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Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	July 17, 2020
Subject:	Zepzelca	**Page:**	1 of 4

Last Review Date: March 8, 2024

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 indication: Zepzelca is indicated for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy (1).

Zepzelca can cause myelosuppression. Treatment with Zepzelca should only be initiated if absolute neutrophil count (ANC) is at least 1,500 cells/mm^3 and platelet count is at least 100,000/mm^3. Blood counts should be monitored including neutrophil count and platelet count prior to each administration. For neutrophil count less than 500 cells/ mm^3 or any value less than lower limit of normal, the use of G-CSF is recommended (1).

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

Diagnosis

Patient must have the following:

Metastatic small cell lung cancer (SCLC)

AND ALL of the following:

a. Disease progression on or after platinum-based chemotherapy
b. Baseline neutrophil count is ≥1,500 cells/mm^3
c. Baseline platelet count is ≥100,000/mm^3
d. Prescriber agrees to monitor for myelosuppression and hepatotoxicity

e. 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
f. 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

Diagnosis

Patient must have the following:

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

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.; July 2023.
2. NCCN Drugs & Biologics Compendium® Lurbinectedein 2024. National Comprehensive Cancer Network, Inc. Accessed on January 22, 2024.

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

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.