Clinical Policy Title:	ixazomib
Policy Number:	RxA.418
Drug(s) Applied:	Ninlaro®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Ixazomib (Ninlaro®) is a proteasome inhibitor. It is indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma (MM) who have received at least one prior therapy.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
ixazomib (Ninlaro®)	MM	4 mg orally on Days 1, 8, and 15 of a 28-day cycle Reduce the starting dose to 3 mg in patients with renal and hepatic impairment	4 mg/week

Dosage Forms

- Capsules: 2.3 mg, 3 mg, 4 mg.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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. Prescribed in combination with dexamethasone and lenalidomide in patients with multiple myeloma who have received at least one prior therapy ;
5. Primary therapy for symptomatic multiple myeloma or for disease relapse after 6 months following primary induction therapy with the same regimen in combination with;
   a. Lenalidomide and dexamethasone (2B recommendation per NCCN);

b. Cyclophosphamide and dexamethasone for transplant patients;

6. Therapy for previously treated multiple myeloma for relapse or progressive disease in combination with:
   a. Dexamethasone and lenalidomide (preferred regimen);
   b. Dexamethasone and pomalidomide for patients who have received at least 2 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 (preferred regimen);
   c. Cyclophosphamide and dexamethasone;
   d. Dexamethasone (used in certain circumstances);
7. Used as maintenance therapy as a single agent for transplant candidates with (off label use):
   a. Symptomatic multiple myeloma after response to primary myeloma therapy;
   b. Response or stable disease following autologous hematopoietic cell transplant;
8. Request meets one of the following (a or b):
   a. Dose does not exceed 4 mg (1 tablet) per week for 3 weeks of a 28-day (4-week) treatment cycle;
   b. Requested dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
   *Prior authorization is required for Revlimid and Pomalyst.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Systemic Light Chain Amyloidosis (off-label) (must meet all):
1. Diagnosis of relapsed or refractory systemic light chain amyloidosis;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Prescribed as single agent or in combination with dexamethasone;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

C. Waldenstrom Macroglobulinemia/ Lymphoplasmacytic Lymphoma (off-label) (must meet all):
1. Diagnosis of waldenstrom macroglobulinemia/ lymphoplasmacytic lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Prescribed in combination with rituximab and dexamethasone;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;

2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 4 mg (1 tablet) per week for 3 weeks of a 28-day (4- week) treatment cycle;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
MM: Multiple Myeloma

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
Pomalyst® (pomalidomide)	Varies	Varies
Revlimid® (lenalidomide)	Varies	Varies
dexamethasone	Varies	Varies

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Strong CYP3A inducers: Avoid concomitant use with Ninlaro®.

References

1. Ninlaro® Prescribing Information. Cambridge, MA: Millennium Pharmaceuticals, Inc.; March 2021. Available at https://ninlaro.com/prescribing-information.pdf. Accessed June 03, 2021.
2. National Comprehensive Cancer Network Drug and Biologics Compendium. Available at www.nccn.org . Accessed June 03, 2021.
3. National Comprehensive Cancer Network. Multiple Myeloma version 7.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf June 03, 2021.
4. National Comprehensive Cancer Network. Systemic Light Chain Amyloidosis version 2.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/amyloidosis.pdf . Accessed June 03, 2021.
5. National Comprehensive Cancer Network. Waldenstrom Macroglobulinemia/ Lymphoplasmacytic Lymphoma;

Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf . Accessed June 03, 2021.
6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology-ip.com/. Accessed June 03, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Line of Business Policy Applies to was updated to all lines of business. 3. Initial and Continued approval duration was updated to include Medicaid, Commercial & HIM approval duration. 4. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 5. References were reviewed and updated.	7/22/2020	9/14/2020
Policy was reviewed: 1. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 2. Initial Approval Criteria I.A.4 was updated to include "with multiple myeloma who have received at least one prior therapy…" 3. Initial Approval Criteria I.A.5 was updated to include "Primary therapy for symptomatic multiple myeloma or for disease…" 4. Initial Approval Criteria I.A.6 was updated to include "Therapy for previously treated multiple myeloma for relapse or progressive disease…" 5. Initial Approval Criteria I.B.4 was updated to include "Prescribed as single agent or in combination with dexamethasone…" 6. Initial Approval Criteria I.C was updated to include off-label indication, "Waldenstrom	06/03/2021	9/14/2021

Macroglobulinemia/ Lymphoplasmacytic Lymphoma (off-label)…” 7. Initial Approval Criteria and Continued Therapy Approval Criteria have been updated to remove HIM approval duration. 8. Continued Therapy Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 9. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 10. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 11. Appendix D was updated to include “Strong CYP3A inducers: Avoid concomitant use with Ninlaro®…” 12. References were reviewed and updated.		