ZEPZELCA®
(lurbinectedin) for injection 4 mg

For your adult patients with metastatic small cell lung cancer (mSCLC) with disease progression on or after platinum-based chemotherapy[1]

When it's time to consider changing course,

PURSUE WHAT MATTERS

#1Rx

ZEPZELCA is the #1-PRESCRIBED medication in the second-line treatment of SCLC* following first-line platinum-based therapies with over 17,000 adult patients treated to date in the United States.[2]

Total number of patients treated is determined as total vials sold divided by 7.3 (average vials per patient) based on SHA claims data from July 2020–May 2023.

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.

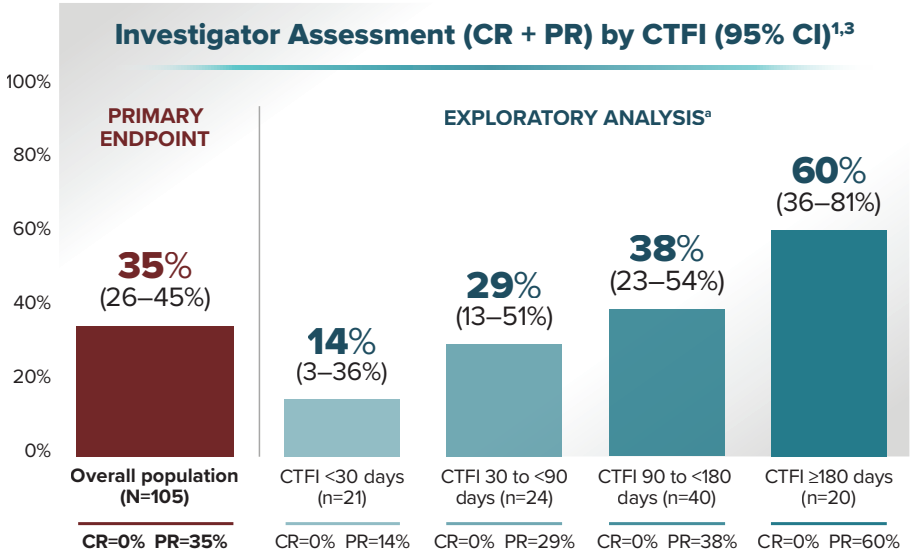
Sepsis occurred in 2% of patients and was fatal in 1% (all cases occurred in patients with solid tumors other than SCLC). Grade 3 or 4 thrombocytopenia occurred in 10%, with a median time to onset of 10 days and a median duration of 7 days. Grade 3 or 4 anemia occurred in 17% of patients.

Please see Important Safety Information throughout and full Prescribing Information.

SCLC=small cell lung cancer.

*Source: Symphony Health Solutions claims data: July 2020–May 2023.

Overall response rate by investigator assessment



Limitations of Data

[a]This exploratory subgroup analysis was not powered to determine statistical significance. Results are descriptive only.

In the overall population, >1 IN 3 PATIENTS ACHIEVED AN OVERALL REPONSE with ZEPZELCA® (lurbinectedin) by the investigator assessment[1]

IMPORTANT SAFETY INFORMATION *(CONTINUED)*

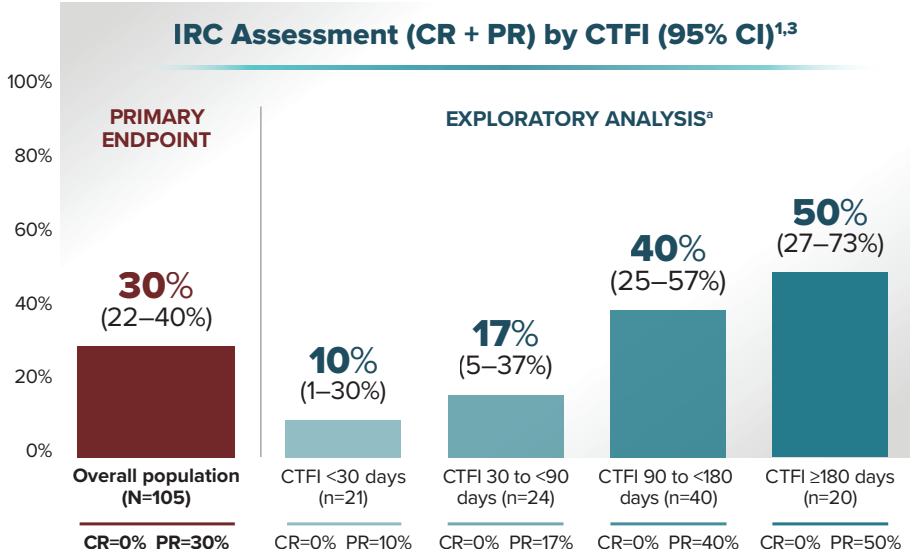
Myelosuppression (*continued*)

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.

Please see Important Safety Information throughout and full Prescribing Information.

Overall response rate by IRC assessment



Limitations of Data

[a]This exploratory subgroup analysis was not powered to determine statistical significance. Results are descriptive only.

Study Design[1,4]

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/m^2 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 PS 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 IRC-assessed ORR using Response Evaluation Criteria in Solid Tumors v1.1.

CR=complete response; CTFI=chemotherapy-free interval; ECOG PS=Eastern Cooperative Oncology Group Performance Status; IRC=independent review committee; ORR=overall response rate; PR=partial response; SCLC=small cell lung cancer.

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.

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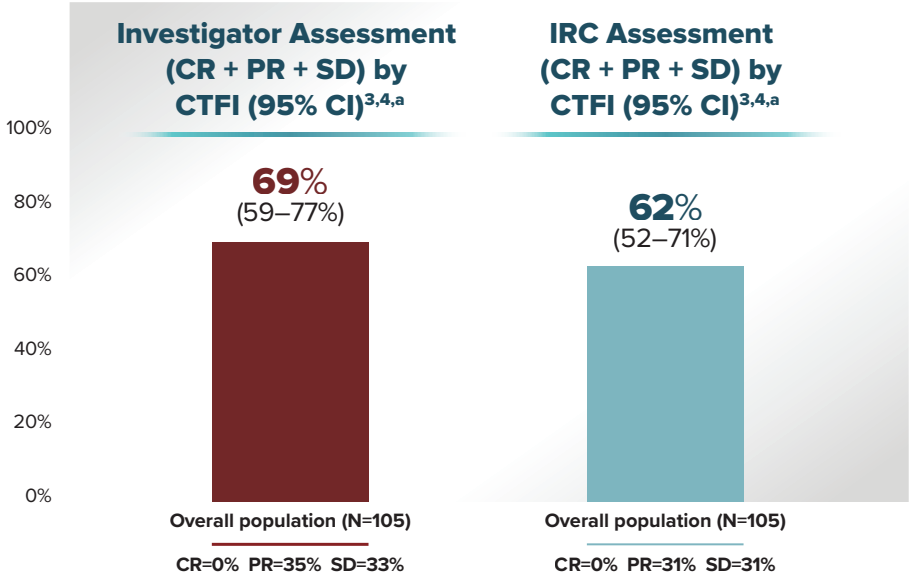
Exploratory analysis of disease control rate



Limitations of Data

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

[a]According to Response Evaluation Criteria in Solid Tumors version 1.1 Complete response (CR): Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to <10 mm. Partial response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Stable disease (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.[5]

IMPORTANT SAFETY INFORMATION *(CONTINUED)*

Hepatotoxicity *(Continued)*

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.

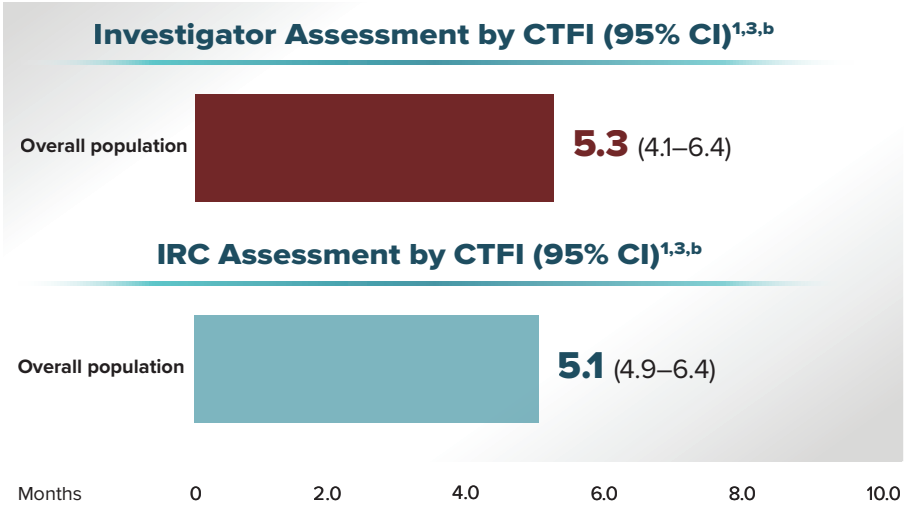
Extravasation Resulting in Tissue Necrosis

Extravasation of ZEPZELCA® (lurbinectedin) 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.

Please see Important Safety Information throughout and full Prescribing Information.

Clinically meaningful duration of response (median, in months)



[b]Duration of response analysis is based on patients who responded to treatment.

Of 8 patients who had received prior immunotherapy as first- or second-line treatment[4,c]:

- Duration of response was consistent with the overall population at a **median of 5.3 months** (range: 2.8–6.4 months)[1,4,c]

Limitations of Data

[c]This exploratory subgroup analysis was post hoc and not powered to determine statistical significance. Results are descriptive only.

CI=confidence interval; CR=complete response; CTFI=chemotherapy-free interval; DCR=disease control rate; IRC=independent review committee; PR=partial response; SCLC=small cell lung cancer; SD=stable disease.

IMPORTANT SAFETY INFORMATION *(CONTINUED)*

Extravasation Resulting in Tissue Necrosis *(Continued)*

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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ZEPZELCA® (lurbinectedin) has an established safety profile

Most adverse reactions were[1,3]
GRADE 1 OR 2

- **1.9% of patients (2 of 105) permanently discontinued due to adverse reactions[1]**
  - Adverse reactions resulting in permanent discontinuation in ≥1% of patients included peripheral neuropathy and myelosuppression[1]
- **Dose 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
- **Dose interruptions due to an adverse reaction occurred in 30.5% of patients[1]**
  - Adverse reactions requiring dosage interruptions in ≥3% of patients included neutropenia and hypoalbuminemia

ADVERSE REACTIONS (≥10%) IN PATIENTS WITH SCLC[1]

Adverse reaction	ZEPZELCA® (lurbinectedin) (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

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 last dose.

Please see Important Safety Information throughout and full Prescribing Information.

ADVERSE REACTIONS (≥10%) IN PATIENTS WITH SCLC[1] (cont'd)

Adverse reaction	ZEPZELCA (N=105)	
	All Grades[a,b] (%)	Grades 3–4 (%)
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain[d]	33	4
Metabolism and nutrition disorders		
Decreased appetite	33	1
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[3]**

IMPORTANT SAFETY INFORMATION *(CONTINUED)*

Embryo-Fetal Toxicity *(Continued)*

Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 4 months after the last 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 last dose.

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Select laboratory abnormalities (≥20%) worsening from baseline[1]

Laboratory abnormalities	ZEPZELCA® (lurbinectedin) (N=105)	
	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 granulocyte colony-stimulating factor (G-CSF) for secondary prophylaxis or therapy for neutropenia, but primary prophylaxis was not allowed[1,4]**

IMPORTANT SAFETY INFORMATION *(CONTINUED)*

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%).

Please see Important Safety Information throughout and full Prescribing Information.

Minimal infusion visits—1-hour dosing, every 21 days

Recommended Dosing[1]

3.2 mg/m² by IV infusion over 60 MINUTES

Repeated EVERY 21 DAYS until disease progression or unacceptable toxicity

Initiate treatment with ZEPZELCA only if absolute neutrophil count (ANC) is at least 1,500 cells/mm^3 and platelet count is at least 100,000/mm^3.

Premedication[1]

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

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

Dose Reduction for ZEPZELCA for Adverse Reactions[1]

Dose Reduction	Total Dose
First:	2.6 mg/m² every 21 days
Second:	2 mg/m² every 21 days

Permanently discontinue ZEPZELCA in patients who are unable to tolerate 2 mg/m² or require a dose delay greater than two weeks.[1]

For full list of dosage modifications of ZEPZELCA for adverse reactions, please refer to the full Prescribing Information.

IV=intravenous.

IMPORTANT SAFETY INFORMATION *(CONTINUED)*

DRUG INTERACTIONS

Effect of CYP3A Inhibitors and Inducers

Avoid coadministration with a strong or a moderate CYP3A inhibitor (including grapefruit and Seville oranges) as this increases lurbinectedin systemic exposure which may increase the incidence and severity of adverse reactions to ZEPZELCA. If coadministration cannot be avoided, reduce the ZEPZELCA dose as appropriate.

Avoid coadministration with a strong CYP3A inducer as it may decrease systemic exposure to lurbinectedin, which may decrease the efficacy of ZEPZELCA.

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In 105 adults with SCLC with disease progression on or after platinum-based chemotherapy,

>1 IN 3 PATIENTS ACHIEVED AN OVERALL RESPONSE

with ZEPZELCA® (lurbinectedin) in the investigator assessment (N=105)[1]

- 35% (95% CI: 26–45%) achieved ORR per IA (CR=0%; PR=35%)
- 30% (95% CI: 22–40%) achieved ORR per IRC assessment (CR=0%; PR=30%)

1.9% OF PATIENTS PERMANENTLY DISCONTINUED

due to an adverse reaction (2 of 105)[1]

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

MINIMAL INFUSION VISITS—1-hour dosing every 21 days[1]

- **The recommended dosage of ZEPZELCA is 3.2 mg/m² by intravenous infusion over 60 minutes every 21 days** until disease progression or unacceptable toxicity
- Initiate treatment with ZEPZELCA only if absolute neutrophil count (ANC) is at least 1,500 cells/mm³ and platelet count is at least 100,000/mm³

EXPLORE ZEPZELCA FOR YOUR PATIENTS

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%).

CI=confidence interval; CR=complete response; IA=investigator assessment; IRC=independent review committee; ORR=overall response rate; PR=partial response; SCLC=small cell lung cancer.

Please see Important Safety Information throughout and full Prescribing Information.

References: 1. ZEPZELCA (lurbinectedin). Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **2.** Data on file. LUR-2023-029. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **3.** Data on file. LUR-2020-003. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **4.** 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. **5.** 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.

Jazz Pharmaceuticals

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