Corporate Medical Policy

Lurbinectedin (Zepzelca™)

File Name: lurbinectedin_zepzelca
Origination: 10/2020
Last CAP Review: n/a
Next CAP Review: 3/2021
Last Review: 10/2020

Description of Procedure or Service

Lurbinectedin (Zepzelca™) is an alkylating drug indicated for the treatment of adults with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.

SCLC is a neuroendocrine tumor that represents approximately 15 percent of all lung cancers and is predominantly attributable to smoking. It is differentiated from most types of non-small cell lung cancer by its rapid doubling time, high growth fraction, and early development of widespread metastases. SCLC is highly responsive to initial chemotherapy and radiotherapy; however, recurrence typically occurs within 14 to 15 months for limited-stage SCLC and within 5 to 6 months for extensive-stage SCLC. There are few treatment options following failure of first-line therapy, and the median survival for relapsed SCLC ranges from 2 to 6 months.

Lurbinectedin (Zepzelca™) is an alkylating drug and selective inhibitor of oncogenic transcription, which was approved by the U.S. Food and Drug Administration (FDA) in June 2020 for the treatment of metastatic SCLC. It works by binding to guanine residues in the minor groove of DNA to form adducts and bend the DNA helix towards the major groove, which affects DNA binding protein activity. Inhibition of oncogenic transcription leads to tumor cell apoptosis.

Related Medical Policies:
PD-1 Inhibitors
Topotecan Hydrochloride (Hycamtin)

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for lurbinectedin (Zepzelca™) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit

design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Lurbinectedin (Zepzelca) is covered

Initial Therapy

Lurbinectedin (Zepzelca) may be considered medically necessary for the treatment of adult patients with small cell lung cancer (SCLC) when the following criteria are met:

- The patient has a diagnosis of SCLC; and
- The patient has metastatic disease; and
- The patient has had disease progression on or after platinum-based chemotherapy.

Initial authorization: 6 months

Continuation Therapy

Continuation of treatment with lurbinectedin (Zepzelca) beyond 6 months after initiation of therapy, and every 12 months thereafter, is considered medically necessary for the treatment of metastatic small cell lung cancer (SCLC) when the following criteria are met:

1. The patient is currently receiving lurbinectedin and continues to meet initial criteria; and
2. The patient has continued clinical benefit on lurbinectedin therapy as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile.

Use of lurbinectedin (Zepzelca) may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either:

- In accordance with FDA label (when clinical benefit has been established, (see Policy Guidelines); **OR**

- In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

When Lurbinectedin (Zepzelca) is not covered

Lurbinectedin (Zepzelca) is considered **investigational** and therefore not covered when the above criteria are not met.

Lurbinectedin (Zepzelca) is considered investigational when used for:

1. Non-cancer indications; **OR**

2. When criteria are not met regarding FDA labeling **OR** strong endorsement/support by nationally recognized compendia, as stated under "When Lurbinectedin (Zepzelca) is covered."

Policy Guidelines

Dosing and Administration

The recommended dose of Zepzelca is 3.2 mg/m^2 given as an intravenous infusion every 21 days until disease progression or unacceptable toxicity. Due to risk of myelosuppression, treatment with Zepzelca should only be initiated if the absolute neutrophil count (ANC) is at least 1,500 cells/mm^3 and platelet count is at least 100,000/mm^3.

Evidence Summary

The efficacy of lurbinectedin (Zepzelca) was evaluated as a single agent in an open-label, multicenter, multi-cohort phase 2 clinical trial of patients with advanced or metastatic solid tumors (NCT02454972). A cohort of patients with small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy (n=105) received lurbinectedin 3.2 mg/m^2 intravenously every 21 days for a median of 4 cycles (range, 1 to 24 cycles). Patients were excluded from the study who had central nervous system (CNS) involvement, grade ≥3 dyspnea, daily intermittent oxygen requirement, hepatitis or cirrhosis, or who were immunocompromised. The primary efficacy endpoint was overall response rate (complete or partial response), which was seen in 37 patients (35.2%; 95% CI 26.2-45.2). An overall response rate of 45% (CI 32-58) was shown in patients with a chemotherapy free interval (CTFI) of ≥90 days (n=60) versus 22% (CI 11-37) in patients with a CTFI <90 days (n=45). Lurbinectedin showed a durable response in some SCLC patients who had progressed on or after platinum-based chemotherapy, and patients with a chemotherapy free interval of ≥90 days demonstrated better outcomes.

Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established and should not be determined to be investigational as defined in Corporate Medical Policy (CMP), "Investigational (Experimental) Services."

Please refer to CMP "Investigational (Experimental) Services" for a summary of evidence standards from nationally recognized compendia.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *J9223, S0353, S0354*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Jazz Pharmaceuticals, Inc. Zepzelca (lurbinectedin) for injection for intravenous use. Highlights of prescribing information. June 2020. Available at: https://pp.jazzpharma.com/pi/zepzelca.en.USPI.pdf. Last accessed September 2020.

U.S. Food and Drug Administration. FDA grants accelerated approval to lurbinectedin for metastatic small cell lung cancer. June 15, 2020. Available at: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-lurbinectedin-metastatic-small-cell-lung-cancer. Last accessed September 2020.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Small Cell Lung Cancer, version 1.2021. Revised August 11, 2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. Last accessed September 2020.

Medical Director review 9/2020

Policy Implementation/Update Information

10/1/20 New policy developed. Zepzelca is considered medically necessary for the treatment of adult patients with small cell lung cancer (SCLC) when specified medical criteria and guidelines are met. Added HCPCS codes C9399, J3490, J3590, J9999, S0353, and S0354 to Billing/Coding section. References added. Medical Director review 9/2020. **Policy notification given 10/1/2020 for effective date 1/1/2021**. (krc)

12/31/20 Added HCPCS code J9223 to Billing/Coding section effective 1/1/2021 and deleted codes C9399, J3490, J3590, and J9999 termed 12/31/2020. (krc)