RXADVANCE
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Clinical Policy Title:	selinexor
Policy Number:	RxA.568
Drug(s) Applied:	Xpovio®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Selinexor (Xpovio®) is a nuclear export inhibitor (XPO1 inhibitor). It is indicated:

- In combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody.
- For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy.

These indications are approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
selinexor (Xpovio®)	RRMM	80 mg in combination with dexamethasone PO on days 1 and 3 of each week	160 mg/week
	DLBCL	60 mg PO on days 1 and 3 of each week.	120 mg/week

Dosage Forms

Tablets: 20 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.

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all):

1. Diagnosis of RRMM;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;

4. Member has received ≥ 4 prior lines of therapy (*see Appendix B for examples)* that include all of the following (a, b, and c):
    a. Two proteasome inhibitors (e.g., bortezomib, Kyprolis®, Ninlaro®)
    b. Two immunomodulatory agents (e.g., Revlimid®, pomalidomide, Thalomid®);
    c. One anti-CD38 monoclonal antibody (e.g., Darzalex®);
5. Request meets one of the following (a or b)*:
    a. Dose does not exceed 160 mg (8 tablets) per week;
    b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Diffuse Large B-Cell Lymphoma (must meet all):

1. Diagnosis of diffuse large B-cell lymphoma (DLBCL) and transformed DLBCL arising from follicular lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Treatment of histologic transformation to diffuse large B-cell lymphoma in patients who have received multiple prior therapies including ≥2 lines of chemoimmunotherapy for indolent or transformed disease;
5. Third line and subsequent therapy (only after at least 2 lines of systemic therapy) for partial response, no response, relapsed, progressive, or refractory disease;
6. Request meets one of the following (a or b)*:
    a. Dose does not exceed 120 mg (6 tablets) per week;
    b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

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 met initial approval criteria for the covered indication and has received this medication for at least 30 days;
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. For RRMM: New dose does not exceed 160 mg (8 tablets) per week and for DLBCL: New dose does not exceed 120 mg (6 tablets) per week;
    b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
RRMM: Relapsed or refractory multiple myeloma
DLBCL: Diffuse large B-cell lymphoma

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	Dose Limit/ Maximum Dose
bortezomib/Revlimid® (lenalidomide) /dexamethasone	Varies	Varies
bortezomib/cyclophosphamide/dexamethasone	Varies	Varies
bortezomib/doxorubicin (or liposomal doxorubicin)/dexamethasone	Varies	Varies
Kyprolis® (carfilzomib)/ Revlimid® (lenalidomide) /dexamethasone	Varies	Varies
Kyprolis® (carfilzomib)/ cyclophosphamide/ dexamethasone	Varies	Varies
Kyprolis® (carfilzomib – weekly or twice weekly)/dexamethasone	Varies	Varies
Ninlaro® (ixazomib)/Revlimid® (lenalidomide)/dexamethasone	Varies	Varies
Ninlaro® (ixazomib)/dexamethasone	Varies	Varies
Ninlaro® (ixazomib)/pomalidomide/dexamethasone	Varies	Varies
bortezomib/dexamethasone	Varies	Varies
bortezomib/Thalomid® (thalidomide)/dexamethasone	Varies	Varies
cyclophosphamide/Revlimid® (lenalidomide)/dexamethasone	Varies	Varies
Revlimid® (lenalidomide)/dexamethasone	Varies	Varies
VTD-PACE (dexamethasone/Thalomid® (thalidomide)/cisplatin/doxorubicin/ cyclophosphamide/etoposide/bortezomib)	Varies	Varies
Revlimid® (lenalidomide)/low-dose dexamethasone	Varies	Varies
Darzalex® (daratumumab)/ bortezomib/ melphan/prednisone	Varies	Varies
Darzalex® (daratumumab)/ bortezomib/dexamethasone	Varies	Varies
Darzalex® (daratumumab)/ Revlimid® (lenalidomide)/ dexamethasone	Varies	Varies
Darzalex® (daratumumab)	Varies	Varies
Darzalex® (daratumumab)/ pomalidomide/ dexamethasone	Varies	Varies
Empliciti® (elotuzumab)/Revlimid® (lenalidomide)/ dexamethasone	Varies	Varies
Empliciti® (elotuzumab)/bortezomib/dexamethasone	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Empliciti® (elotuzumab)/pomalidomide/dexamethasone	Varies	Varies
bendamustine/bortezomib/dexamethasone	Varies	Varies
bendamustine/Revlimid® (lenalidomide)/ dexamethasone	Varies	Varies
panobinostat/bortezomib/dexamethasone	Varies	Varies
panobinostat/Kyprolis® (carfilzomib)	Varies	Varies
panobinostat/Revlimid® (lenalidomide)/ dexamethasone	Varies	Varies
pomalidomide/cyclophosphamide/dexamethasone	Varies	Varies
pomalidomide/dexamethasone	Varies	Varies
pomalidomide/bortezomib/dexamethasone	Varies	Varies
pomalidomide/ Kyprolis® (carfilzomib)/ dexamethasone	Varies	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/Boxed Warnings

- Contraindication(s):
  - None.

- Boxed Warning(s):
  - None.

APPENDIX D: General Information

- Xpovio® (selinexor) is the first and only FDA-approved oral XPO1 inhibitor that gets to the cell's core to cause cell cycle arrest and apoptosis.
- Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma (NHL), a cancer of the immune system.
- The most common adverse reactions (incidence ≥20%) in patients with multiple myeloma are thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infection.
- The most common adverse reactions (incidence ≥20%) in patients with DLBCL, excluding laboratory abnormalities, are fatigue, nausea, diarrhea, appetite decrease, weight decrease, constipation, vomiting, and pyrexia. Grade 3-4 laboratory abnormalities (≥15%) are thrombocytopenia, lymphopenia, neutropenia, anemia, and hyponatremia.

References

1. Xpovio Prescribing Information. Newton, MA: Karyopharm Therapeutics Inc.; June 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212306s000lbl.pdf. Accessed October 01, 2020.
2. FDA Briefing Document, Oncologic Drugs Advisory Committee Meeting: NDA 212306 Selinexor; February 26, 2019. Available at: https://www.fda.gov/media/121667/download. Accessed October 01, 2020.
3. National Comprehensive Cancer Network. Multiple Myeloma Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed October 01, 2020.

4. National Comprehensive Cancer Network. B-cell lymphoma Version 4.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed October 01, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title was updated as “selinexor”. 2. Line of business policy applies to all lines of business. 3. Dosing information updated with DLBCL indication. 4. Initial approval criteria updated with “Diffuse Large B-Cell Lymphoma info. added”. 5. Continued therapy approval criteria II.A.1 was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance..” 6. Appendix D updated with common adverse effects. 7. References were reviewed and updated.	09/30/2020	12/07/2020