CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

Lurbinectedin (Zepzelca)

(Jazz Pharmaceuticals Canada Inc.)

Indication: metastatic small cell lung cancer (SCLC)

August 18, 2022

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0281-000
Brand name (generic)	Lurbinectidin (Zepzelca)
Indication(s)	Treatment of adult patients with Stage III or metastatic small cell lung cancer (SCLC) who have progressed on or after platinum-containing therapy.
Organization	Ontario Health (CCO) Lung Cancer Drug Advisory Committee
Contact information[a]	Name: Dr. Donna Maziak

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
The DAC agrees with the negative recommendation.		

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

[a] CADTH may contact this person if comments require clarification.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please list any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☒
Ontario Health provided secretariat function to the DAC.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☒
	Yes	☐
If yes, please list the clinicians who contributed input and whose declarations have not changed: - Dr. Sara Kuruvilla		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Dr. Donna Maziak*
Position	*Lead, Ontario Health (CCO) Lung Cancer Drug Advisory Committee*
Date	*17/08/2022*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.	

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0281-000
Brand name (generic)	Lurbinectedin (Zepzelca)
Indication(s)	Treatment of adult patients with Stage III or metastatic small cell lung cancer (SCLC) who have progressed on or after platinum-containing therapy.
Organization	Lung Cancer Canada – Clinician Group
Contact information[a]	[redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☒
Lung Cancer Canada agreed that the absence of phase III data makes direct comparison of efficacy, toxicity and HRQOL difficult in this situation. The current ongoing Phase III study is in the early stage of enrollment and results are not anticipated until at least 4 years from now. Recurrent small-cell lung cancer patients are often very symptomatic which negatively affects their HRQoL, especially for those with platinum-refractory disease. Response to therapy is likely going to improve disease-related symptoms even in the presence of side effects. Current available options for platinum-refractory small-cell lung cancer have an ORR of 5% and mPFS of less than 2 months, as reported in the literature, options like lurbinectedin may provide a better chance of symptoms improvement. With the current enrollment status of the ongoing phase 3 study, such patients may not have access of a potentially more efficacious and tolerable option than topotecan or cyclophosphamide/doxorubicin/vincristine (CAV). Lurbinectedin also requires less chair time to administer and fewer trips for the patient to a cancer centre since it is given only on day 1 of each 21 day cycle for 1 hour (topotecan given daily on day 1-5 of 21 day cycle). Lurbinectedin is not known to carry the risks of hemorrhagic cystitis, neuropathy, and cardiac dysfunction seen with CAV.		
Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
If not, what aspects are missing from the draft recommendation?		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
	Yes	☒

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

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  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
1. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

B. Previously Disclosed Conflict of Interest		
3. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Dr. Quincy Chu • Dr. Stephanie Snow • Dr. Ron Burkes • Dr. Paul Wheatley-Price • Dr. Donna Maziak • Dr. Geoffery Liu • Dr. Rosalyn Juergens • Dr. Kevin Jao • Dr. David Dawe		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*

Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2

Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3

Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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Company	Check Appropriate Dollar Range			
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Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0281
Name of the drug and Indication(s)	Lurbinectedin for metastatic small cell lung cancer (SCLC)
Organization Providing Feedback	PAG

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.		
Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	☐
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	X
	No requested revisions	☐

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
None.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
In Table 3 Cost and Cost-effectiveness, in the treatment row, PAG is requesting adding the dosing schedule.
b) Reimbursement conditions and related reasons
None.
c) Implementation guidance
None.

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0281-000
Brand name (generic)	Lurbinectedin (Zepzelca)
Indication(s)	Treatment of adult patients with Stage III or metastatic small cell lung cancer (SCLC) who have progressed on or after platinum-containing therapy.
Organization	Lung Cancer Canada – Patient Group
Contact information[a]	[redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Lung Cancer Canada is disappointed with the negative recommendation by CADTH for the reimbursement of lurbinectedin for advanced small cell lung cancer (SCLC). Although the uncertainty in the clinical trial data and lack of comparator (control group) in the trial posed a valid rationale for the uncertainty in clinical benefit for patients treated with lurbinectedin, there are still benefits highlighted that patients on the treatment experienced. This was not concluded by pERC as stated in the final 2 lines under "Rationale for the Recommendation".

Although there are existing treatment options in the chemotherapy space for small cell lung cancer, there is still a huge unmet need for a wider variety of treatment options for SCLC patients in comparison to the waves of research that NSCLC has had in the past few decades. As the prognosis for those with SCLC is slim and disheartening due to the aggressive nature of the disease and rapid progression that follows, patients are eager for a treatment that can be effective at delaying disease progression and managing symptoms. As outlined in our initial submission, lurbinectedin allowed some patients the ability to return to a level of functionality that wasn't possible before, while being effective at delaying progression and carrying less toxic side effects than other chemotherapies. It also mitigates some travel-related barriers for patients due to its 21-day cycle, meaning fewer trips to the hospital, less travel time for patients, and greater flexibility to enjoy their lives and time they have.

With the approval of lurbinectedin representing the first progress in the SCLC treatment setting in more than a decade, there is a huge unmet need in these patients and due to the high symptom burden, rapid spread and progression of the disease, there are few viable treatment options. The currently ongoing phase 3 LAGOON clinical trial will showcase response to treatment and overall survival benefits, bringing in more real-world evidence that is needed. LCC hopes that CADTH takes these patient values into consideration, as patients are ultimately bearing the brunt of the decisions regarding treatment reimbursement.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐

If not, what aspects are missing from the draft recommendation?

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
N/A		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
N/A		

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Appendix 1. Conflict of Interest Declarations for Patient Groups

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A. Patient Group Information	
Name	*Shem Singh*
Position	*Executive Director*
Date	*Aug 11/2022*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
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Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	Lurbinectedin
Brand name (generic)	Zepzelca
Indication(s)	Metastatic small cell lung cancer
Organization	Lung Health Foundation
Contact information[a]	Name: Peter Glazier [redacted] [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒
Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale. We strongly disagree with CADTH's decision to not recommend reimbursement. There is an urgent need for treatment options for advanced stage small cell lung cancer patients. There are no existing options available for this population of patients, if their disease progresses on chemotherapy. The lack of options is creating inequities among lung cancer patients.		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒
If not, what aspects are missing from the draft recommendation?		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by CADTH.

Appendix 1. Conflict of Interest Declarations for Patient Groups

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A. Patient Group Information	
Name	*Jessica Sopher*
Position	*Director, Public Affairs*
Date	*09-08-2022*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
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	Yes	☒

D. New or Updated Conflict of Interest Declaration

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Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0281-000
Brand name (generic)	Zepzelca® (lurbinectedin)
Indication(s)	Treatment of adult patients with Stage III or metastatic small cell lung cancer (SCLC) who have progressed on or after platinum-containing therapy
Organization	Jazz Pharmaceuticals
Contact information[a]	Name: [redacted] Title: Market Access and Government Relations Email: [redacted] Phone: [redacted] Mailing Address: 4080 Confederation Parkway, Suite 602, Mississauga, Ontario, L5B 0G1

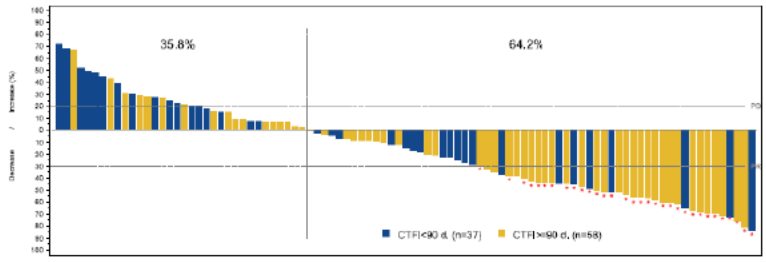
Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation?	Yes	☐
	No	☒

Jazz Pharmaceuticals **does <u>not</u> agree** with the pERC initial recommendation which is not aligned with the sentiments and feedback provided by the clinician and patient groups as well as the clinical experts consulted by CADTH. After careful review of the pERC initial recommendation and associated feedback reports, Jazz asks that the pERC reconsiders several aspects of the submitted evidence:

1. **The phase II, B-005 study demonstrated that lurbinectedin is an active therapy for patients with relapsed small cell lung cancer (SCLC)** (1)

- This multicentre, multinational study recruited 105 relapsed SCLC patients with platinum refractory, resistant and sensitive disease and included patients with ECOG PS ≤2 (1).
- Overall response assessed by the investigators was 35.2%. These results are supported by the durability of responses, with duration of ≥6 months in 43% of patients who had a response.
- According to the independent review committee, 61 (64%) patients had reduction in target lesions, including 20 (19%) with a chemotherapy-free interval (CTFI) of <90 days and 41 (81%) of those with a CTFI of ≥90 days (see Figure 1).
- It is important to remember that SCLC is an aggressive and rapidly progressing disease with poor outcomes. At data cut-off, median overall survival (mOS) was 9.3 months, which is noteworthy in the second-line SCLC setting, especially for a population that included patients with refractory/ resistant disease.

Figure 1: Waterfall plot showing maximum variation in target lesion size



2. Uncertainty in clinical benefit has been addressed by three submitted indirect treatment comparisons (ITC); the breadth of which demonstrate a net clinical benefit in favor of lurbinectedin compared to other available treatments.

- Jazz Pharmaceuticals disagrees with pERC's assessment that "*the limitations in all 3 ITCs that meant conclusions could not be drawn for any of them*" (2).
- Each submitted ITC concluded that lurbinectedin offers positive clinical outcomes to patients with SCLC including longer median overall survival (mOS).
- In particular, a population-level, Canadian synthetic control arm (SCA) study evaluated the treatment efficacy of lurbinectedin compared to standard of care (SOC) in patients with relapsed SCLC in Alberta following exposure to platinum therapy (3). In their review, CADTH notes the consulted clinical experts agreed that "*the set of patients seemed generalizable to the population of patients with SCLC in Alberta and likely to the rest of the Canadian provinces and territories*".
- In the SCA, the unadjusted mOS was 6.7 months (95% CI: 6.0 - 7.7) and the CTFI and stage-standardized median OS was 6.1 months (5.4 - 7.7) compared to 9.3 months (6.3 - 11.8) in the lurbinectedin trial. <u>This represents a potential >3 months survival benefit in favor of lurbinectedin</u>. Considering that the current SOC of care was adopted two decades ago with no new advances since, the magnitude of this potential survival benefit cannot be ignored.

3. Lurbinectedin is associated with low levels of treatment-related adverse events, a widely accepted proxy for Quality of Life (QoL) improvement.

- Canadian clinicians have expressed significant support for the adoption of lurbinectedin within the Canadian treatment algorithm. In their feedback to CADTH, the clinical experts repeatedly stressed the difficulties SCLC patients experience with available treatments in the second and subsequent lines, especially IV topotecan and CAV, which they described as "*terribly harsh*" (2). They felt that severe hematological toxicities occurred less frequently in patients receiving lurbinectedin in the B-005 study compared with their clinical experience with IV topotecan and CAV in the second- and third-line setting. Patients who had experience with lurbinectedin felt that the drug had reduced or stabilized tumour size, delayed disease progression, helped them continue or resume activities of daily living including employment, and had more manageable side effects and a shorter recovery time compared with other SCLC therapies they had received.
- Furthermore, with the use of available therapies, most individuals in the Canadian SCA (67%) experienced one or more hospitalizations or ER visits within six-months of initiating post-platinum therapy (a clinical proxy for serious adverse events [SAEs]). These findings suggest a potentially high degree of treatment-related toxicity in this disease setting and highlight the need for more tolerable therapies (3).
- By comparison, in the B-005 trial (1), lurbinectedin had an acceptable and manageable safety profile:
    - SAEs occurred in 11 (10%) patients.
    - No treatment-related deaths were reported with lurbinectedin.
    - Only two (2%) patients discontinued lurbinectedin therapy because of treatment-related adverse events.

4. New Data: Five (5) additional analyses suggest that SCLC patients treated with lurbinectedin experience similar outcomes to those observed in the B-005 study.

Over the course of the CADTH reimbursement review, new data has become available from five additional studies which further support that patients treated with lurbinectedin experience similar clinical improvements to those observed in the B-005 study These studies are summarized in the table below:

Study	Key Takeaway
1. EMERGE 402 – Phase IV Evidence (presented at World Congress of Lung Cancer (WCLC) 2022) (4).	From EMERGE-402, the real-world safety profile of lurbinectedin is generally consistent with the B-005 study, with no new safety signals.
2. Flatiron Real World Outcomes Analysis of Lurbinectedin in Adult Small Cell Lung Cancer Patients in the US (not yet presented; accepted to ESMO 2022) (5).	Patients treated with lurbinectedin as 2L monotherapy in this real-world setting had outcomes within the bounds observed in the B-005 clinical trial.
3. Characterization of Real-World Use of Lurbinectedin in Adult Small Cell Lung Cancer Patients in the United States from the Flatiron Health EHR database (presented at WCLC 2022) (6).	In the United States, lurbinectedin use to date reflects per-label treatment in metastatic SCLC patients who previously received platinum-based chemotherapy.
4. Concert AI US EMR – Real World Comparative Arm study (presented at ASCO 2022) (7).	Lurbinectedin monotherapy demonstrated improved median OS, lower risk of death at 3 and 6 months, and higher response rate compared to other SOC treatments in relapsed/refractory SCLC.
5. Analysis of patients with relapsed small cell lung cancer (SCLC) receiving single-agent lurbinectedin in the phase 3 ATLANTIS trial (presented at ASCO 2022) (8).	Patients who completed 10 cycles of lurbinectedin + DOX combination and switched to lurbinectedin monotherapy tended to maintain or improve their tumor response (including an increase in complete responses), with favorable OS and duration of response (DOR) and acceptable tolerability with no new safety signals.

5. **Lurbinectedin has been recognized as a clinically meaningful treatment that addresses an immediate need for new therapies in Canada.**

- Results from the LAGOON Phase III Study (NCT05153239) will not be available for 3 years (estimated: 2025). Although this study is in active recruitment, Canadian SCLC patients do not have the luxury of time to wait for its completion. The predicted 1-year survival rates for SCLC in Canada range from 20-43% and decline to the single digits by 5 years (9).
- An immediate need for new therapies in relapsed SCLC is further validated by.
    - Regulatory bodies: The FDA granted orphan drug designation and priority review for lurbinectedin for relapsed SCLC patients under an expedited program (Project Orbis) (10). Health Canada also granted accelerated approval with a notice of compliance with conditions (11).
    - Guidelines: NCCN practice guidelines have already adopted and recognized lurbinectedin regimen as the preferred therapy for SCLC patients with relapse ≤6 months and as a recommended regimen for patients with relapse >6 months (12). The ESMO guidelines have similarly recognized the value of lurbinectedin for these patients (13).
    - Canadian Clinicians: Canadian clinicians have expressed significant adoption of lurbinectedin as a valuable treatment option for Canadian patients. In the time since it has become available in Canada (Dec 2021), lurbinectedin has been requested for [redacted] patients by [redacted] clinicians across the country (as of Aug 17, 2022) (14).
- Jazz notes that CADTH has issued positive recommendations for drugs with similar data packages (phase II & ITCs), similar magnitude of benefit and with ongoing Phase III trials in difficult to treat disease sites with high unmet need. Given these similarities, Jazz believes the lurbinectedin submission should be reconsidered.

Summary

The phase II, B-005 study demonstrated that lurbinectedin is an active therapy for patients with relapsed SCLC. Uncertainty in clinical benefit has been addressed by three submitted ITCs; the breadth of which demonstrate a meaningful survival benefit in favor of lurbinectedin compared to other available treatments.

Further validation of the meaningful clinical benefit of lurbinectedin and the unmet need is evident via the clinician and patient input into CADTH, as well as the fact that priority review was granted by both Health Canada and the FDA. Additionally, the NCCN practice guidelines have already adopted and recognized lurbinectedin regimen as the preferred therapy for SCLC patients with relapse ≤6 months and as a recommended regimen for patients with relapse >6 months. The ESMO guidelines have similarly recognized the value of lurbinectedin for these patients. On the basis of clinical benefit alone – lurbinectedin represents an important option for a disease with devastating historical outcomes and provides hope for a patient population who have not benefited from new therapies in decades – especially after the progression of disease.

Given the final data presented in the submission, newly available data, along with the feedback from the clinical experts, clinician and patient input, and the urgent need for SCLC patients to access a new safe and efficacious regimen - Jazz respectfully requests CADTH to reconsider its negative initial recommendation and its potential impact on patients' ability to access an important therapy.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐
Not applicable		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
Not applicable		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
Not applicable		

[a] CADTH may contact this person if comments require clarification.

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