

Positive Quality Intervention: Lurbinectedin (Zepzelca™) for Small Cell Lung Cancer

Description: The purpose of this PQI is to evaluate the use of lurbinectedin for the treatment of adult patients with metastatic small cell lung cancer with disease progression on or after platinum-based chemotherapy.

Background: Small cell lung cancer (SCLC), which accounts for around 15% of all lung cancer diagnoses, is typically highly aggressive with poor survival outcomes.¹ The recommended first-line treatment is a platinum-based chemotherapy regimen.³ Few options exist for treatment of patients with SCLC after failure of first-line treatment. Lurbinectedin is an alkylating agent that inhibits oncogenic transcription, approved as second-line therapy in patients with metastatic SCLC. The United States Food & Drug Administration approval of lurbinectedin in this setting is based on a single-arm, open-label, phase 2, multi-centered basket trial in Europe and the US.² Patients enrolled in the trial were adults (aged ≥ 18 years) with a pathologically proven diagnosis of SCLC, ECOG performance status ≤ 2 , measurable disease, absence of brain metastasis, adequate organ function, and pre-treated with only one previous chemotherapy-containing line of treatment. The primary outcome was overall response (ORR) as assessed by the investigators according to RECIST 1.1. In the 105 patients who were enrolled and treated with lurbinectedin, ORR was demonstrated in 37 patients (35.2%; 95% CI 26.2-45.2). The most common grade 3-4 adverse events included hematological abnormalities such as anemia (9%), leucopenia (29%), neutropenia (46%), and thrombocytopenia (7%). Serious treatment-related adverse events occurred in 10% of the patients, of which neutropenia and febrile neutropenia were the most common (5% patients for each). No treatment-related deaths were reported.^{2,4}

PQI Process:

- Screen for drug interactions; avoid coadministration with strong/moderate CYP3A inhibitors/inducers
- Recommended dosage is 3.2 mg/m² administered over 60 minutes. Treatment is given every 21 days until disease progression or unacceptable toxicity
- No initial dose adjustment recommended for baseline renal or hepatic impairment (limited data available)
- Initiate treatment only if baseline ANC $\geq 1,500$ cells/mm³ and platelet count is $\geq 100,000$ /mm³
- Lurbinectedin is available as a single-dose, preservative free vial with 4 mg lyophilized powder per vial
- Pre-medications for antiemetic prophylaxis:
 - Corticosteroids (dexamethasone 8 mg intravenously or equivalent)
 - Serotonin antagonists (ondansetron 8 mg intravenously or equivalent)
- Preparation:
 - Inject 8 mL of SWFI into the vial, yielding a solution containing 0.5 mg/mL lurbinectedin
 - Shake the vial until complete dissolution. 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: Volume (mL) = Body Surface Area (m²) x Individual Dose (mg/m²)/0.5 mg/mL
 - 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 or 5% Dextrose)

Important notice: NCODA has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.

Patient Centered Activities:

- Counsel patient on lurbinectedin
- Ensure patient has access to supportive medications: Supply patient with as needed antiemetic medication prescriptions to be used at home
- Instruct patient to report any adverse events, such as diarrhea, nausea/vomiting, mouth sores, or inflammation

Medication Access Assistance

<https://jazzcares.com/hcp/zepzelca/>

1-833-533-JAZZ (5299) Monday-Friday, 8 AM-8 PM ET

Supplemental Information:

Cautions & Warnings

- Myelosuppression: Monitor blood counts prior to each administration. Withhold, reduce the dose, or permanently discontinue lurbinectedin based on severity. For neutrophil count less than 500 cells/mm³ or any value less than lower limit of normal, the use of myeloid growth factor (G-CSF) is recommended.
- Hepatotoxicity: Monitor liver function tests prior to initiating, periodically during treatment and as clinically indicated. Withhold, reduce dose, or permanently discontinue based on severity.
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females and males of reproductive potential of the potential risk to a fetus and to use an effective method of contraception.

Most common adverse reactions (≥20%): leukopenia, lymphopenia, fatigue, anemia, neutropenia, increased creatinine, increased alanine aminotransferase, increased glucose, thrombocytopenia, nausea, decreased appetite, musculoskeletal pain, decreased albumin, constipation, dyspnea, decreased sodium, increased aspartate aminotransferase, vomiting, cough, decreased magnesium and diarrhea.

Dose Reduction for Lurbinectedin for Adverse Reactions

- 1st dose reduction - 2.6 mg/ m² every 21 days
- 2nd dose reduction - 2 mg/m² every 21 days
- Permanently discontinue if unable to tolerate 2 mg/m² or dose delay greater than two weeks

Adverse Reaction	Severity	Dose Modification
Neutropenia	Grade 4 or any grade febrile neutropenia	Hold until ≤ Grade 1 Resume at reduced dose
Thrombocytopenia	Grade 3 with bleeding or Grade 4	Hold until platelets ≥ 100,00/mm ³ Resume at reduced dose
Hepatotoxicity	Grade 2/3/4	Hold until ≤ Grade 1 Resume at reduced dose

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References:

1. Basumallik N, Agarwal M. Small Cell Lung Cancer. 2021 Jul 17. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. PMID: 29494065.
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. Small Cell Lung Cancer. Version 1.2021. National Comprehensive Cancer Network. Available at: http://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. Accessed 2021.
4. Singh S, Jaigirdar AA, Mulkey F, et al. FDA Approval Summary: Lurbinectedin for the Treatment of Metastatic Small Cell Lung Cancer. *Clin Cancer Res.* 2021;27(9):2378-2382.

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