Clinical Policy: Lurbinectedin (Zepzelca)

Reference Number: CP.PHAR.500
Effective Date: 09.01.20
Last Review Date: 08.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Coding Implications
Revision Log

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

Description

Lurbinectedin (Zepzelca®) is an alkylating drug.

FDA Approved Indication(s)

Zepzelca is indicated in combination with atezolizumab or atezolizumab and hyaluronidase-tqjs, for the maintenance treatment of adult patients with extensive-stage small cell lung cancer (SCLC) whose disease has not progressed after first-line induction therapy with atezolizumab or atezolizumab and hyaluronidase-tqjs, carboplatin and etoposide.

Policy/Criteria

Provider must submit documentation (including 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 Zepzelca is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Small Cell Lung Cancer (must meet all)**:**

1. Diagnosis of SCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in one of the following ways (a or b):
   a. Both of the following (i and ii; *off-label*):
      i. As single-agent therapy;
      ii. Disease is advanced or metastatic and has progressed on or after platinum-containing regimen (e.g., cisplatin, carboplatin);
   b. For extensive-stage SCLC: In combination with Tecentriq® or Tecentriq Hybreza™ for maintenance therapy following combination use with Tecentriq or Tecentriq Hybreza, carboplatin and etoposide;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 3.2 mg/m^2 every 21 days;
   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/ICHRA – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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. Small Cell Lung Cancer (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Zepzelca 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. New dose does not exceed 3.2 mg/m^2 every 21 days;
   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:
Medicaid/HIM/ICHRA – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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
SCLC: small cell lung cancer

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
cisplatin- or carboplatin-containing chemotherapy	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

Appendix D: General Information
On September 30, 2026, the FDA withdrew Zepzelca's accelerated approval for adults with metastatic small cell lung cancer whose disease progressed during or after platinum-based chemotherapy. The indication was initially granted in June 2020 based on tumor response rate and response duration; however, the phase 3 LAGOON confirmatory trial did not meet its primary endpoint.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
SCLC	3.2 mg/m^2 IV every 21 days	3.2 mg/m^2 per 21 days

VI. Product Availability

Single-dose vial: 4 mg

VII. References

1. Zepzelca Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; September 2026. Available at: https://www.zepzelca.com. Accessed October 15, 2026.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org. Accessed October 15, 2026.
3. National Comprehensive Cancer Network. Small Cell Lung Cancer Version 1.2027. Available at: https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. Accessed October 15, 2026.

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
J9223	Injection, lurbinectedin, 0.1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2022 annual review: no significant changes; removed option to bypass platinum containing regimen if contraindicated or clinically significant adverse effects are experienced per prescribing information; references reviewed and updated.	04.27.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.03.22	
3Q 2023 annual review: added monotherapy requirement per NCCN; references reviewed and updated.	04.13.23	08.23
3Q 2024 annual review: revised Commercial approval durations to "6 months or to the member's renewal date, whichever is longer" for this injectable drug; references reviewed and updated.	05.06.24	08.24
3Q 2025 annual review: no significant changes; references reviewed and updated.	04.09.25	08.25
RT4: added option for combination use with Tecentriq or Tecentriq Hybreza following combination use with Tecentriq or Tecentriq Hybreza, carboplatin and etoposide for extensive-stage SCLC per prescribing information; extended initial approval duration from 6 to 12 months for this maintenance medication for a chronic condition.	12.02.25	
3Q 2026 annual review: for continued therapy, removed single-agent requirement; added ICHRA line of business; references reviewed and updated.	04.15.26	08.26
RT4: updated FDA Approved Indication(s) section for withdrawal of SCLC monotherapy accelerated approval indication and added "off-label" parenthetical notation for the corresponding criteria per current NCCN support.	10.15.26	

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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