



## FDA Approves Zepzelca® (lurbinectedin) and Atezolizumab (Tecentriq®) Combination as First-Line Maintenance Therapy for Extensive-Stage Small Cell Lung Cancer

October 02, 2025

*Combination reduced the risk of disease progression or death by 46% and risk of death by 27% in pivotal Phase 3 IMforte trial*

*Zepzelca and atezolizumab combination added to National Comprehensive Cancer Network® Guidelines for SCLC*

*For U.S. media and investors only*

DUBLIN, Oct. 2, 2025 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the U.S. Food and Drug Administration (FDA) has granted approval for Zepzelca® (lurbinectedin) in combination with atezolizumab (Tecentriq®) or atezolizumab and hyaluronidase-tqjs (Tecentriq Hybreza®) as a maintenance treatment for adults with extensive-stage small cell lung cancer (ES-SCLC) whose disease has not progressed after first-line induction therapy with atezolizumab, carboplatin and etoposide.<sup>1</sup> The approval marks the first combination therapy for first-line maintenance treatment of ES-SCLC, a fast-growing and aggressive cancer with limited treatment options.

The National Comprehensive Cancer Network® (NCCN®) updated the NCCN Clinical Practice Guidelines in Oncology® (NCCN Guidelines®) for SCLC to include the Zepzelca and atezolizumab combination as a preferred regimen for patients whose disease has not progressed following four cycles of platinum-based chemotherapy and atezolizumab induction.

"For people with extensive-stage small cell lung cancer and their families, the period after induction therapy is often filled with uncertainty, given the high risk of relapse," said Roy Herbst, M.D., Ph.D., deputy director and chief of medical oncology and hematology at Yale Cancer Center and Smilow Cancer Hospital. "The Zepzelca and Tecentriq combination provides a new option and a proactive approach in this setting shown to improve progression-free and overall survival in patients who haven't progressed after standard induction chemotherapy with Tecentriq and chemotherapy. The approval may lead to a meaningful shift in how we manage this challenging disease and gives us a new tool to help to delay disease progression and extend survival."

"ES-SCLC patients have good initial responses but then quickly progress. Extending the time to progression, and ultimately survival, will be clinically valuable, in particular in this fast-moving cancer," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development, and chief medical officer of Jazz Pharmaceuticals. "The introduction of a new maintenance approach offers a new way to manage this aggressive disease and gives patients and their physicians a new treatment option with the potential to increase both PFS and OS. We're proud to advance the standard of care for ES-SCLC and we continue to pursue opportunities in cancer research that improve lives."

The FDA approval is based on results from the Phase 3 IMforte trial ([NCT05091567](#)), which showed that the Zepzelca and atezolizumab combination reduced the risk of disease progression or death by 46% and the risk of death by 27%, compared to atezolizumab maintenance therapy alone. Following four cycles of induction therapy, from the point of randomization the median overall survival (OS) for the Zepzelca and atezolizumab regimen was 13.2 months versus 10.6 months for atezolizumab alone (stratified hazard ratio [HR]=0.73; 95% CI: 0.57–0.95; p=0.0174). From the point of randomization, median progression-free survival (PFS) by independent assessment was 5.4 months versus 2.1 months, respectively (stratified HR=0.54, 95% CI: 0.43–0.67; p<0.0001). These results were presented at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting and simultaneously published in *The Lancet*.

The most common adverse reactions for Zepzelca in combination with atezolizumab including laboratory abnormalities, (≥ 30%) are decreased lymphocytes, decreased platelets, decreased hemoglobin, decreased leukocytes, decreased neutrophils, nausea, and fatigue/asthenia.

### About Small Cell Lung Cancer

In the U.S., approximately 13 percent of lung cancers are small cell.<sup>2</sup> Approximately 30,000 new cases of small cell lung cancer (SCLC) are reported in the U.S. each year.<sup>2,3</sup> The risk for developing SCLC is much higher among current or former tobacco smokers; however, SCLC can also be caused by exposure to secondhand smoke, asbestos, some inhaled chemicals, radiation and air pollution. People with a family history of lung cancer may also be at a higher risk, too.<sup>4</sup> SCLC is the most aggressive form of lung cancer and it tends to spread quickly to other parts of the body including the brain, liver and bone.<sup>5,6</sup> A large percentage of SCLC patients on treatment briefly achieve a response, although the cancer often returns and is usually more aggressive and resistant to regimens that were previously effective.<sup>5</sup>

### About Zepzelca® (lurbinectedin)

Zepzelca is an alkylating drug that binds guanine residues within DNA. This triggers a cascade of events that can affect the activity of DNA binding proteins, including some transcription factors, and DNA repair pathways, resulting in disruption of the cell cycle and potentially cell death.<sup>1</sup>

In October 2025, the FDA approved Zepzelca in combination with atezolizumab or atezolizumab and hyaluronidase-tqjs, as maintenance treatment for adults 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.

In June 2020, the FDA approved Zepzelca under accelerated approval 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 ORR and DOR. 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<sup>3</sup> and platelet count of at least 100,000/mm<sup>3</sup>. 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<sup>3</sup> or any value less than lower limit of normal, administer G-CSF. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.

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 neutrophils 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.

### **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.

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).

### **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.

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.

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**

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 each), 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%).

### **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.

### **GERIATRIC USE**

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  $\geq 65$  years of age and patients  $< 65$  years of age (33% vs. 29%, respectively). There was a higher incidence of Grade 3 or 4 adverse reactions in patients  $\geq 65$  years of age compared to younger patients (45% vs. 31%, 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 accompanying full [Prescribing Information](https://pp.jazzpharma.com/pi/zepzelca.en.USPI.pdf).** <https://pp.jazzpharma.com/pi/zepzelca.en.USPI.pdf>

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### **About Jazz Pharmaceuticals**

Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharma company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing potentially life-changing medicines for people with serious diseases – often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines, including leading therapies for sleep disorders and epilepsy, and a growing portfolio of cancer treatments. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics in oncology and neuroscience. Jazz is headquartered in Dublin, Ireland with research and development laboratories, manufacturing facilities and employees in multiple countries committed to serving patients worldwide. Please visit [www.jazzpharmaceuticals.com](http://www.jazzpharmaceuticals.com) for more information.

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<sup>1</sup>ZEPZELCA (lurbinectedin) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

<sup>2</sup>Alvarado-Lunda G, Morales-Espinosa D. Treatment for small cell lung cancer, where are we now? – A review. Transl Lung Cancer Res. 2016;5(1):26-38.

<sup>3</sup>SEER Explorer Lung and Bronchus Cancer, Recent Trends in SEER Incidence Rates, 2000-2016, by Age, <https://seer.cancer.gov/explorer> Updated June 27, 2024. Accessed October 1, 2025.

<sup>4</sup>American Cancer Society. Small cell lung cancer causes, risk factors, and prevention. <https://www.cancer.org/content/dam/CRC/PDF/Public/8709.00.pdf>. Updated May 16, 2016. Accessed September 22, 2025.

<sup>5</sup>American Cancer Society. What is lung cancer? <https://www.cancer.org/cancer/lung-cancer/about/what-is.html>. Updated January 29, 2024. Accessed October 1, 2025.

<sup>6</sup>American Cancer Society. Small cell lung cancer stages. <https://www.cancer.org/cancer/lung-cancer/detection-diagnosis-staging/staging-sclc.html>. Updated January 29, 2024. Accessed October 1, 2025.



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