ZEPZELCA®
(lurbinectedin) for injection 4 mg

NOW APPROVED for First-Line Maintenance

Billing and Coding Guide

For more information, contact your Jazz Pharmaceuticals Oncology Business Manager:

Name: _____ **Phone number:** _____

Email: _____

INDICATIONS

ZEPZELCA (lurbinectedin) for injection 4 mg, in combination with atezolizumab or atezolizumab and hyaluronidase-tqjs, is indicated for the maintenance treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) whose disease has not progressed after first-line induction therapy with atezolizumab or atezolizumab and hyaluronidase-tqjs, carboplatin and etoposide.

ZEPZELCA (lurbinectedin) for injection 4 mg, as a single agent, 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 severe and fatal myelosuppression including febrile neutropenia and sepsis, thrombocytopenia and anemia.

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. To reduce the risk of febrile neutropenia during treatment with ZEPZELCA in combination with atezolizumab or atezolizumab and hyaluronidase-tqjs, administer granulocyte colony-stimulating factor (G-CSF). Monitor blood counts including neutrophils, red blood cells and platelets prior to each ZEPZELCA 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.

Introduction

This guide provides an overview of coding and coverage information related to ZEPZELCA. Healthcare providers can use this guide to determine for themselves the appropriate claims to file for ZEPZELCA-related services. Jazz Pharmaceuticals does not guarantee payment or coverage for any product or service. Information specific to billing and coding should be verified by the provider for each patient prior to treatment. Providers should contact payers directly for any revised or additional requirements, information, or guidance. It is the provider's responsibility to determine the appropriate healthcare setting, and to submit true and correct claims for the products and services rendered.

ZEPZELCA billing and coding requirements will vary based on many factors, including the site of service where the drug is administered, the type of insurance the patient has, and the benefit under which ZEPZELCA is covered.

Site of Service

ZEPZELCA may be administered in physicians' offices, or in hospital outpatient departments. For most payers, the site of service will affect the billing and coding requirements. This guide focuses on coverage, coding, and billing for ZEPZELCA when administered in physicians' offices and hospital outpatient settings.

ZEPZELCA Coverage Guidance

Physician offices and hospital outpatient facilities:

- For patients enrolled in Medicaid, a Medicare Advantage plan, or a commercial health plan, coverage of ZEPZELCA will vary by payer and may also be subject to utilization restrictions
- For Medicare patients, ZEPZELCA will be covered under Medicare Part B when used for an FDA-approved indication and when medically reasonable and necessary. There are no precertification requirements for ZEPZELCA under traditional fee-for-service

Benefit Category

Most payers cover physician-administered products such as ZEPZELCA under a medical benefit rather than a pharmacy benefit. For Medicare, while ZEPZELCA will typically be covered under Part B, private payers and Medicaid, including managed Medicaid, may require that physicians obtain ZEPZELCA through a specialty pharmacy. Specialty pharmacies may bill the payer under the medical or pharmacy benefit, depending on what that payer requires.

IMPORTANT SAFETY INFORMATION (cont.)

Myelosuppression (cont.)

- *ZEPZELCA with Intravenous Atezolizumab*
  - In the IMforte study, primary prophylaxis of G-CSF was administered to 84% of patients. Based on laboratory values, decreased neutrophil occurred in 36%, including 18% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased neutrophil cells was 31 days and a median duration of 10 days. Febrile neutropenia occurred in 1.7%. Sepsis occurred in 1%. There were 7 fatal infections: pneumonia (n=3), sepsis (n=3), and febrile neutropenia (n=1).
  - Based on laboratory values, decreased platelets occurred in 54%, including 15% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased platelet cells was 31 days and a median duration of 12 days.
  - Based on laboratory values, decreased hemoglobin occurred in 51%, including 13% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased hemoglobin was 64 days and a median duration of 8 days.

Please see Important Safety Information throughout and full Prescribing Information.

Ordering and Distribution

Specialty Distributors and Group Purchasing Organizations (GPOs)

ZEPZELCA is available for purchase from the authorized **Specialty Distributors and GPOs** 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.

cencora

AmerisourceBergen Specialty Distribution	Oncology Supply
• **Phone:** 1-800-746-6273 • **Fax:** 1-800-547-9413 • **Online:** https://www.asdhealthcare.com/home • **Email:** service@asdhealthcare.com	• **Phone:** 1-800-633-7555 • **Fax:** 1-800-248-8205 • **Online:** https://www.oncologysupply.com/ • **Email:** service@oncologysupply.com

CardinalHealth™

Cardinal Specialty Pharmaceutical Distribution

- **Phone:** 1-800-453-3972
- **Fax:** 1-800-274-9897
- **Online for hospitals:** https://orderexpress.cardinalhealth.com
- **Online for oncology clinics:** https://specialtyonline.cardinalhealth.com
- **Email:** SPDOncologyTeam@cardinalhealth.com

McKESSON

McKesson Plasma and Biologics	McKesson Specialty Health
• **Phone:** 1-800-625-2566 • **Fax:** 1-800-752-7626 • **Online:** https://connect.mckesson.com • **Email:** MPBOrders@mckesson.com	• **Phone:** 1-800-482-6700 • **Fax:** 1-800-289-9285 • **Online:** https://mscs.mckesson.com/ • **Email:** MSH-CustomerCare@mckesson.com

GPOs

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

IMPORTANT SAFETY INFORMATION (cont.)

Myelosuppression (cont.)

• *ZEPZELCA as a Single-Agent*

— In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA as a single agent, 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.

ZEPZELCA® (lurbinectedin) for injection 4 mg

Dosing and Administration[1]

The **recommended dosage of ZEPZELCA as a single-agent and as a combination** with atezolizumab or atezolizumab and hyaluronidase-tqjs is:

Recommended dose	Schedule
3.2 mg/m^2 by IV infusion over 60 minutes	**Once every 21 days** • Continue until disease progression or unacceptable toxicity

IV=intravenous.

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.

ZEPZELCA with Intravenous Atezolizumab or atezolizumab and hyaluronidase-tqjs

When administering ZEPZELCA on the same day as atezolizumab or atezolizumab and hyaluronidase-tqjs, administer the chosen atezolizumab drug first. For the recommended dosage of atezolizumab or atezolizumab and hyaluronidase-tqjs, refer to the respective Prescribing Information.

If discontinuation of atezolizumab or atezolizumab and hyaluronidase-tqjs is required due to an immune-related severe adverse event, treatment with ZEPZELCA may be continued at the same dose as a single agent. If immune toxicity does not resolve or recurs despite discontinuation of atezolizumab, permanently discontinue ZEPZELCA. ZEPZELCA is a hazardous drug. Follow applicable special handling and disposal procedures.

Preparation and administration

- Inject 8 mL of Sterile Water for Injection USP into the vial, yielding a solution containing 0.5 mg/mL lurbinectedin. 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, free of visible particles.
- Calculate the required volume of reconstituted solution as follows:

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

- For administration through a 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 (0.9% Sodium Chloride Injection USP or 5% Dextrose Injection USP).
- For administration through a 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 (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 (cont.)

Hepatotoxicity

ZEPZELCA can cause hepatotoxicity which may be severe.

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.

Please see Important Safety Information throughout and full Prescribing Information.

How Supplied, Storage and Handling[1]

- ZEPZELCA for injection is supplied as a sterile, preservative-free, white to off-white lyophilized powder in a single-dose clear glass vial
- Each carton (NDC 68727-712-01) contains 4 mg in one single-dose vial
- Store refrigerated at 2°C to 8°C (36°F to 46°F)
- Storage of infusion solution: 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 refrigeration at 2°C to 8°C (36°F to 46°F) conditions
- ZEPZELCA is a hazardous drug. Follow applicable special handling and disposal procedures

IMPORTANT SAFETY INFORMATION (cont.)

Hepatotoxicity (cont.)

- *ZEPZELCA with Intravenous Atezolizumab*
  - In the IMforte study, based on laboratory values, increased alanine aminotransferase (ALT) occurred in 25%, including 3% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. Increased aspartate aminotransferase (AST) occurred in 24% including 3% Grade 3 or Grade 4. The median time to onset of Grade ≥3 elevation in transaminases was 52 days (range: 6 to 337).
- *ZEPZELCA as a Single-Agent*
  - In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA as a single agent, 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.

Please see Important Safety Information throughout and full Prescribing Information.

ZEPZELCA® (lurbinectedin) for injection 4 mg

Sample Coding

This section provides sample codes for hospitals and physician offices for small cell lung cancer. Note that many of the codes are the same for both sites of care.

ICD-10-CM codes[2]

Code	Description
C33	Malignant neoplasm of trachea
C34.00–C34.02	Malignant neoplasm of bronchus and lung; main bronchus
C34.10–C34.12	Malignant neoplasm of bronchus and lung; upper lobe
C34.2	Malignant neoplasm of bronchus and lung; middle lobe
C34.30–C34.32	Malignant neoplasm of bronchus and lung; lower lobe
C34.80–C34.82	Malignant neoplasm of bronchus and lung; overlapping sites
C34.90–C34.92	Malignant neoplasm of bronchus and lung; unspecified part

ICD-10-CM=International Classification of Diseases, 10th Revision, Clinical Modification.

Revenue codes[3]

Code	Description
0250	General pharmacy
0260	General IV therapy
0510	Clinic, general
0636	Pharmacy, drugs requiring detailed coding

IV=intravenous.

Permanent J-code

Permanent J-code for ZEPZELCA[4]	Description[4]	HCPCS code dosage (billing units)[4]	Example
J9223	Infusion: 3.2 mg/m^2	0.1 mg = 1 unit	4 mg vial[1] = 40 units

HCPCS=Healthcare Common Procedure Coding System.

These are sample codes based on publicly available information and are informational only and not a guarantee or promise of coverage. Appropriate codes can vary by patient, setting of care, and payer. Correct coding is the responsibility of the provider submitting the claim for the item or service. Please check with the payer to verify codes and special billing requirements.

IMPORTANT SAFETY INFORMATION (cont.)

Extravasation Resulting in Tissue Necrosis

Extravasation of ZEPZELCA can cause skin and soft tissue injury, including necrosis requiring debridement. 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.

Sample Coding (cont.)

NDC[1]

Payers may require a 10-digit or 11-digit NDC. Both are provided for your convenience.

10-digit	11-digit	Description
68727-712-01	68727-0712-01	ZEPZELCA for injection is supplied as a sterile, preservative-free, white to off-white lyophilized powder in a 4 mg single-dose clear glass vial. Each carton contains one single-dose vial.

NDC=National Drug Code.

CPT codes[5]

Code	Description
96413	Chemotherapy administration, IV infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, IV infusion technique; each additional hour (list separately in addition to code for primary procedure)
96417	Chemotherapy administration, IV infusion technique; each additional sequential infusion (different substance/drug), up to 1 hour (list separately in addition to code for primary procedure)

CPT=Current Procedural Terminology; IV=intravenous.

These are sample codes based on publicly available information and are informational only and not a guarantee or promise of coverage. Appropriate codes can vary by patient, setting of care, and payer. Correct coding is the responsibility of the provider submitting the claim for the item or service. Please check with the payer to verify codes and special billing requirements.

IMPORTANT SAFETY INFORMATION (cont.)

Extravasation Resulting in Tissue Necrosis (cont.)

ZEPZELCA with Intravenous Atezolizumab

– In the IMforte study, extravasation resulting in skin necrosis occurred in one patient who received ZEPZELCA in combination with atezolizumab.

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.

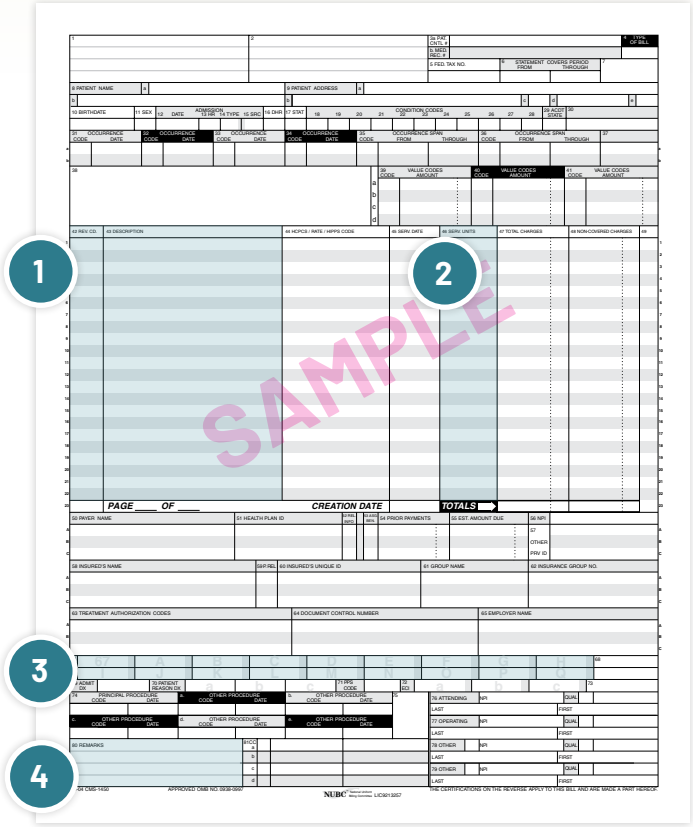
Please see Important Safety Information throughout and full Prescribing Information.

ZEPZELCA® (lurbinectedin) for injection 4 mg

Sample Forms

Sample Medicare Claim Form: CMS-1450 Form (Hospital Outpatient)

This sample claim form is provided only as an example. The healthcare provider is responsible for determining appropriate codes for an individual patient for related and/or separate procedures and for completing the appropriate forms.



1 Fields 42 and 43

Enter the appropriate revenue code (Field 42) and description (Field 43) corresponding to the permanent J-code (Field 44).

2 Field 46

Enter the number of units billed that corresponds to the vial size used (Lurbinectedin 4 mg vial[1] = 40 units). Contact your Medicare contractor and/or all other contracted/non-contracted payer(s) for any questions regarding filling guidelines for coverage, coding, and payment.

3 Field 67

Enter the diagnosis code.

4 Field 80

Product information: Billing with a specific J-code allows for faster payment through electronic billing. Manual billing may still be required in certain circumstances. In those cases, it may be necessary to provide the following product information for payment: NDC, quantity of the drugs administered (expressed in unit of measure applicable to the drug or biological), and the date the drug was administered to the patient.

IMPORTANT SAFETY INFORMATION (cont.)

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.

ZEPZELCA with Intravenous Atezolizumab

– In the IMforte study, among 235 patients who had a creatine phosphokinase laboratory evaluation, increased creatine phosphokinase occurred in 9% who received ZEPZELCA in combination with atezolizumab.

Please see Important Safety Information throughout and full Prescribing Information.

ZEPZELCA® (lurbinectedin) for injection 4 mg

Sample Forms (cont.)

Sample Medicare Claim Form: CMS-1500 Form (Physician Office)

This sample claim form is provided only as an example. The healthcare provider is responsible for determining appropriate codes for an individual patient for related and/or separate procedures and for completing the appropriate forms. Guidance is provided below for how to incorporate the permanent J-code (J9223).

1 Field 19

This area may be used to list the drug name, NDC,[a,b] dosage, strength, and route of administration.

2 Field 21

Enter the appropriate ICD-10-CM diagnosis code corresponding to the patient's diagnosis.

3 Field 23

If required, report the prior authorization number here.

4 Field 24, Column D

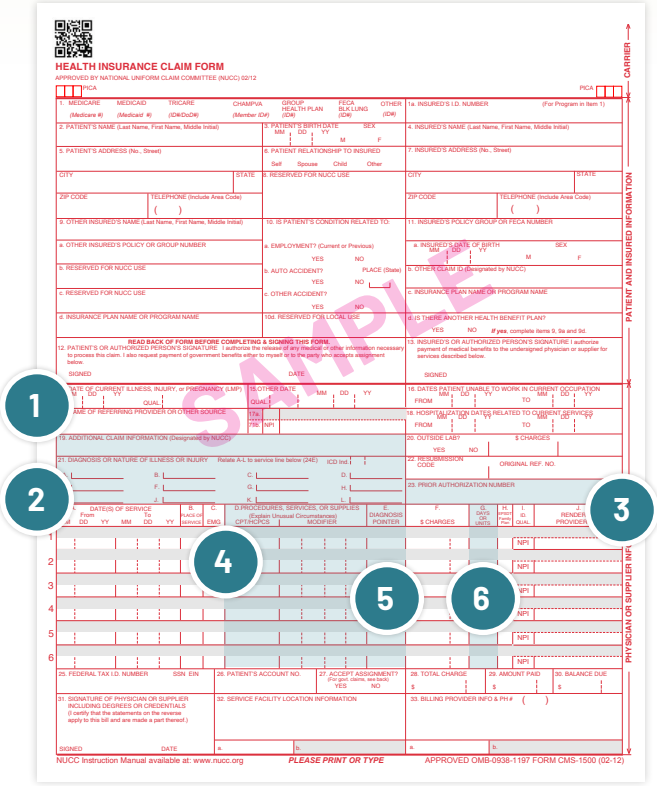
Enter the permanent J-code to report the use of ZEPZELCA. Also include the CPT code representing procedures performed as well as the appropriate modifier (append modifier if needed/appropriate).

5 Field 24, Column E

Specify diagnosis from Box 21 relating to each CPT/J-code listed in Field 24, Column D.

6 Field 24, Column G

Enter the appropriate number of units administered (0.1 mg = 1 unit). Also, on a separate line, enter the appropriate number of units discarded (if applicable) using the JW modifier.[b,c]



[a]Please note that for billing purposes, the NDC requires 11 digits (thus a zero has been entered into the sixth digit). This is consistent with the Red Book and First DataBank listings.

[b]Contact your Medicare contractor and/or all other contracted/non-contracted payer(s) for any questions regarding filling guidelines for coverage, coding, and payment.

[c]JW modifier: Providers and suppliers are required to report the JW modifier on Part B drug claims for discarded drugs and biologicals. Also, providers and suppliers must document the amount of discarded drugs or biologicals in Medicare beneficiaries' medical records.

IMPORTANT SAFETY INFORMATION (cont.)

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. 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.

Please see Important Safety Information throughout and full Prescribing Information.

ZEPZELCA® (lurbinectedin) for injection 4 mg

Checklists and Sample Letters

Benefits Verification and Prior Authorization Checklist

This sample claim form is provided only as an example. When calling a payer to verify benefits and inquire about prior authorization, the following key questions should be considered.

Verify patient eligibility and benefits with the payer before providing ZEPZELCA.

☐ **What is the patient's copayment, coinsurance, deductible, or out-of-pocket maximum?**
- Has it been met? If not, what amount has been applied to date?

☐ **Does the patient have an annual or lifetime benefit maximum?**
- Has it been met? If not, what amount has been applied to date?

☐ **Does the patient have other insurance benefits that will need to be coordinated?**

☐ **Is prior authorization required? If so, what are the submission requirements for ZEPZELCA?**
- J-code to report ZEPZELCA
- Number of units
- Where and how to submit prior authorizations
- Prior authorization process
- Required documentation (eg, forms, prescribing information, and statement of medical necessity)
- Is there a medical policy in place for small cell lung cancer and/or ZEPZELCA?
- How long will it take?

☐ **Check criteria for reauthorization and obtain appropriate documentation**

IMPORTANT SAFETY INFORMATION (cont.)

ADVERSE REACTIONS

- *ZEPZELCA with Intravenous Atezolizumab*
  - Serious adverse reactions occurred in 31% of patients receiving ZEPZELCA in combination with atezolizumab. Serious adverse reactions occurring in >2% were pneumonia (2.5%), respiratory tract infections (2.1%), dyspnea (2.1%), and decreased platelet count (2.1%). Fatal adverse reactions occurred in 5% of patients receiving ZEPZELCA with atezolizumab including pneumonia (3 patients), sepsis (3 patients), cardio-respiratory arrest (2 patients), myocardial infarction (2 patients), and febrile neutropenia (1 patient).
  - The most common adverse reactions (≥30%), including laboratory abnormalities, in patients who received ZEPZELCA with atezolizumab were decreased lymphocytes (55%), decreased platelets (54%), decreased hemoglobin (51%), decreased neutrophils (36%), nausea (36%), and fatigue/asthenia (32%).
- *ZEPZELCA as a Single-Agent*
  - Serious adverse reactions occurred in 34% of patients who received ZEPZELCA. Serious adverse reactions in ≥3% of patients included pneumonia, febrile neutropenia, neutropenia, respiratory tract infection, anemia, dyspnea, and thrombocytopenia.

Please see Important Safety Information throughout and full Prescribing Information.

ZEPZELCA® (lurbinectedin) for injection 4 mg

Checklists and Sample Letters (cont.)

Claims Filing Checklist

The following tips may assist you with successfully filing claims for an infusion therapy.

- ☐ **Use appropriate codes to report the patient's condition, the drugs the patient received, and the services you have provided.**
  - J-code
  - CPT code
  - ICD-10-CM code
  - Document waste if necessary per payer protocol
- ☐ **Include additional information requested by the payer in box 19 of the CMS-1500 form or in box 80 of the CMS-1450.**
  - ZEPZELCA
  - Dosage
  - National Drug Code number
  - Route of administration
  - Unit description
- ☐ **Attach additional information to the claim if necessary.**
  - Letter of medical necessity
  - Prescribing information
  - Patient notes
- ☐ **Review claim for accuracy, including patient identification numbers, coding, and number of units.**
- ☐ **File claim as soon as possible and within payer filing time limits.**
- ☐ **Reconcile claim reports promptly and thoroughly to ensure claims have been appropriately processed and paid.**
- ☐ **Verify that payment amounts correspond with your public payer allowables and your private payer contracts.**

IMPORTANT SAFETY INFORMATION (cont.)

ADVERSE REACTIONS (cont.)

— 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.

ZEPZELCA® (lurbinectedin) for injection 4 mg

Checklists and Sample Letters (cont.)

Letter of Medical Necessity Checklist

This section provides information and sample letter components that can help ensure your communications with health plans regarding medical necessity are as complete as possible. These samples describe the type of information that will usually be required. You can refer to the checklist on this page as you develop and complete your own letters.

Below is a checklist of items that may be needed to support the development of your letter of medical necessity:

Patient information

- ☐ Patient name
- ☐ Patient date of birth
- ☐ Insurance ID
- ☐ Insurance group number
- ☐ Case ID (if applicable)

Clinical rationale

- ☐ Patient diagnosis
- ☐ Comprehensive list of previous treatment therapies used
- ☐ Information about the patient's previous treatments
- ☐ Rationale for selecting ZEPZELCA
- ☐ Test results and chart notes
- ☐ Hospital admission and/or emergency room notes

Additional supporting documentation may vary between health plans, but may include:

- ☐ Prescribing information
- ☐ Documentation required by prior authorization, if any
- ☐ Relevant peer-reviewed articles

IMPORTANT SAFETY INFORMATION (cont.)

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.

Please see Important Safety Information throughout and full Prescribing Information.

ZEPZELCA® (lurbinectedin) for injection 4 mg

Checklists and Sample Letters (cont.)

Sample Letter of Medical Necessity

This is an example of what payers may require in a letter of medical necessity. Be sure to understand the specific payer requirements for your patient.

[Date]
[Payer name]
[Payer street address]
[Payer city, state, ZIP code]

Patient name: [Patient full name]
Date of birth: [Patient birth date]
Member ID: [Patient member ID number]
Policy or group number: [Patient policy or group number]
Case ID number: [Case ID number (if applicable)]

To Whom It May Concern,

Patient's clinical/medical history:

- Patient age
- Patient's diagnosis (ICD-10-CM code)
- Date of diagnosis
- Patient's first visit, date of referral
- Previous treatments including drug names, duration of treatment(s), responses to those treatments
- Confirmation of whether or not disease has progressed following 1L treatment
- Complications associated with the patient's small cell lung cancer

Treatment plan:

- Include plan of treatment (eg, dosage, frequency of infusion, length of treatment)
- Clinical rationale for the ZEPZELCA prescription

Enclosures:

- Prescribing information
- Clinical notes/medical records
- Test results
- Relevant peer-reviewed articles

Sincerely,

_____
[Physician name and signature]
[Physician address]
[Physician phone number]

IMPORTANT SAFETY INFORMATION (cont.)

GERIATRIC USE

- *ZEPZELCA with Intravenous Atezolizumab*
  - Of the 242 patients with ES-SCLC treated with ZEPZELCA and atezolizumab in IMforte, 124 (51%) patients were 65 years of age and older, while 29 (12%) patients were 75 years of age and older. No overall differences in effectiveness were observed between older and younger patients. There was no overall difference in the incidence of serious adverse reactions in patients ≥65 years of age and patients <65 years of age (33% vs. 29%, respectively). There was no higher incidence of Grade 3 or 4 adverse reactions in patients >65 years of age compared to younger patients (45% vs. 31%, respectively).

Please see Important Safety Information throughout and full Prescribing Information.

ZEPZELCA® (lurbinectedin) for injection 4 mg

Checklists and Sample Letters (cont.)

Letter of Appeal Checklist

This section provides information and examples that can help ensure your communications with health plans regarding an appeal are as complete as possible. These samples provide the type of information that will usually be required. Refer to this checklist as you develop and complete your own letters. One sample appeals letter is provided on the next page. Incorrect or incomplete submissions may delay the review process or result in an automatic denial of the request.

Below is a checklist of items that may be needed to support the development of your letter of appeal:

Patient information

- ☐ Patient name
- ☐ Patient date of birth
- ☐ Insurance ID
- ☐ Insurance group number
- ☐ Case ID (if applicable)

Clinical rationale

- ☐ Patient diagnosis
- ☐ Comprehensive list of previous treatment therapies used
- ☐ Information about the patient's previous treatments
- ☐ Rationale for selecting ZEPZELCA
- ☐ Test results and chart notes
- ☐ Hospital admission and/or emergency room notes

Additional supporting documentation may vary between health plans, but may include:

- ☐ Prescribing information
- ☐ Relevant peer-reviewed articles
- ☐ For 2nd- and 3rd-level appeals, include a copy of the previous denial letter(s)

IMPORTANT SAFETY INFORMATION (cont.)

GERIATRIC USE (cont.)

- *ZEPZELCA as a Single-Agent*
  - 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%). There was a higher incidence of Grade 3 or 4 adverse reactions in patients ≥65 years of age compared to younger patients (76% vs. 50%, respectively).

Please see Important Safety Information throughout and full Prescribing Information.

ZEPZELCA® (lurbinectedin) for injection 4 mg

Checklists and Sample Letters (cont.)

Sample Letter of Appeal – Step Edit

To Whom It May Concern:

We have read and acknowledged your policy for the responsible management of drugs in the small cell lung cancer (SCLC) category. We are writing to request that you reconsider your denial of coverage for ZEPZELCA. This letter is being submitted on behalf of the above referenced patient for the treatment of SCLC [diagnosis code].

The reason given for the denial was [state reason from insurer's letter]. A copy of the most recent denial letter is included along with medical notes in response to the denial. After reviewing the denial letter, we continue to feel that ZEPZELCA [dose, frequency] is the appropriate therapy. The relevant clinical history is summarized below.

This plan currently lists [required step edit therapies] to be attempted prior to treatment with ZEPZELCA. These step edit therapies are not viable for this patient. We are requesting that the step edit therapy requirement be bypassed.

Document the patient's history, diagnosis, current condition, and symptoms; for example, confirm the patient:

_____ Diagnosis of small cell lung cancer (ICD-10-CM code)

_____ Adult patient aged >18 years

_____ Previous treatments including drug names, duration of treatment(s), responses to those treatments

_____ Confirmation of whether or not disease has progressed following 1L treatment

_____ Rationale and clinical support for why other treatments are not appropriate for this patient

Previous therapies:	**Reason for discontinuation:**	**Duration of therapy:**

(Provide rationale for prescribing ZEPZELCA.)

(Provide clinical support for your recommendation.)

The ordering physician is [physician name, NPI #]. The PA decision may be faxed to [fax #] or mailed to [physician business office address]. Please also send a copy of the coverage determination decision to [patient name].

Sincerely,

_____

[Physician name and signature] [Patient name and signature]
[Name of practice]
[Phone number]
Encl:

IMPORTANT SAFETY INFORMATION (cont.)

HEPATIC IMPAIRMENT

Avoid administration of ZEPZELCA in patients with severe hepatic impairment. If administration cannot be avoided, reduce the dose. Monitor for increased adverse reactions in patients with severe hepatic impairment.

Reduce the dose of ZEPZELCA in patients with moderate hepatic impairment. Monitor for increased adverse reactions in patients with moderate hepatic impairment.

No dose adjustment of ZEPZELCA is recommended for patients with mild hepatic impairment.

Please see Important Safety Information throughout and full Prescribing Information.

ZEPZELCA® (lurbinectedin) for injection 4 mg

Access and Patient Support

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

JazzCares is committed to **helping patients get access** to their ZEPZELCA medication and **providing personalized support** throughout their treatment.

JazzCares supports patients and practices[a]

Helps patients understand their insurance coverage and provides information and support on benefits investigation, prior authorization, appeals, billing and coding, and referrals to other financial assistance

Savings Card for eligible patients[a]

Commercially insured patients can reduce their out-of-pocket cost for their ZEPZELCA medication to as little as $10, subject to an annual maximum

Patient Assistance Program for eligible patients[b]

Uninsured or underinsured patients who meet certain financial criteria may be eligible to receive ZEPZELCA at no cost

Oncology Business Managers provide expertise and support

- Patient-specific issues
- Access and reimbursement
- Coding and billing
- Purchasing, procurement, and distribution

To learn more about JazzCares support offerings, call **1-833-533-JAZZ (5299)** Monday-Friday, 8 AM to 8 PM ET, visit **JazzCares**, or contact your **Oncology Business Manager**

[a]Insurance coverage and plans may vary. The JazzCares Program 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.

[b]Subject to financial and residency eligibility criteria.

Please see Important Safety Information throughout and full Prescribing Information.

ZEPZELCA® (lurbinectedin) for injection 4 mg

IMPORTANT SAFETY INFORMATION

Myelosuppression

ZEPZELCA can cause severe and fatal myelosuppression including febrile neutropenia and sepsis, thrombocytopenia and anemia.

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. To reduce the risk of febrile neutropenia during treatment with ZEPZELCA in combination with atezolizumab or atezolizumab and hyaluronidase-tqjs, administer granulocyte colony-stimulating factor (G-CSF). Monitor blood counts including neutrophils, red blood cells and platelets prior to each ZEPZELCA 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.

- *ZEPZELCA with Intravenous Atezolizumab*
  - In the IMforte study, primary prophylaxis of G-CSF was administered to 84% of patients. Based on laboratory values, decreased neutrophils occurred in 36%, including 18% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased neutrophil cells was 31 days and a median duration of 10 days. Febrile neutropenia occurred in 1.7%. Sepsis occurred in 1%. There were 7 fatal infections: pneumonia (n=3), sepsis (n=3), and febrile neutropenia (n=1).
  - Based on laboratory values, decreased platelets occurred in 54%, including 15% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased platelet cells was 31 days and a median duration of 12 days.
  - Based on laboratory values, decreased hemoglobin occurred in 51%, including 13% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased hemoglobin was 64 days and a median duration of 8 days.
- *ZEPZELCA as a Single-Agent*
  - In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA as a single agent, 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.

Hepatotoxicity

ZEPZELCA can cause hepatotoxicity which may be severe.

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.

- *ZEPZELCA with Intravenous Atezolizumab*
  - In the IMforte study, based on laboratory values, increased alanine aminotransferase (ALT) occurred in 25%, including 3% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. Increased aspartate aminotransferase (AST) occurred in 24% including 3% Grade 3 or Grade 4. The median time to onset of Grade ≥3 elevation in transaminases was 52 days (range: 6 to 337).
- *ZEPZELCA as a Single-Agent*
  - In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA as a single agent, 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.

Extravasation Resulting in Tissue Necrosis

Extravasation of ZEPZELCA can cause skin and soft tissue injury, including necrosis requiring debridement. 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.

ZEPZELCA® (lurbinectedin) for injection 4 mg

IMPORTANT SAFETY INFORMATION (cont.)

Extravasation Resulting in Tissue Necrosis (cont.)

ZEPZELCA with Intravenous Atezolizumab

— In the IMforte study, extravasation resulting in skin necrosis occurred in one patient who received ZEPZELCA in combination with atezolizumab.

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.

ZEPZELCA with Intravenous Atezolizumab

— In the IMforte study, among 235 patients who had a creatine phosphokinase laboratory evaluation, increased creatine phosphokinase occurred in 9% who received ZEPZELCA in combination with atezolizumab.

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. 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.

ADVERSE REACTIONS

- *ZEPZELCA with Intravenous Atezolizumab*
  - — Serious adverse reactions occurred in 31% of patients receiving ZEPZELCA in combination with atezolizumab. Serious adverse reactions occurring in >2% were pneumonia (2.5%), respiratory tract infections (2.1%), dyspnea (2.1%), and decreased platelet count (2.1%). Fatal adverse reactions occurred in 5% of patients receiving ZEPZELCA with atezolizumab including pneumonia (3 patients), sepsis (3 patients), cardio-respiratory arrest (2 patients), myocardial infarction (2 patients), and febrile neutropenia (1 patient).
  - — The most common adverse reactions (≥30%), including laboratory abnormalities, in patients who received ZEPZELCA with atezolizumab were decreased lymphocytes (55%), decreased platelets (54%), decreased hemoglobin (51%), decreased neutrophils (36%), nausea (36%), and fatigue asthenia (32%).
- *ZEPZELCA as a Single-Agent*
  - — Serious adverse reactions occurred in 34% of patients who received ZEPZELCA. Serious adverse reactions in ≥3% of patients included pneumonia, febrile neutropenia, neutropenia, respiratory tract infection, anemia, dyspnea, and thrombocytopenia.
  - — 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%).

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.

Please see Important Safety Information throughout and full Prescribing Information.

ZEPZELCA® (lurbinectedin) for injection 4 mg

IMPORTANT SAFETY INFORMATION (cont.)

GERIATRIC USE

- *ZEPZELCA with Intravenous Atezolizumab*
  - Of the 242 patients with ES-SCLC treated with ZEPZELCA and atezolizumab in IMforte, 124 (51%) patients were 65 years of age and older, while 29 (12%) patients were 75 years of age and older. No overall differences in effectiveness were observed between older and younger patients. There was no overall difference in the incidence of serious adverse reactions in patients ≥65 years of age and patients <65 years of age (33% vs. 29%, respectively). There was no higher incidence of Grade 3 or 4 adverse reactions in patients >65 years of age compared to younger patients (45% vs. 31%, respectively).
- *ZEPZELCA as a Single-Agent*
  - 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%). There was a higher incidence of Grade 3 or 4 adverse reactions in patients ≥65 years of age compared to younger patients (76% vs. 50%, respectively).

HEPATIC IMPAIRMENT

Avoid administration of ZEPZELCA in patients with severe hepatic impairment. If administration cannot be avoided, reduce the dose. Monitor for increased adverse reactions in patients with severe hepatic impairment.

Reduce the dose of ZEPZELCA in patients with moderate hepatic impairment. Monitor for increased adverse reactions in patients with moderate hepatic impairment.

No dose adjustment of ZEPZELCA is recommended for patients with mild hepatic impairment.

Please see full Prescribing Information.

For more information about ZEPZELCA, visit www.ZEPZELCAPro.com.

Reimbursement information provided by Jazz Pharmaceuticals Inc. is gathered from third-party sources and is presented for illustrative purposes only. This information does not constitute reimbursement or legal advice, and Jazz Pharmaceuticals Inc. makes no representation or warranty regarding this information or its completeness, accuracy, or timeliness. Laws, regulations, and payer policies concerning reimbursement are complex and change frequently, and service providers are responsible for all decisions relating to coding and reimbursement submissions. Accordingly, Jazz Pharmaceuticals Inc. strongly recommends that you consult with your payers, reimbursement specialist, and/or legal counsel regarding coding, coverage, and reimbursement matters.

Insurance coverage and plans may vary. This is 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.

References: 1. ZEPZELCA® (lurbinectedin) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc. **2.** Centers for Medicare & Medicaid Services. ICD-10-CM tabular list of diseases and injuries. https://ftp.cdc.gov/pub/health_statistics/nchs/Publications/ICD10CM/2022/icd10cm-tabular-2022-April-1.pdf. April 1, 2022. Accessed June 9, 2025. **3.** Noridian Healthcare Solutions. Revenue codes. https://med.noridianmedicare.com/web/jea/topics/claim-submission/revenue-codes. Updated March 18, 2024. Accessed June 9, 2025. **4.** Centers for Medicare & Medicaid Services website. Centers for Medicare & Medicaid Services (CMS) Healthcare Common Procedure Coding System (HCPCS) application summaries and coding decisions. https://www.cms.gov/files/document/2020-hcpcs-application-summary-quarter-3-2020-drugs-and-biologics.pdf. Accessed June 9, 2025. **5.** Coalition of Hematology and Oncology Practices. Welcome to coding guidelines presentation focusing on oncology billing. https://www.choptx.org/wp-content/uploads/2017/12/Coding-for-Oncology-Presentation-Final.v2pptx.pdf. Accessed June 9, 2025.

ZEPZELCA is a registered trademark of PharmaMar, S.A. used by Jazz Pharmaceuticals under license.
©2025 Jazz Pharmaceuticals. US-LUR-2000177 Rev1025

Jazz Pharmaceuticals PharmaMar

ZEPZELCA® (lurbinectedin) for injection 4 mg