mg/m^2 on Days 1 and 2 and 56 mg/m^2 on Days 8, 9, 15 and 16 o Cycle 2 and later: administer Kyprolis 56 mg/m^2 on Days 1, 2, 8, 9, 15 and 16 • Dose: o Starting dose of Kyprolis: 20 mg/m^2 on Cycle 1, Days 1 and 2 o If tolerated, escalate Kyprolis to 56 mg/m^2 on Day 8 of Cycle 1 o See prescribing information for Sarclisa dosing___ _____ *Calculate the Kyprolis dose using the patient's actual body surface area at baseline. In patients with a body surface area greater than 2.2 m^2, calculate the dose based upon a body surface area of 2.2 m^2.*	

VI. Product Availability

Single-dose vial: 10 mg, 30 mg, 60 mg

VII. References

1. Kyprolis Prescribing Information. Thousand Oaks: Onyx Pharmaceuticals, Inc.; June 2022. Available at: http://www.kyprolis.com. Accessed July 12, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 12, 2022.
3. National Comprehensive Cancer Network. Multiple Myeloma Version 05.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed July 12, 2022.
4. National Comprehensive Cancer Network. Waldenstrom's macroglobulinemia-lymphoplasmacytic lymphoma Version 01.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed July 12, 2022.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9047	Injection, carfilzomib, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New Policy Created	10/2018	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019	
4Q 2020 annual review: Kyprolis dosing as monotherapy and in combination with dexamethasone added per PI; MM - FDA approved regimen added: in combination with Darzalex and dexamethasone, and NCCN recommended regimen added: in combination with dexamethasone and cyclophosphamide ± Thalomid; references reviewed and updated.	10/2020	
4Q 2021 annual review: added primary therapy and revised therapy for previous treated for relapsed or refractory disease and updated Appendix B Therapeutic Alternatives as per NCCN recommendation; updated Section V Dosage and Administration and Section VI Product Availability; references reviewed and updated.	10/2021	
4Q 2022 annual review: RT4 – added new indication in combination with Sarclisa plus dexamethasone and Darzalex Faspro plus dexamethasone for MM after one to three lines of therapy; per NCCN Compendium added additional MM uses as primary therapy in combination with dexamethasone, lenalidomide, and Darzalex, added previously treated MM combination regimens, added criteria set for systemic light chain amyloidosis; references reviewed and updated.	10/2022	