



Federal Employee Program.

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Section:	Prescription Drugs	Effective Date:	January 1, 2026
Subsection:	Antineoplastic Agents	Original Policy Date:	July 17, 2020
Subject:	Zepzelca	Page:	1 of 5

Last Review Date: December 12, 2025

Zepzelca

Description

Zepzelca (lurbinectedin)

Background

Zepzelca (lurbinectedin) is an alkylating drug that binds guanine residues in the minor groove of DNA, forming adducts and resulting in a bending of the DNA helix towards the major groove. Adduct formation triggers a cascade of events that can affect the subsequent activity of DNA binding proteins, including some transcription factors, and DNA repair pathways, resulting in perturbation of the cell cycle and eventual cell death (1).

Regulatory Status

FDA-approved indications: Zepzelca is an alkylating drug indicated: (1)

- In combination with atezolizumab or atezolizumab and hyaluronidase-tqjs, for maintenance treatment of adult patients with extensive-stage small cell lung cancer whose disease has not progressed after first-line induction therapy with atezolizumab or atezolizumab and hyaluronidase-tqjs, carboplatin and etoposide.
- For the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.

Zepzelca can cause myelosuppression. Treatment with Zepzelca should only be initiated if absolute neutrophil count (ANC) is at least 1,500 cells/mm³ and platelet count is at least 100,000/mm³. Blood counts should be monitored including neutrophil count and platelet count prior to each administration. For neutrophil count less than 500 cells/ mm³ or any value less than lower limit of normal, the use of G-CSF is recommended (1)

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Zepzelca can cause hepatotoxicity. Liver function tests should be monitored prior to initiation, periodically during treatment, and as clinically indicated (1).

Zepzelca can cause fetal harm when administered to a pregnant woman. Female patients of reproductive potential should be advised to use effective contraception during treatment with Zepzelca and for 6 months after the final dose. Male patients with female partners of reproductive potential should be advised to use effective contraception during treatment with Zepzelca and for 4 months after the final dose (1).

The safety and effectiveness of Zepzelca in pediatric patients less than 18 years of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Zepzelca may be considered **medically necessary** if the conditions indicated below are met.

Zepzelca may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Extensive-stage small cell lung cancer (SCLC)
 - a. Used for maintenance treatment
 - b. Used in combination with Tecentriq (atezolizumab) or Tecentriq Hybreza (atezolizumab and hyaluronidase-tqjs)

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- c. Disease has not progressed after first-line induction therapy with Tecentriq (atezolizumab) or Tecentriq Hybreza (atezolizumab and hyaluronidase-tqjs), carboplatin and etoposide
- 2. Metastatic small cell lung cancer (SCLC)
 - a. Disease progression on or after platinum-based chemotherapy

AND ALL of the following:

- a. Baseline neutrophil count is $\geq 1,500$ cells/mm³
- b. Baseline platelet count is $\geq 100,000$ /mm³
- c. Prescriber agrees to monitor for myelosuppression and hepatotoxicity
- d. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Zepzelca and for 6 months after the final dose
- e. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Zepzelca and for 4 months after the final dose

Prior – Approval Renewal Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

- 1. Extensive-stage small cell lung cancer (SCLC)
- 2. Metastatic small cell lung cancer (SCLC)

AND ALL of the following:

- a. **NO** disease progression or unacceptable toxicity
- b. Prescriber agrees to monitor for myelosuppression and hepatotoxicity
- c. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Zepzelca and for 6 months after the final dose
- d. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Zepzelca and for 4 months after the final dose

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Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval Renewal Limits

Same as above

Rationale

Summary

Zepzelca (lurbinectedin) is an alkylating drug that binds guanine residues in the minor groove of DNA, forming adducts and resulting in a bending of the DNA helix towards the major groove. Adduct formation triggers a cascade of events that can affect the subsequent activity of DNA binding proteins, including some transcription factors, and DNA repair pathways, resulting in perturbation of the cell cycle and eventual cell death. The safety and effectiveness of Zepzelca in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Zepzelca while maintaining optimal therapeutic outcomes.

References

1. Zepzelca [package insert]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; October 2025.
2. NCCN Drugs & Biologics Compendium® Lurbinectedein 2025. National Comprehensive Cancer Network, Inc. Accessed on November 5, 2025.

Policy History

Date	Action
July 2020	Addition to PA
September 2020	Annual review
December 2021	Annual review and reference update
December 2022	Annual review and reference update
March 2023	Annual review and reference update
March 2024	Annual review and reference update

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September 2024 Annual review and reference update
March 2025 Annual review and reference update
October 2025 Per PI update, added indication of extensive-stage small cell lung cancer
December 2025 Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 12, 2025 and is effective on January 1, 2026.