ZEPZELCA® (lurbinectedin) for injection 4 mg

A GUIDE TO *ZEPZELCA®* (lurbinectedin)

FOR ADVANCED PRACTICE PROVIDERS AND PHARMACISTS

Pursue more at **ZEPZELCAPro.com**

INDICATION

ZEPZELCA® (lurbinectedin) is indicated for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

Myelosuppression

ZEPZELCA can cause myelosuppression. In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA, Grade 3 or 4 neutropenia occurred in 41% of patients, with a median time to onset of 15 days and a median duration of 7 days. Febrile neutropenia occurred in 7% of patients.

Sepsis occurred in 2% of patients and was fatal in 1% (all cases occurred in patients with solid tumors other than SCLC). Grade 3 or 4 thrombocytopenia occurred in 10%, with a median time to onset of 10 days and a median duration of 7 days. Grade 3 or 4 anemia occurred in 17% of patients.

Please see pages 14 and 15 for Important Safety Information and accompanying full Prescribing Information.

For adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy,

PURSUE A RESPONSE WITH *ZEPZELCA*® (lurbinectedin)

105 adults with SCLC with disease progression received at least 1 prior line of platinum-based chemotherapy

ECOG PS ≤2

→

ZEPZELCA 3.2 mg/m²

administered as a 60-minute infusion every 21 days

→

Treatment continued until disease progression or unacceptable toxicity

Study design[1,2]

The phase 2 study was a multicenter, open-label, multi-cohort trial evaluating ZEPZELCA as a single agent in 105 adult patients with advanced or metastatic SCLC with disease progression on or after platinum-based chemotherapy. Patients received ZEPZELCA 3.2 mg/m² by intravenous infusion every 21 days (one cycle) for a median of 4 cycles (range: 1 to 24 cycles). The median age was 60 years (range: 40 to 83 years). Baseline ECOG Performance Status was 0–1 in 92% of patients. The major efficacy outcome measure was confirmed investigator-assessed ORR. Additional efficacy outcome measures included duration of response and an independent review committee (IRC)-assessed ORR using Response Evaluation Criteria In Solid Tumors version 1.1. The proportion of patients with disease control (a complete response [CR], partial response [PR], or stable disease [SD]) was an exploratory outcome measure.

ZEPZELCA inhibits transcription, a key process in SCLC pathology[1,3,4]

ZEPZELCA binds to guanine residues in the minor groove of DNA, affecting activity of transcription factors, which stalls RNA polymerase II, affects DNA repair pathways, and results in eventual cell death.[1,5]

*According to Response Evaluation Criteria In Solid Tumors v1.1. CR: Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to <10 mm. PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. SD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease, taking as reference the smallest sum diameters while on study.[6]

†Includes 5 patients with partial response not confirmed.[2,7]

‡Median in months.

In the overall population,

>1 in 3 patients achieved ORR by the investigator assessment[1]

- 35% (95% CI: 26–45) by investigator assessment
  — CR=0%; PR=35%
- 30% (95% CI: 22–40) by IRC assessment
  — CR=0%; PR=30%

Exploratory analysis of disease control rate (DCR) with ZEPZELCA

- **69%** (95% CI: 58.8–77.3) of patients achieved **DCR** (CR + PR + SD) by investigator assessment[2*]
  — CR=0%; PR=35%; SD=33%†
- **62%** (95% CI: 51.9–71.2) of patients achieved **DCR** by IRC assessment[7*†]
  — CR=0%; PR=31%; SD=31%†

Limitations of DCR data

No conclusions about efficacy can be drawn from these descriptive data because they are results from exploratory end points in a phase 2, single-arm study.

In a phase 2, single-arm study of 105 adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy

ZEPZELCA demonstrated clinically meaningful duration of response (N=105)[1]

- **5.3 months**‡ (95% CI: 4.1–6.4) by investigator assessment
- **5.1 months**‡ (95% CI: 4.9–6.4) by IRC assessment

CR=complete response; ECOG=Eastern Cooperative Oncology Group; ORR=overall response rate; PR=partial response; SD=stable disease.

IMPORTANT SAFETY INFORMATION (*CONTINUED*)

Myelosuppression (*continued*)

Administer ZEPZELCA only to patients with baseline neutrophil count of at least 1,500 cells/mm³ and platelet count of at least 100,000/mm³.

Monitor blood counts 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. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.

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ONE-HOUR DOSING, EVERY 21 DAYS MEANS MINIMAL INFUSION VISITS

Recommended Dosage of ZEPZELCA® (lurbinectedin)[1]

ZEPZELCA for injection	60-minute IV infusions	Administered every 21 days
		 Until disease progression or unacceptable toxicity

Initiate treatment with ZEPZELCA only if absolute neutrophil count is ≥1,500 cells/mm^3 and platelet count is ≥100,000/mm^3.[1]

Premedication[1]

Consider administering the following pre-infusion medications to antiemetic prophylaxis:

- Corticosteroids (intravenous dexamethasone 8 mg or equivalent)
- Serotonin antagonists (intravenous ondansetron 8 mg or equivalent)

A Straightforward Dose-Reduction Schedule to Help Manage Adverse Reactions[1]

First dose reduction	Second dose reduction
2.6 mg/m^2 every 21 days	2 mg/m^2 every 21 days

Permanently discontinue ZEPZELCA in patients who are unable to tolerate 2 mg/m^2 or require a dose delay greater than 2 weeks.[1]

Discontinue ZEPZELCA if patients are unable to tolerate 2 mg/m^2 every 21 days.[1]

IMPORTANT SAFETY INFORMATION (*CONTINUED*)

Hepatotoxicity

ZEPZELCA can cause hepatotoxicity. In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA, Grade 3 elevations of ALT and AST were observed in 6% and 3% of patients, respectively, and Grade 4 elevations of ALT and AST were observed in 0.4% and 0.5% of patients, respectively. The median time to onset of Grade ≥3 elevation in transaminases was 8 days (range: 3 to 49), with a median duration of 7 days.

Monitor liver function tests, prior to initiating ZEPZELCA, periodically during treatment, and as clinically indicated. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.

Dosage Modification for Adverse Reactions[1]

Adverse reaction	Severity[a]	Dosage modification
Neutropenia[b]	Grade 4 or any grade febrile neutropenia	• Withhold ZEPZELCA until Grade ≤1 • Resume ZEPZELCA at a reduced dose
Thrombocytopenia	Grade 3 with bleeding or Grade 4	• Withhold ZEPZELCA until platelet ≥100,000/mm^3 • Resume ZEPZELCA at reduced dose
Hepatotoxicity	Grade 2	• Withhold ZEPZELCA until Grade ≤1 • Resume ZEPZELCA at same dose
	Grade ≥3	• Withhold ZEPZELCA until Grade ≤1 • Resume ZEPZELCA at reduced dose or permanently discontinue
Rhabdomyolysis	Grade 2	• Withhold ZEPZELCA until Grade ≤1 • Resume ZEPZELCA at same dose
	Grade ≥3	• Permanently discontinue ZEPZELCA
Other Adverse Reactions	Grade 2	• Withhold ZEPZELCA until Grade ≤1 • Resume ZEPZELCA at same dose
	Grade ≥3	• Withhold ZEPZELCA until Grade ≤1 • Resume ZEPZELCA at reduced dose or permanently discontinue

[a]National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.0.
[b]Patients with isolated Grade 4 neutropenia (neutrophil count less than 500 cells/mm^3) may receive G-CSF=granulocyte colony-stimulating factor prophylaxis rather than undergo lurbinectedin dose reduction.

- For neutrophil count <500 cells/mm^3 or any value less than lower limit of normal, the use of G-CSF is recommended[1]

IMPORTANT SAFETY INFORMATION (*CONTINUED*)

Extravasation Resulting in Tissue Necrosis

Extravasation of ZEPZELCA resulting in skin and soft tissue injury, including necrosis requiring debridement, can occur. Consider use of a central venous catheter to reduce the risk of extravasation, particularly in patients with limited venous access. Monitor patients for signs and symptoms of extravasation during the ZEPZELCA infusion.

If extravasation occurs, immediately discontinue the infusion, remove the infusion catheter, and monitor for signs and symptoms of tissue necrosis. The time to onset of necrosis after extravasation may vary.

Administer supportive care and consult with an appropriate medical specialist as needed for signs and symptoms of extravasation. Administer subsequent infusions at a site that was not affected by extravasation.

Rhabdomyolysis

Rhabdomyolysis has been reported in patients treated with ZEPZELCA.

Monitor creatine phosphokinase (CPK) prior to initiating ZEPZELCA and periodically during treatment as clinically indicated. Withhold or reduce the dose based on severity

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PREPARATION, ADMINISTRATION, AND STORAGE

ZEPZELCA® (lurbinectedin) is a hazardous drug. Follow applicable special handling and disposal procedures.[1]

Preparation[1]

- Inject 8 mL of Sterile Water for Injection USP into the vial, yielding a solution containing 0.5 mg/mL of ZEPZELCA. Shake the vial until complete dissolution
- Visually inspect the solution for particulate matter and discoloration. The reconstituted solution is a clear, colorless, or slightly yellowish solution, essentially free of visible particles
- Calculate the required volume of reconstituted solution as follows:

$$\text{Volume (mL)} = \frac{\text{Body Surface Area (m}^2\text{) x Individual Dose (mg/m}^2\text{)}}{\text{0.5 mg/mL}}$$

- Central venous line: Withdraw the appropriate amount of reconstituted solution from the vial and add to an infusion container containing at least 100 mL of diluent*
- Peripheral venous line: Withdraw the appropriate amount of reconstituted solution from the vial and add to an infusion container containing at least 250 mL of diluent*

Administration[1]

- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If particulate matter is observed, do not administer
- ZEPZELCA can be administered with or without an in-line filter. If infusion lines containing in-line filters are utilized for administration of ZEPZELCA, polyethersulfone (PES) in-line filters with pore sizes of 0.22 micron are recommended
  - Do not use in-line nylon membrane filters when the reconstituted ZEPZELCA solution is diluted using 0.9% Sodium Chloride Injection, USP. Adsorption of ZEPZELCA to the nylon membrane filters has been observed when 0.9% Sodium Chloride Injection, USP is used as the diluent
- Compatibility with other intravenous administration materials and the diluted ZEPZELCA solution has been demonstrated in the following materials:
  - Polyolefin containers (polyethylene, polypropylene, and mixtures)
  - Polyvinyl Chloride (PVC) (non-DEHP-containing), polyurethane, and polyolefin infusion sets (polyethylene, polypropylene, and polybutadiene)
  - Implantable venous access systems with titanium and plastic resin ports and with polyurethane or silicone intravenous catheters
- Do not co-administer ZEPZELCA and other intravenous drugs concurrently within the same intravenous line

Storage of Infusion Solution[1]

- If not used immediately after reconstitution or dilution, the ZEPZELCA solution can be stored prior to administration for up to 24 hours following reconstitution, including infusion time, at either room temperature/ambient light or under refrigerated (2 °C–8 °C; 36 °F–46 °F) conditions†

*Diluent for ZEPZELCA should be 0.9% Sodium Chloride Injection USP or 5% Dextrose Injection USP.
†Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If particulate matter is observed, do not administer.

IMPORTANT SAFETY INFORMATION (*CONTINUED*)

Embryo-Fetal Toxicity

ZEPZELCA can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise female patients of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 6 months after the final dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 4 months after the final dose.

Lactation

There are no data on the presence of ZEPZELCA in human milk, however, because of the potential for serious adverse reactions from ZEPZELCA in breastfed children, advise women not to breastfeed during treatment with ZEPZELCA and for 2 weeks after the final dose.

MOST COMMON ADVERSE REACTIONS

The most common adverse reactions, including laboratory abnormalities, (≥20%) are leukopenia (79%), lymphopenia (79%), fatigue (77%), anemia (74%), neutropenia (71%), increased creatinine (69%), increased alanine aminotransferase (66%), increased glucose (52%), thrombocytopenia (37%), nausea (37%), decreased appetite (33%), musculoskeletal pain (33%), decreased albumin (32%), constipation (31%), dyspnea (31%), decreased sodium (31%), increased aspartate aminotransferase (26%), vomiting (22%), decreased magnesium (22%), cough (20%), and diarrhea (20%).

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ZEPZELCA® (lurbinectedin) DEMONSTRATED A SAFETY PROFILE WITH A LOW DISCONTINUATION RATE DUE TO ADVERSE REACTIONS

Most adverse reactions were Grade 1 or 2[1,7]

Adverse Reactions (≥10%) in Patients With SCLC[1]

Adverse reaction	ZEPZELCA (N=105)	
	All Grades[a,b] (%)	Grades 3–4 (%)
General disorders		
Fatigue	77	12
Pyrexia	13	0
Chest pain	10	0
Gastrointestinal disorders		
Nausea	37	0
Constipation	31	0
Vomiting	22	0
Diarrhea	20	4
Abdominal pain[c]	11	1
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain[d]	33	4
Metabolism and nutrition disorders		
Decreased appetite	33	1

IMPORTANT SAFETY INFORMATION (*CONTINUED*)

DRUG INTERACTIONS

Strong and Moderate CYP3A Inhibitors
Avoid coadministration with a strong or a moderate CYP3A inhibitor as this increases lurbinectedin systemic exposure which may increase the incidence and severity of adverse reactions to ZEPZELCA. If coadministration of ZEPZELCA with a moderate CYP3A inhibitor cannot be avoided, consider dose reduction of ZEPZELCA, if clinically indicated.

Strong and Moderate CYP3A Inducers
Avoid coadministration with a strong or moderate CYP3A inducer. Coadministration with a strong CYP3A inducer decreases lurbinectedin systemic exposure which may reduce ZEPZELCA efficacy.

Adverse Reactions (≥10%) in Patients With SCLC[1] (*continued*)

Adverse reaction	ZEPZELCA (N=105)	
	All Grades[a,b] (%)	Grades 3–4 (%)
Respiratory, thoracic, and mediastinal disorders		
Dyspnea	31	6
Cough[e]	20	0
Infections and infestations		
Respiratory tract infection[f]	18	5
Pneumonia[g]	10	7
Nervous system disorders		
Peripheral neuropathy[h]	11	1
Headache	10	1

[a]Graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) 4.0.
[b]No grade 5 adverse reactions were reported.
[c]Includes abdominal pain, abdominal pain upper, and abdominal discomfort.
[d]Includes musculoskeletal pain, back pain, arthralgia, pain in extremity, musculoskeletal chest pain, neck pain, bone pain, and myalgia.
[e]Includes cough and productive cough.
[f]Includes upper respiratory tract infection, viral upper respiratory tract infection, respiratory tract infection, and bronchitis.
[g]Includes pneumonia and lung infection.
[h]Includes neuropathy peripheral, neuralgia, paresthesia, peripheral sensory neuropathy, hypoesthesia, and hyperesthesia.

Alopecia occurred in 1% of patients[7]

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ZEPZELCA® (lurbinectedin) DEMONSTRATED A SAFETY PROFILE WITH A LOW DISCONTINUATION RATE DUE TO ADVERSE REACTIONS (*CONTINUED*)

Select Laboratory Abnormalities (≥20%) Worsening From Baseline[1]

	ZEPZELCA (N=105)	
Laboratory abnormalities	**All Grades[a,b] (%)**	**Grades 3–4 (%)**
Hematology		
Decreased leukocytes	79	29
Decreased lymphocytes	79	43
Decreased hemoglobin	74	10
Decreased neutrophils	71	46
Decreased platelets	37	7
Chemistry		
Increased creatinine	69	0
Increased alanine aminotransferase	66	4
Increased glucose	52	5
Decreased albumin	32	1
Decreased sodium	31	7
Increased aspartate aminotransferase	26	2
Decreased magnesium	22	0

[a]The denominator used to calculate the rate varied from 95 to 105 based on the number of patients with a baseline value and at least one post-treatment value.
[b]Graded per NCI CTCAE 4.0.

- In the phase 2 study, 22% of patients received G-CSF for secondary prophylaxis or therapy for neutropenia, but primary prophylaxis was not allowed[1,2]

Permanent discontinuation due to an adverse reaction occurred in 1.9% of patients with SCLC (2 of 105).[1]

- Adverse reactions resulting in permanent discontinuation in ≥1% of patients included peripheral neuropathy and myelosuppression

Dosage interruptions due to an adverse reaction occurred in 30.5% of patients.[1]

- Adverse reactions requiring dosage interruption in ≥3% of patients included neutropenia and hypoalbuminemia

Dosage reductions due to an adverse reaction occurred in 25% of patients.[1]

- Adverse reactions requiring dosage reductions in ≥3% of patients included neutropenia, febrile neutropenia, and fatigue

MONITORING GUIDELINES FOR *ZEPZELCA*

Monitoring[1]	
Myelosuppression	• Administer ZEPZELCA only to patients with baseline neutrophil count of at least 1,500 cells/mm^3 and platelet count of at least 100,000/mm^3 • Monitor blood counts 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 • Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity
Hepatotoxicity	• Monitor liver function tests prior to initiating ZEPZELCA and periodically during treatment as clinically indicated • Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity
Extravasation Resulting in Tissue Necrosis	• Consider use of a central venous catheter to reduce the risk of extravasation, particularly in patients with limited venous access • Monitor patients for signs and symptoms of extravasation during the ZEPZELCA infusion • If extravasation occurs, immediately discontinue the infusion, remove the infusion catheter, and monitor for signs and symptoms of tissue necrosis • The time to onset of necrosis after extravasation may vary • Administer supportive care and consult with an appropriate medical specialist as needed for signs and symptoms of extravasation • Administer subsequent infusions at a site that was not affected by extravasation
Rhabdomyolysis	• Monitor creatine phosphokinase (CPK) prior to initiating ZEPZELCA and periodically during treatment as clinically indicated • Withhold or reduce the dose based on severity

IMPORTANT SAFETY INFORMATION (*CONTINUED*)

GERIATRIC USE

Of the 105 patients with SCLC administered ZEPZELCA in clinical studies, 37 (35%) patients were 65 years of age and older, while 9 (9%) patients were 75 years of age and older. No overall difference in effectiveness was observed between patients aged 65 and older and younger patients.

There was a higher incidence of serious adverse reactions in patients ≥65 years of age than in patients <65 years of age (49% vs 26%, respectively). The serious adverse reactions most frequently reported in patients ≥65 years of age were related to myelosuppression and consisted of febrile neutropenia (11%), neutropenia (11%), thrombocytopenia (8%), and anemia (8%).

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PATIENT SUPPORT

JazzCares™
Making a difference in Patients' lives, one Patient at a time

JazzCares is committed to helping your patients get access to their ZEPZELCA® (lurbinectedin) medication and providing personalized support throughout their treatment

Dedicated JazzCares specialists assist patients and practices with:

- Benefit investigation—helps patients understand their insurance coverage for ZEPZELCA
- Prior authorization support
- Appeals support
- Billing and coding information
- Referrals to other financial assistance

Reduction of out-of-pocket costs for ZEPZELCA for eligible patients

Savings Card—eligible, commercially insured patients can pay as little as $10 for their ZEPZELCA medication, subject to an annual maximum

Free drug program for eligible patients

Learn more about JazzCares support offerings by calling 1-833-533-JAZZ (5299) Monday–Friday, 8 AM to 8 PM ET, or visit JazzCares.com

Insurance coverage and plans may vary. The JazzCares program at Jazz Pharmaceuticals provides general information only and is not a guarantee of any coverage or reimbursement outcome. All treatment decisions rest solely with the treating physician or qualified healthcare professional. Jazz Pharmaceuticals reserves the right to terminate or modify this program at any time with or without notice. Other terms and conditions apply.

ORDERING INFORMATION

J-code for ZEPZELCA

Permanent, product-specific HCPCS J-code for ZEPZELCA	J9223

Order ZEPZELCA through our distribution partners

Specialty distributors

ZEPZELCA is available for purchase from the authorized Specialty Distributors listed below. Verify that your facility has an account with their Specialty Distributor before ordering. If not, they should contact their Specialty Distributor. The facility should also contact their Specialty Distributor with questions regarding product returns.

AmerisourceBergen

ASD Healthcare	Oncology Supply
ASD Healthcare Phone/Fax: (800) 746-6273/(800) 547-9413 Online: https://www.asdhealthcare.com/home	Oncology Supply Phone/Fax: (800) 633-7555/(800) 248-8205 Online: https://www.oncologysupply.com

Cardinal Health

Cardinal Health
Phone/Fax: (877) 453-3972/(877) 274-9897 Online: Order Express (Hospitals) https://orderexpress.cardinalhealth.com Specialty Online (Clinics): https://specialtyonline.cardinalhealth.com

McKesson

McKesson Plasma and Biologics (MPB)	McKesson Specialty Health (MSH)
Phone/Fax: (877) 625-2566/(888) 752-7626 Online: https://connect.mckesson.com	Phone/Fax: (800) 482-6700/(800) 289-9285 Online: http://MSCS.McKesson.com

Group Purchasing Organizations (GPOs)
ZEPZELCA is available through:

- ION Solutions (AmerisourceBergen®)
- Unity GPO (The US Oncology Network/McKesson)
- Onmark® GPO (McKesson)
- VitalSource™ (Cardinal Health™)

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Extravasation Resulting in Tissue Necrosis

Extravasation of ZEPZELCA resulting in skin and soft tissue injury, including necrosis requiring debridement, can occur. Consider use of a central venous catheter to reduce the risk of extravasation, particularly in patients with limited venous access. Monitor patients for signs and symptoms of extravasation during the ZEPZELCA infusion.

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Rhabdomyolysis

Rhabdomyolysis has been reported in patients treated with ZEPZELCA.

Monitor creatine phosphokinase (CPK) prior to initiating ZEPZELCA and periodically during treatment as clinically indicated. Withhold or reduce the dose based on severity.

Embryo-Fetal Toxicity

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Lactation

There are no data on the presence of ZEPZELCA in human milk, however, because of the potential for serious adverse reactions from ZEPZELCA in breastfed children, advise women not to breastfeed during treatment with ZEPZELCA and for 2 weeks after the final dose.

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DRUG INTERACTIONS

Strong and Moderate CYP3A Inhibitors

Avoid coadministration with a strong or a moderate CYP3A inhibitor as this increases lurbinectedin systemic exposure which may increase the incidence and severity of adverse reactions to ZEPZELCA. If coadministration of ZEPZELCA with a moderate CYP3A inhibitor cannot be avoided, consider dose reduction of ZEPZELCA, if clinically indicated.

Strong and Moderate CYP3A Inducers

Avoid coadministration with a strong or moderate CYP3A inducer. Coadministration with a strong CYP3A inducer decreases lurbinectedin systemic exposure which may reduce ZEPZELCA efficacy.

GERIATRIC USE

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Please see accompanying full Prescribing Information.

References: 1. ZEPZELCA (lurbinectedin). Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **2.** 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;21(5):645-654. **3.** Farago AF, Drapkin BJ, Lopez-Vilarino de Ramos JA, et al. ATLANTIS: a Phase III study of lurbinectedin/doxorubicin versus topotecan or cyclophosphamide/doxorubicin/vincristine in patients with small-cell lung cancer who have failed one prior platinum-containing line. *Future Oncol.* 2019;15(3):231-239. **4.** Christensen CL, Kwiatkowski N, Abraham BJ, et al. Targeting transcriptional addictions in small cell lung cancer with a covalent CDK7 inhibitor. *Cancer Cell.* 2014;26(6):909-922. **5.** Santamaría Nuñez G, Robles CM, Giraudon C, et al. Lurbinectedin specifically triggers the degradation of phosphorylated RNA polymerase II and the formation of DNA breaks in cancer cells. *Mol Cancer Ther.* 2016;15(10):2399-2412. **6.** Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer.* 2009;45(2):228-247. **7.** Data on file. LUR-2020-003. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **8.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Small Cell Lung Cancer. V.2.2022.

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✔ NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[8]*

- **Lurbinectedin (ZEPZELCA) is a category 2A recommended treatment option** for patients with SCLC who relapse **≤6 months** *or* **>6 months**† following first-line platinum-based chemotherapy‡
- **Lurbinectedin is a category 2A, preferred treatment option** for patients with SCLC who relapse ≤6 months with ECOG PS 0–2‡

*See the NCCN Guidelines® for SCLC for detailed recommendations, including other treatment options.
†Other recommended regimen.
‡**Category 2A:** Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate. Note that *Category 2A* and *Preferred* are two separate recommendations.[8]

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Important Patient Counseling Information[1]

Myelosuppression
Advise patients to immediately contact their healthcare provider for fever, other signs of infection, unusual bruising, bleeding, tiredness or pallor.

Hepatotoxicity
Advise patients to contact their healthcare provider immediately for signs and symptoms suggestive of hepatotoxicity.

Extravasation Resulting in Tissue Necrosis
Advise patients to contact their healthcare provider immediately for signs and symptoms extravasation. The time to onset of necrosis after extravasation may vary.

Rhabdomyolysis
Advise patients to contact their healthcare provider immediately for signs and symptoms rhabdomyolysis.

Embryo-Fetal Toxicity
- Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females to inform their healthcare provider of a known or suspected pregnancy.
- Advise females of reproductive potential to use effective contraception during treatment with ZEPZELCA® (lurbinectedin) and for 6 months after the final dose.
- Advise males with female partners of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 4 months after the final dose.

Lactation
Advise women not to breastfeed during treatment with ZEPZELCA and for at least 2 weeks after the final dose.

Drug Interactions
Advise patients to inform their healthcare providers of all concomitant medications, herbal and dietary supplements. Advise patients to avoid grapefruit products during treatment with ZEPZELCA.

Please see pages 14 and 15 for Important Safety Information and accompanying full Prescribing Information.

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