## Zepzelca™ (lurbinectedin) – New orphan drug approval

- On June 15, 2020, Jazz Pharmaceuticals and PharmaMar announced the FDA approval of Zepzelca (lurbinectedin), 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).
- 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 resulting in disruption of the cell cycle and eventual cell death.
- The efficacy of Zepzelca was established in an open-label, multi-cohort study in patients with advanced or metastatic solid tumor. The study included a cohort of patients (N = 105) with SCLC with disease progression on or after platinum-based chemotherapy. The major efficacy outcome measure was overall response rate (ORR). An additional efficacy outcome measure was duration of response (DOR).
    - The overall ORR was 35% (95% CI: 26, 45) and the median DOR was 5.3 months (95% CI: 4.1, 6.4).
- Warnings and precautions for Zepzelca include myelosuppression, hepatotoxicity, and embryo-fetal toxicity.
- The most common adverse reactions, including laboratory abnormalities (≥ 20%), with Zepzelca use were 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.
- The recommended dose of Zepzelca is 3.2 mg/$m^2$ by intravenous infusion over 60 minutes every 21 days until disease progression or unacceptable toxicity.
    - Zepzelca should only be initiated if absolute neutrophil count is at least 1,500 cells/$mm^3$ and platelet count is at least 100,000/$mm^3$.
    - Premedication with corticosteroids and serotonin antagonists can be considered for antiemetic prophylaxis.
- Jazz Pharmaceuticals plans to launch Zepzelca in early July. Zepzelca will be available as a 4 mg lyophilized powder in a single-dose vial.



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