Zepzelca® (lurbinectedin) and Atezolizumab (Tecentriq®) Combination Granted U.S. FDA Priority Review for First-Line Maintenance Treatment of Extensive-Stage Small Cell Lung Cancer

June 10, 2025

Target Action (PDUFA) Date set for October 7, 2025

Application based on data from IMforte, the first Phase 3 trial demonstrating statistically significant and clinically meaningful improvements in both progression-free and overall survival in the ES-SCLC first-line maintenance setting

Jazz to host investor webcast on Tuesday, June 10 at 4:30 p.m. EDT / 9:30 p.m. IST to review Zepzelca data

For U.S. media and investors only

DUBLIN, June 10, 2025 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced the U.S. Food and Drug Administration (FDA) has accepted the supplemental New Drug Application (sNDA) for Zepzelca® (lurbinectedin) in combination with atezolizumab (Tecentriq®) as a first-line maintenance treatment for people with extensive-stage small cell lung cancer (ES-SCLC) whose disease has not progressed after first-line induction therapy with atezolizumab, carboplatin, and etoposide for Priority Review, with a Prescription Drug User Fee Act (PDUFA) action date of October 7, 2025. Priority Review is granted to applications for drugs that have the potential to significantly improve the treatment, prevention, or diagnosis of serious conditions.

"The FDA's Priority Review designation for *Zepzelca* in combination with atezolizumab as a first-line maintenance treatment highlights the urgent need for new approaches and the potential benefit of *Zepzelca* for patients with extensive-stage small cell lung cancer, a disease with limited therapeutic options and high unmet need," 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. "We are pleased to have received this review designation after presenting the IMforte trial data at ASCO 2025 with simultaneous publication in *The Lancet.* Together, these milestones bring us a step closer to potentially offering patients a new first-line maintenance option that could help extend the time they live without their disease progressing."

The sNDA submission is based on results from the Phase 3 IMforte trial of *Zepzelca* in combination with atezolizumab, which met both primary endpoints, demonstrating statistically significant improvements in progression-free survival (PFS) and overall survival (OS) compared to atezolizumab alone. Following induction therapy with carboplatin, etoposide and atezolizumab, patients who did not have disease progression were randomized to receive *Zepzelca* plus atezolizumab or atezolizumab alone. From the point of randomization, which occurred after patients completed the induction phase of four cycles of platinum-based chemotherapy plus atezolizumab, the median PFS was 5.4 months for the *Zepzelca* plus atezolizumab combination versus 2.1 months for atezolizumab alone (stratified HR = 0.54, 95% CI: 0.43–0.67; p < 0.0001), and median OS was 13.2 months versus 10.6 months (stratified hazard ratio [HR] = 0.73; 95% CI: 0.57–0.95; p = 0.0174). The combination reduced the risk of disease progression or death by 46% and the risk of death by 27% compared to atezolizumab alone. The *Zepzelca* plus atezolizumab combination had no new or unexpected safety signals.

Webcast Details
IMforte trial results were first presented in an oral session at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting and published simultaneously in *The Lancet*. The Company will host an investor webcast on June 10 at 4:30 p.m. EDT / 9:30 p.m. IST to review these data. The webcast will include commentary from a leading small cell lung cancer expert and Company senior management. The webcast may be accessed from the Investors section of the Jazz Pharmaceuticals website at www.jazzpharmaceuticals.com.

About Small Cell Lung Cancer
In the U.S., approximately 13 percent of lung cancers are small cell.[1] Approximately 30,000 new cases of small cell lung cancer (SCLC) are reported in the U.S. each year.[1,2] 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.[1] 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.[2,3] 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.[2]

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.[4]

The FDA approved *Zepzelca* under accelerated approval in June 2020 for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy. The approval is based on overall response rate (ORR) and duration of response (DOR) demonstrated in an open-label, monotherapy clinical study. In December 2021, Jazz and PharmaMar announced the initiation of LAGOON, a confirmatory Phase 3 clinical trial of *Zepzelca* for the treatment of patients with relapsed SCLC. If positive, LAGOON could confirm the benefit of *Zepzelca* in the treatment of SCLC when patients progress following 1L treatment with a platinum-based regimen and support full approval in the U.S.

ZEPZELCA (lurbinectedin) for injection 4 mg, is indicated for the treatment of adult patients with metastatic 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 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.

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

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.

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.

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.

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%).

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 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%).

Please see accompanying full Prescribing Information.

ZEPZELCA is a trademark of Pharma Mar, S.A. used by Jazz Pharmaceuticals under license.

Tecentriq (atezolizumab) is a registered trademark of Genentech, a member of the Roche Group.

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 for more information.

Jazz Pharmaceuticals plc Caution Concerning Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements related to Zepzelca's potential as a first-line maintenance therapy for extensive-stage small cell lung cancer and other statements that are not historical facts. These forward-looking statements are based on Jazz Pharmaceuticals' current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with the successful completion of regulatory activities and uncertain regulatory approval, and other risks and uncertainties affecting Jazz Pharmaceuticals and its development programs, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals plc's Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including Jazz Pharmaceuticals' Annual Report on Form 10-K for the year ended December 31, 2024, as supplement by Jazz Pharmaceuticals' Quarterly Report on Form 10-Q for the quarter ended March 31, 2025, and future filings and reports by Jazz Pharmaceuticals. Other risks and uncertainties of which Jazz Pharmaceuticals is not currently aware may also affect Jazz Pharmaceuticals' forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. The forward-looking statements herein are made only as of the date hereof or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by Jazz Pharmaceuticals on its website or otherwise. Jazz Pharmaceuticals undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

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[1] 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 June 10, 2025.

[2] American Cancer Society. What is lung cancer? https://www.cancer.org/cancer/lung-cancer/about/what-is.html. Updated October 1, 2019. Accessed June 10, 2025.

[3] American Cancer Society. Small cell lung cancer stages. https://www.cancer.org/cancer/lung-cancer/detection-diagnosis-staging/staging-sclc.html. Updated October 1, 2019. Accessed June 10, 2025.

[4] ZEPZELCA (lurbinectedin) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

combination-granted-us-fda-priority-review-for-first-line-maintenance-treatment-of-extensive-stage-small-cell-lung-cancer-302477581.html

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