Clinical Policy: Selinexor (Xpovio)
Reference Number: CP.PHAR.431
Effective Date: 07.16.19
Last Review Date: 08.20
Line of Business: Commercial, HIM, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Selinexor (Xpovio®) is a nuclear export inhibitor (XPO1 inhibitor).

FDA Approved Indication(s)
Xpovio is indicated:
- In combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (MM) 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 (NOS), 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 these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial.

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 health plans affiliated with Centene Corporation® that Xpovio 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. Disease is relapsed or refractory;
      5. Member has received ≥ 4 prior therapies (see Appendix B) including 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®);*  
         *Prior authorization may be required
      6. 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:**
Medicaid/HIM – 6 months
Commercial – Length of Benefit

**B. Diffuse Large B-Cell Lymphoma** (must meet all):
1. Diagnosis of DLBCL, NOS, including DLBCL arising from follicular lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Disease is relapsed or refractory;
5. Member has received ≥ 2 prior therapies* for relapsed or refractory disease *(see Appendix B)*;

*Prior authorization may be required

6. Request meets one of the following (a or b):*
   a. Dose does not exceed 60 mg (3 tablets) twice weekly;
   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:**
Medicaid/HIM – 6 months
Commercial – Length of Benefit

**C. Other diagnoses/indications**
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid

**II. Continued Therapy**

**A. All Indications in Section I** (must meet all):
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Xpovio for a 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 MM: New dose does not exceed 160 mg (8 tablets) per week;
   b. For DLBCL: New dose does not exceed 60 mg (3 tablets) twice weekly;
   c. 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:**
Medicaid/HIM – 12 months
Commercial – Length of Benefit
B. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via health plan benefit and documentation supports
      positive response to therapy.
      Approval duration: Duration of request or 6 months (whichever is less); or
   2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT
      specifically listed under section III (Diagnoses/Indications for which coverage is
      NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance
      marketplace and CP.PMN.53 for Medicaid.

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 policies –
      CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and
      CP.PMN.53 for Medicaid or evidence of coverage documents

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   DLBCL: diffuse large B-cell lymphoma
   FDA: Food and Drug Administration
   MM: multiple myeloma
   NCCN: National Comprehensive Cancer Network
   NOS: not otherwise specified

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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>MM: regimens containing proteasome inhibitors, immunomodulatory agents and/or anti-CD38 monoclonal antibodies (examples - NCCN)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>bortezomib / Revlimid (lenalidomide) or pomalidomide or Thalomid (thalidomide) / dexamethasone</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Kyprolis (carfilzomib – weekly or twice weekly) / dexamethasone</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Kyprolis / Revlimid / dexamethasone</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Ninlaro (ixazomib) / Revlimid / dexamethasone</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Darzalex (daratumumab) / bortezomib / dexamethasone ± Thalomid</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Darzalex / Revlimid / dexamethasone</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>DLBCL NOS: second-line/subsequent regimens (examples - NCCN)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GemOx (gemcitabine, oxaliplatin) ± rituximab</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Polatuzumab vedotin ± rituximab ± bendamustine</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>DHAP (dexamethasone, cisplatin, cytarabine) ± rituximab</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>DHAX (dexamethasone, cytarabine, oxaliplatin) ± rituximab</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Yescarta® (axicabtagene ciloleucel)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
</tbody>
</table>
Drug Name | Dosing Regimen | Dose Limit/Maximum Dose
---|---|---
Kymriah® (tisagenlecleucel) | 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
None reported

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>MM</td>
<td>80 mg in combination with dexamethasone PO on days 1 and 3 of each week</td>
<td>160 mg/week</td>
</tr>
<tr>
<td>DLBCL</td>
<td>60 mg PO on Days 1 and 3 of each week</td>
<td>60 mg/day</td>
</tr>
</tbody>
</table>

VI. Product Availability
Tablet: 20 mg

VII. References

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Policy created</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>07.16.19</td>
<td>08.19</td>
<td></td>
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<tr>
<td>Finalized line of businesses on policy to include HIM per SDC and prior clinical guidance.</td>
<td>12.02.19</td>
<td></td>
</tr>
<tr>
<td>3Q 2020 annual review: criteria added for new FDA-approved indication: DLBCL; references reviewed and updated.</td>
<td>07.01.20</td>
<td>08.20</td>
</tr>
</tbody>
</table>

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program
approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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