Clinical Policy Title:	lurbinectedin
Policy Number:	RxA.642
Drug(s) Applied:	Zepzelca™
Original Policy Date:	07/26/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Lurbinectedin (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(s).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
lurbinectedin (Zepzelca™)	Metastatic SCLC with disease progression on or after platinum-based chemotherapy	3.2 mg/m^2 once every 21 days until disease progression or unacceptable toxicity	3.2 mg/m^2 per 21-day cycle

Dosage Forms

- IV injection: 4 mg lyophilized powder in a single-dose vial.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Metastatic Small Cell Lung Cancer (must meet all)**:**

1. Diagnosis of recurrent, advanced, or metastatic SCLC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Patient's performance Score is 0-2 and be used as a single agent (see Appendix D for reference ranges);
5. Member has disease progression on or after platinum-based chemotherapy;
6. Trial and failure of topotecan orally or intravenously unless contraindicated or clinically adverse effects

are experienced;
7. Dose does not exceed 3.2 mg/m^2 per 21-day cycle.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Metastatic Small Cell Lung Cancer (must meet all)**:**
1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Dose does not exceed 3.2 mg/m^2 per 21-day cycle.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
SCLC: Small Cell Lung Cancer
CNS: Central Nervous System
AUC: Area under the curve

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
topotecan (Hycamtin®)	Oral: 2.3 mg/m^2/day for 5 consecutive days every 21 days. Intravenous: 1.5 mg/m^2/day for 5 consecutive days every 21 days.	Oral: 2.3 mg/m2 per day PO Intravenous: 4 mg IV
Tecentriq®	ES - SCLC: 840 mg intravenously every 2 weeks; OR 1,200 mg intravenously every 3 weeks; OR 1,680 mg intravenously every 4 weeks until disease progression or unacceptable toxicity. Administer in combination with carboplatin (AUC 5 IV on day 1) and etoposide (100 mg/m^2 IV on days 1, 2, and 3), every 3 weeks for 4 cycles. Administer atezolizumab prior to chemotherapy when given on the same day.	1,680 mg/4 weeks

Drug Name	Dosing Regimen	Maximum Dose
Imfinzi™	ES - SCLC: Weight 30 kg and more: With etoposide and either carboplatin or cisplatin, administer Imfinzi™ 1500 mg every 3 weeks in combination with chemotherapy, and then 1500 mg every 4 weeks as a single agent. Weight less than 30 kg: With etoposide and either carboplatin or cisplatin, administer Imfinzi™ 20 mg/kg every 3 weeks in combination with chemotherapy, and then 10 mg/kg every 2 weeks as a single agent	1500 mg every 3 weeks
etoposide (Etopophos®)	SCLC: Intravenous: Administered in combination with cisplatin, as first-line treatment. 35 mg/m^2 per day administered intravenously over 5 minutes to 3.5 hours for 4 days or 50 mg/m^2 per day administered intravenously over 5 minutes to 3.5 hours for 5 days. Oral: 70 mg/m^2 orally once daily on days 1 to 4 in combination with other approved chemotherapeutic agents, every 3 to 4 weeks. Alternatively, administer etoposide 100 mg/m^2 orally once daily on days 1 to 5 in combination with other approved chemotherapeutic agents, every 3 to 4 weeks. Round the dose to the nearest capsule strength. The recommended dose of etoposide capsules is two times the intravenous dose, rounded to the nearest 50 mg.	Intravenous: 200 mg/m^2 per day Oral: 100 mg/m^2 per day.

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Strong/moderate CYP3A inducers and inhibitors: Avoid coadministration.
- Zepzelca™ has not been studied in patients with the following conditions: Central nervous system (CNS) involvement, grade ≥3 dyspnea, daily intermittent oxygen requirement, hepatitis or cirrhosis, and immunocompromised patients. Caution should be exercised in using Zepzelca™ with these patients.

- Reference ranges for performance score:

Grade	ECOG Performance Status
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
5	Dead

References

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6. .Etopophos® Prescribing Information. Montgomery, AL: H2-Pharma, LLC; December 2019. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7499fc35-fae8-44ad-bbab-9a1a589bf3ee . Accessed July 01, 2021.
7. Imfinzi™ Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2021. Available at: https://www.imfinzi.com . Accessed July 01, 2021.
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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	07/27/2020	09/14/2020
Policy was reviewed: 1. Background was updated to include	07/01/2021	09/14/2021

generic drug name Lurbinectedin. 2. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 3. Initial Approval Criteria I.A.4 was updated to include “Patient’s performance Score is 0-2…”. 4. Initial Approval Criteria I.A.6.b was updated to remove “dose is supported by practice guidelines or peer-reviewed literature for the related off-label use…”. 5. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving the medication that has been authorized by..." 6. Continued Therapy Approval Criteria II.A.2.b was updated to remove “dose is supported by practice guidelines or peer-reviewed literature for the related off-label use…”. 7. Appendix A was updated to include abbreviations CNS and AUC. 8. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 9. Appendix B: Therapeutic Alternatives was updated to include alternative drugs Tecentriq, Imfinzi, and etoposide as well as their respective dosing regimens and maximum doses. 10. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only. 11. Appendix D was updated to include “Reference ranges for performance score…” and subsequent ECOG Performance Status reference table. 12. References were reviewed and updated.		
