Zepzelca® (lurbinectedin)
(Intravenous)

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I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 6 months.
- Renewal: Prior authorization validity may be renewed every 6 months thereafter

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- 80 billable units every 21 days

III. Initial Approval Criteria [1]

Prior authorization validity is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Small Cell Lung Cancer † ‡ Φ [1-5,1e-4e]

- Used in combination with atezolizumab (intravenous or subcutaneous) as maintenance therapy; **AND**
  - Disease has not progressed following 4 cycles of first-line therapy with atezolizumab (intravenous or subcutaneous), carboplatin, and etoposide †; **AND**
    - Patient has extensive stage disease (ES-SCLC); **OR**
  - Disease has progressed or relapsed after a prolonged disease-free interval ‡; **AND**
    - Patient has at least stable disease following 4 cycles of subsequent therapy with atezolizumab (intravenous or subcutaneous), carboplatin, and etoposide; **AND**
    - Lurbinectedin has not been used previously; **AND**
    - Patient has an Eastern Cooperative Oncology Group (ECOG) performance status of 0-1; **AND**
    - Patient has no history of brain metastases; **OR**

- Used as a single agent; **AND**
  - Used for one of the following if not previously used:
    - Metastatic disease †
    - Relapsed or progressive disease ‡; **AND**
  - Patient has disease progression on or after platinum-based chemotherapy (i.e., cisplatin, carboplatin) †

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Prior authorization validity may be renewed based on the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: myelosuppression (e.g., neutropenia, thrombocytopenia, anemia, etc.), hepatotoxicity, extravasation resulting in tissue necrosis, rhabdomyolysis, etc.

V. Dosage/Administration [1]

Indication	Dose
Small Cell Lung Cancer	Administer 3.2 mg/m^2 by intravenous infusion every 21 days until disease progression or unacceptable toxicity.
** If discontinuation of atezolizumab (intravenous or subcutaneous) is required due to an immune-related severe adverse event, treatment with lurbinectedin may be continued at the same dose as a single agent.* ** If immune toxicity does not resolve or recurs despite discontinuation of atezolizumab (intravenous or subcutaneous), permanently discontinue lurbinectedin.*	

VI. Billing Code/Availability Information

HCPCS Code:

- J9223 – Injection, lurbinectedin, 0.1 mg; 1 billable unit = 0.1 mg

NDC:

- Zepzelca 4 mg single-dose vial for injection: 68727-0712-xx

VII. References (STANDARD)

1. Zepzelca [package insert]. Palo Alto, CA; Jazz Pharmaceuticals, Inc.; October 2025. Accessed October 2025.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) lurbinectedin. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed October 2025.
3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Small Cell Lung Cancer Version 2.2026. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed October 2025.
4. Trigo J, Subbiah V, Besse B, et al. Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial. Lancet Oncol. 2020 May;21(5):645-654. doi: 10.1016/S1470-2045(20)30068-1. Epub 2020 Mar 27.
5. Paz-Ares L, Borghaei H, Liu SV, et al. Efficacy and safety of first-line maintenance therapy with lurbinectedin plus atezolizumab in extensive-stage small-cell lung cancer (IMforte): a randomised, multicentre, open-label, phase 3 trial. *Lancet*. 2025;405(10495):2129-2143. doi:10.1016/S0140-6736(25)01011-6.

VIII. References (ENHANCED)

1e. von Pawel J, Schiller JH, Shepherd FA, et al. Topotecan versus cyclophosphamide, doxorubicin, and vincristine for the treatment of recurrent small-cell lung cancer. J Clin Oncol. 1999 Feb;17(2):658-67. doi: 10.1200/JCO.1999.17.2.658.

2e. O'Brien ME, Ciuleanu TE, Tsekov H, et al. Phase III trial comparing supportive care alone with supportive care with oral topotecan in patients with relapsed small-cell lung cancer. J Clin Oncol. 2006 Dec 1;24(34):5441-7. doi: 10.1200/JCO.2006.06.5821.

3e. Eckardt JR, von Pawel J, Pujol JL, et al. Phase III study of oral compared with intravenous topotecan as second-line therapy in small-cell lung cancer. J Clin Oncol. 2007 May 20;25(15):2086-92. doi: 10.1200/JCO.2006.08.3998. Erratum in: J Clin Oncol. 2007 Aug 1;25(22):3387.

4e. Edelman MJ, Dvorkin M, Laktionov K, et al. Randomized phase 3 study of the anti-disialoganglioside antibody dinutuximab and irinotecan vs irinotecan or topotecan for second-line treatment of small cell lung cancer. Lung Cancer. 2022;166:135-142
5e. Ahn MJ, Cho BC, Felip E, et al; DeLLphi-301 Investigators. Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer. N Engl J Med. 2023 Nov 30;389(22):2063-2075. doi: 10.1056/NEJMoa2307980. Epub 2023 Oct 20.
6e. Baize N, Monnet I, Greillier L, et al. Carboplatin plus etoposide versus topotecan as second-line treatment for patients with sensitive relapsed small-cell lung cancer: an open-label, multicentre, randomised, phase 3 trial. Lancet Oncol 2020;21:1224-1233.
7e. Paz-Ares L, Dvorkin M, Chen Y, Reinmuth N, Hotta K, et al. Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial. Lancet. 2019 Nov 23;394(10212):1929-1939. doi: 10.1016/S0140-6736(19)32222-6. Epub 2019 Oct 4. PMID: 31590988.
8e. Prime Therapeutics Management. Zepzelca Clinical Literature Review Analysis. Last updated October 2025. Accessed October 2025.

Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	No: PA not a priority
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus

ICD-10	ICD-10 Description
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C7A.1	Malignant poorly differentiated neuroendocrine tumors
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.12	Personal history of malignant neoplasm of trachea

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC