Evolent Clinical Guideline 3028 for Zepzelca™ (lurbinectedin)

Guideline Number:	Applicable Codes	
Evolent_CG_3028		
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Original Date:	**Last Revised Date:**	**Implementation Date:**
July 2020	February 2025	February 2025

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STATEMENT

Purpose

To define and describe the accepted indications for Zepzelca (lurbinectedin) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Small Cell Lung Cancer (SCLC)

- NOTE: Zepzelca (lurbinectedin) use is not supported by Evolent Policy for the treatment of metastatic/extensive stage Small Cell Lung Cancer (SCLC). The above policy position is supported by the following:
  - The FDA approval of Zepzelca (lurbinectedin) was an accelerated approval that was based on a phase II basket trial. The latter trial used surrogate endpoints such as Overall Response Rate. No confirmatory, randomized data are available to show superior survival, compared to other available standard-of-care alternatives (e.g., intravenous topotecan or the CAV regimen).
  - The ATLANTIS trial (referenced below), a randomized phase III trial, failed to show an overall survival benefit for Zepzelca (lurbinectedin) + doxorubicin over standard of care (e.g., intravenous topotecan or the CAV regimen) for second line therapy for extensive stage Small Cell Lung Cancer
  - There are no available randomized trial data to show superior outcomes with Zepzelca compared to standard of care second line therapy for extensive stage small cell lung cancer (e.g., intravenous topotecan or the CAV regimen).
  - Please refer to alternative agents/regimens recommended by Evolent at **Evolent Pathways**

CONTRAINDICATIONS/WARNINGS

- None

EXCLUSION CRITERIA

- Any neuro-endocrine carcinoma that is of non-lung (non-pulmonary) origin, for example, poorly differentiated neuroendocrine carcinoma of GI, GU, Head and Neck, and metastatic poorly differentiated neuroendocrine carcinoma of an Unknown Primary Origin. This exclusion is based on the lack of clinical trial evidence supporting the use of Zepzelca (lurbinectedin) in the above settings.
- Dosing exceeds single dose limit of Zepzelca (lurbinectedin) 3.2 mg/m^2.
- Investigational use of Zepzelca (lurbinectedin) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
  - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
  - Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
  - That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
  - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
  - That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J9223 - Injection, lurbinectedin, 0.1 mg

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
February 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1408 Zepzelca (lurbinectedin) • Updated exclusion criteria
February 2024	• Updated exclusion criteria • Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. Aix SP, et al. Combination lurbinectedin and doxorubicin versus physician's choice of chemotherapy in patients with relapsed small-cell lung cancer (ATLANTIS): a multicentre, randomised, open-label, phase 3 trial. *Lancet Respir Med*. 2023 Jan;11(1):74-86. doi: 10.1016/S2213-2600(22)00309-5.
2. Trigo J, 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.
3. Zepzelca prescribing information. Jazz Pharmaceuticals, Inc. Palo Alto, CA 2023.
4. Clinical Pharmacology Elsevier Gold Standard 2025.
5. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
6. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
7. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.
8. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
9. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.
10. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.