Clinical Policy: Iberdomide (Zenbexus)

Reference Number: CP.PHAR.809
Effective Date: 12.01.26
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid Revision Log

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

Description

Iberdomide (Zenbexus™) is a cereblon-modulating protein degrader.

FDA Approved Indication(s)

Zenbexus is indicated in combination with daratumumab and hyaluronidase-fihj and dexamethasone for the treatment of adult patients with multiple myeloma (MM) who have received at least 1 prior line of therapy including a proteasome inhibitor and an immunomodulatory agent.

This indication is approved under accelerated approval based on minimal residual disease-negative complete response at any time. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

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 Zenbexus 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. Failure of both of the following (a and b), unless clinically significant adverse effects are experienced or all are contraindicated:*
   a. An immunomodulatory agent (e.g., lenalidomide, Pomalyst®, Thalomid®);
   b. A proteasome inhibitor (e.g., bortezomib, Kyprolis®, Ninlaro®);
   **Prior authorization may be required for immunomodulatory agents and proteasome inhibitors.*
5. Prescribed in combination with both of the following (a and b):
   a. Darzalex Faspro® (daratumumab/hyaluronidase-fihj);
   b. Dexamethasone;
6. For Zenbexus requests, member must use generic iberdomide, unless contraindicated or clinically significant adverse effects are experienced;

7. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii) on days 1-21 of repeated 28-day cycles:
      i. 1 mg per day;
      ii. 1 capsule per day;
   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: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Multiple Myeloma (meets all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Zenbexus for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Zenbexus requests, member must use generic iberdomide, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed both of the following (i and ii) on days 1-21 of repeated 28-day cycles:
      i. 1 mg per day;
      ii. 1 capsule per day;
   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: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, 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.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
MM: multiple myeloma

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
Examples of immunomodulatory agents		
lenalidomide (Revlimid®)	25 mg PO QD days 1-21 of repeated 28-day cycles	25 mg/day
Pomalyst (pomalidomide)	4 mg PO QD days 1-21 of repeated 28-day cycles	4 mg/day
Thalomid® (thalidomide)	200 mg PO QD	200 mg/day
Examples of proteasome inhibitors		
bortezomib (Velcade®)	1.3 mg/m^2/dose SC or IV; frequency of administration varies based on specific use	1.3 mg/m^2/dose

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Kyprolis® (carfilzomib)	20 mg/m^2, 27 mg/m^2, and/or 56 mg/m^2 IV; frequency of administration varies based on specific use	Varies
Ninlaro® (ixazomib)	4 mg PO once weekly on days 1, 8, 15 of a 28-day treatment cycle	4 mg/day

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): pregnancy
- Boxed warning(s): embryo-fetal toxicity and serious venous and arterial thromboembolism

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MM	1 mg PO QD on days 1-21 of a 28-day cycle, until disease progression or unacceptable toxicity, in combination with daratumumab and hyaluronidase-fihj and dexamethasone	1 mg/day

VI. Product Availability

Capsules: 0.75 mg, 1 mg

VII. References

1. Zenbexus Prescribing Information. Princeton, NJ: Bristol-Myers Squibb Company; August 2026. Available at: https://www.zenbexus.com. Accessed August 19, 2026.
2. National Comprehensive Cancer Network. Multiple Myeloma Version 5.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed August 19, 2026.
3. Clinical Pharmacology [database online]. Tampa, FL: Elsevier; 2026. URL: www.clinicalkeys.com/pharmacology. Accessed August 19, 2026.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.19.26	11.26

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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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