RXADVANCE
2 Park Central Drive
Southborough, MA 01772

NEW DRUG APPROVAL

Brand Name	ZEPZELCA™
Generic Name	lurbinectedin
Drug Manufacturer	Jazz Pharmaceuticals, Inc.

New Drug Approval

ZEPZELCA™ is an alkylating drug 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.

Limitation Of Use: Initiate treatment only if absolute neutrophil count (ANC) is greater than or equal to 1,500 cells/mm$^{(3)}$ or greater and platelet count is greater than or equal to 100,000/mm$^{(3)}$.

FDA Approval Date: June 15, 2020

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Small cell lung cancer (SCLC) is a fast-growing type of lung cancer. It spreads much more quickly than non-small cell lung cancer. There are two types of SCLC:

- Small cell carcinoma (oat cell cancer)
- Combined small cell carcinoma

Most SCLCs are of the oat cell type. About 15% of all lung cancer cases are SCLC. Small cell lung cancer is slightly more common in men than women.

Almost all cases of SCLC are due to cigarette smoking. SCLC is very rare in people who have never smoked.

SCLC is the most aggressive form of lung cancer. It usually starts in the breathing tubes (bronchi) in the center of the chest. Although the cancer cells are small, they grow very quickly and create large tumors. These tumors often spread rapidly (metastasize) to other parts of the body, including the brain, liver, and bone.

Lung cancer is the leading cause of cancer death in the United States and around the world. Almost as many Americans die of lung cancer as of prostate, breast, and colon cancer combined every year. Siegel and colleagues reviewed recent cancer data and estimated a total of 239,320 new cases of lung cancer and 161,250 deaths from lung cancer in the United States in 2010.

In the United States, cancer of the lung and bronchus ranks second in both genders, with an estimated 115,060 new cases in men (14% of all new cancers) and 106,070 in women (14% of all new cancers). The age-adjusted incidence rate of lung cancer is 62 per 100,000 men and women per year in the United States, with the incidence rate higher in men than in women (75.2 vs 52.3 per 100,000).[3] Lung cancer in both genders tops the list on the number of estimated deaths yearly (85,600, or 28% of all cancer deaths for men, and 71,340, or 26% of all cancer deaths for women).

Efficacy

Efficacy was demonstrated in the PM1183-B-005-14 trial (Study B-005; NCT02454972), a multicenter open-label, multi-cohort study enrolling 105 patients with metastatic SCLC who had disease progression on or after platinum-

based chemotherapy. Patients received lurbinectedin 3.2 mg/m^2 by intravenous infusion every 21 days until disease progression or unacceptable toxicity.

The main efficacy outcome measures were confirmed overall response rate (ORR) determined by investigator assessment using RECIST 1.1 and response duration. Among the 105 patients, the ORR was 35% (95% CI: 26%, 45%), with a median response duration of 5.3 months (95% CI: 4.1, 6.4). The ORR as per independent review committee was 30% (95% CI: 22%, 40%) with a median response duration of 5.1 months (95% CI: 4.9, 6.4).

Safety

ADVERSE EVENTS

The most common adverse reactions, including laboratory abnormalities, (≥20%) are 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.

WARNINGS & PRECAUTIONS

- Myelosuppression: Monitor blood counts prior to each administration. Initiate treatment with ZEPZELCA™ only if baseline neutrophil count greater than or equal to 1,500 cells/mm^3 and platelet count is greater than or equal to 100,000/mm^3. Withhold, reduce the dose, or permanently discontinue ZEPZELCA™ based on severity.
- Hepatotoxicity: 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.
- 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.

CONTRAINDICATIONS

Specific contraindications have not been determined.

Clinical Pharmacology

MECHANISMS OF ACTION

lurbinectedin is an alkylating drug that binds guanine residues in the minor groove of DNA, forming adducts and resulting in a bending of the DNA helix towards the major groove. Adduct formation triggers a cascade of events that can affect the subsequent activity of DNA binding proteins, including some transcription factors, and DNA repair pathways, resulting in perturbation of the cell cycle and eventual cell death.

Dose & Administration

ADULTS

- Premedication, consider corticosteroids (eg, dexamethasone 8 mg IV or equivalent) and serotonin antagonists (e.g., ondansetron 8 mg IV or equivalent) prior to infusion
- 3.2 mg/m^2 IV infusion over 60 minutes every 21 days until disease progression or unacceptable toxicity

PEDIATRICS

Safety and effectiveness in pediatric patients have not been established.

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GERIATRICS

No overall difference in effectiveness was observed between patients aged 65 and older and younger patients.

RENAL IMPAIRMENT

There are no dosage adjustments provided in the manufacturer's labeling for CrCl 30 to 89 mL/minute. For CrCl <30 mL/minute there are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

HEPATIC IMPAIRMENT

No dose adjustment of ZEPZELCA™ is recommended for patients with mild hepatic impairment (total bilirubin ≤ ULN and AST > ULN, or total bilirubin 1.0-1.5 × ULN and any AST).

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Lyophilized powder for injection in a single-dose vial: 4 mg