

Drug Policy:

Zepzelca™ (lurbinectedin)

POLICY NUMBER UM ONC_1408	SUBJECT Zepzelca™ (lurbinectedin)	DEPT/PROGRAM UM Dept	PAGE 1 of 3
DATES COMMITTEE REVIEWED 07/08/20, 07/14/21, 11/15/21, 03/09/22, 05/11/22, 02/08/23, 03/08/23	APPROVAL DATE March 8, 2023	EFFECTIVE DATE March 31, 2023	COMMITTEE APPROVAL DATES 07/08/20, 07/14/21, 11/15/21, 03/09/22, 05/11/22, 02/08/23, 03/08/23
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee	
URAC STANDARDS HUM v8: UM 1-2; UM 2-1	NCQA STANDARDS UM 2	ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS	APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

I. 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.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH 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.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this NCH policy provided:

1. The requested medication was used within the last year, **AND**
2. The member has not experienced disease progression and/or no intolerance to the requested medication, **AND**
3. Additional medication(s) are not being added to the continuation request.

B. Small Cell Lung Cancer (SCLC)

1. NOTE: Per NCH Policy, Zepzelca (lurbinectedin) is not approvable for the treatment of metastatic/extensive stage Small Cell Lung Cancer (SCLC). The above Policy Position is supported by the following:
 - a. The FDA approval of Zepzelca was an accelerated approval that was based on a phase II basket trial that used surrogate endpoints such as Overall Response Rate. No confirmatory data are available.
 - b. The ATLANTIS trial (referenced below), a randomized phase III trial, failed to show an Overall Survival benefit for Zepzelca + doxorubicin over standard of care second line therapy for extensive stage Small Cell Lung Cancer (e.g., intravenous topotecan or the CAV regimen).
 - c. 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.
 - d. Please refer to alternative agents/regimens recommended by NCH at <http://pathways.newcenturyhealth.com>.

III. EXCLUSION CRITERIA

- A. Disease progression while taking Zepzelca (lurbinectedin).
- B. Dosing exceeds single dose limit of Zepzelca (lurbinectedin) 3.2 mg/m².
- C. 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 lurbinectedin in the above settings.
- D. 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:
 1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
 2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
 3. 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.
 4. 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).
 5. 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.
 6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
 7. 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.

IV. MEDICATION MANAGEMENT

- A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

- A. Review – Utilization Management Department
- B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

- A. None

VII. REFERENCES

- A. 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.
- B. 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.
- C. Zepzelca prescribing information. Jazz Pharmaceuticals, Inc. Palo Alto, CA 2022.
- D. Clinical Pharmacology Elsevier Gold Standard 2023.
- E. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023.
- F. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.
- G. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2023.
- H. 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.
- I. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: <https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf>.
- J. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: <http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm>.
- K. NCQA UM 2023 Standards and Elements.