CADTH

CADTH REIMBURSEMENT REVIEW

# Stakeholder Feedback on Draft Recommendation

## LUTETIUM (177Lu) VIPIVOTIDE TETRAXETAN (Pluvicto)

(Advanced Accelerator Applications USA, Inc.)

**Indication:** The treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have received at least one androgen receptor pathway inhibitor (ARPI) and taxane-based chemotherapy.

**February 16, 2023**

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# CADTH Reimbursement Review

# Feedback on Draft Recommendation

| Stakeholder information | |
|---|---|
| CADTH project number | PC0297 |
| Name of the drug and Indication(s) | lutetium ($^{177}$Lu) vipivotide tetraxetan for prostate cancer |
| Organization Providing Feedback | PAG |

| 1. Recommendation revisions<br>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<br>Complete this section if major or minor revisions are requested |
|---|
| None |

| 3. Clarity of the recommendation<br>Complete this section if editorial revisions are requested for the following elements |
|---|
| **a) Recommendation rationale** |
| None |
| **b) Reimbursement conditions and related reasons** |
| Under Table 1 for Reimbursement conditions for initiation, PAG is requesting the following revisions:<br><br>For the implementation guidance, to remove Ga-68 from criteria 1,2,3,4 . Suggest to specify the criteria to have at least one PSMA-11 positive lesion. Given the variation of facilities to |

accessing 68-Ga vs other isotopes such as F-18, omitting the details on Ga-68 can avoid potential implementation challenge.

**c) Implementation guidance**

Please provide high-level details regarding the information that requires clarification. You can provide specific comments in the draft recommendation found in the next section. Additional implementation questions can be raised here.

1.1 Initiation & PSMA positive / 10.2 Feasibility of adoption - Access to PSMA-PET-CT

- At the moment, only F-18 labelled PSMA-PET agents are available for PSMA PET scanning in certain jurisdictions (e.g., F-18 DCFPyL and F-18 PSMA 1007). To support equitable access to therapy with PLUVICTO and help address ongoing challenges in PSMA PET agent availability/accessibility, eligibility should not be limited Ga-68 PET-CTs, but to also include PET-CT scans performed with F-18 labelled agents, or other PSMA radiopharmaceuticals that may be adopted by the jurisdictions as evidence evolves.
- Current guidelines from the Advanced Prostate Cancer Consensus Conference (APCCC) 2021 support using Ga-68 or F-18 labelled PSMA PET agents (https://www.sciencedirect.com/science/article/pii/S0302283822018073?via%3Dihub

4. Prescribing

- Given the interdependencies, $^{177}$Lu vipivotide tetraxetan should be prescribed by "an oncology specialist with expertise in radioligand therapy, in the context of a multidisciplinary approach to care including Nuclear Medicine Physician/Radiologist, Medical/ Radiation Oncologist and any other relevant clinical specialties."
    - Patient evaluation for eligibility includes imaging, laboratory values, and medications; a team approach ensures appropriate patients are selected and addresses any concerns with complications, adverse events and disease progression.
    - Some facilities' approach to radioligand therapy includes Nuclear Medicine Physician's prescribing the therapy, while in discussion with relevant healthcare professionals through regular tumour board meetings.
- Prescribing physicians should also work closely with nuclear imaging radiologists in cases of equivocal positive cases to determine eligibility.

10.1 Feasibility of adoption – organizational feasibility

- Not all centres will be able to support the delivery costs which may limit access. Implementation will need to consider cost of delivery, in addition to the cost of lutetium

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| Stakeholder information | |
|---|---|
| CADTH project number | PC0297-000 |
| Brand name (generic) | Pluvicto (lutetium vipivotide tetraxetan) |
| Indication(s) | Treatment of adults with prostate-specific membrane antigen-positive metastatic castration-resistant prostate cancer who have received at least one androgen receptor pathway inhibitor and taxane-based chemotherapy. |
| Organization | Canadian Cancer Society |
| Contact information | Name: Sasha Frost [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.

| 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?

Related to page 9: Patient input (specifically perspectives from patients who tried the drug under evaluation) was sparce in the draft recommendation. Patients experiences with the drug under review (side effect tolerability for Pluvicto, patient perspectives on the tolerability of being radioactive for several days, how they felt about the route/frequency of administration in hospital, the QoL improvements noted etc.) were not mentioned in the stakeholder section of the report. This section also did not mention concerns about access to PSMA PET scanners and local treatment access (however this was highlighted in other sections of this report). Although details on patient perspectives were sparse in the report, the overall recommendation reflected patient values as noted in the patient submission.

| 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.

Related to page 5: The implementation issues were clearly stated in the recommendation, however, more clarity on the ICER of $50,000 per QALY gained (including why this benchmark has been set for oncology drugs, if it has been inflation adjusted and if this is comparable to benchmarks internationally) would be helpful.

| **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

- 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.

| **A. Patient Group Information** | |
|---|---|
| **Name** | *Sasha Frost* |
| **Position** | *Senior Advocacy Specialist (Public Engagement)* |
| **Date** | *Please add the date form was completed (15-02-2023)* |
| ☒ | 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** | | | |
|---|---|---|---|---|
| | **$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* | ☐ | ☐ | ☐ | ☐ |

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# CADTH Reimbursement Review
# Feedback on Draft Recommendation

| Stakeholder information | |
|---|---|
| CADTH project number | PC0297-000 |
| Brand name (generic) | lutetium ($^{177}$Lu) vipivotide tetraxetan |
| Indication(s) | The treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have received at least one androgen receptor pathway inhibitor (ARPI) and taxane-based chemotherapy. |
| Organization | Advanced Accelerator Applications Canada Inc. (AAA) |
| Contact information[a] | [redacted] |

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

Advanced Accelerator Applications Canada Inc. agrees with the pCODR Expert Review Committee's (pERC) draft recommendation for PLUVICTO™ (lutetium [$^{177}$Lu] vipivotide tetraxetan) for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have received at least one androgen receptor pathway inhibitor (ARPI) and taxane-based chemotherapy.

However, the sponsor would like to provide additional clarity to the implementation guidance surrounding PSMA testing found in Table 1, on page 4 of the draft recommendation. Although $^{68}$Ga-PSMA-11 was used in the VISION trial, other PSMA imaging tracers (e.g., F-18 piflufolastat PSMA) can be used to ascertain PSMA status in prostate cancer, as per NCCN guidelines. Therefore, the sponsor kindly requests that the implementation guidance clarify that PSMA-positivity should be assessed using a validated tracer combined with PET-CT imaging.

Regarding the economic analysis, CADTH was not able to derive conclusions regarding the relative effectiveness of PLUVICTO™ compared to cabazitaxel, and ultimately suggested PLUVICTO™ was dominated by cabazitaxel in the base case (Table 2, page 21). AAA would like to emphasize that the totality of evidence submitted by the sponsor demonstrated a likelihood of benefit of PLUVICTO™ over cabazitaxel (e.g., statistically significant primary endpoint readouts from TheraP, NMA, and RWE OS data). This aligns with clinician input stating that "in the TheraP trial, lutetium vipivotide tetraxetan compared favourably with cabazitaxel in men with mCRPC leading to a higher PSA response and fewer grade 3 or 4 adverse events" (Clinical Review Report, Clinician Input section, p122).

Furthermore, AAA would like to clarify the point of "CADTH identified concerns regarding the both the internal and external validity of the VISION results, in particular, imbalanced censoring between patients in $^{177}$Lu vipivotide tetraxetan and BSC/BSoC arms may bias the results for rPFS and SSE, favouring $^{177}$Lu vipivotide tetraxetan" (Table 2, page 21). There is no data to support or refute the hypotheses of early dropouts favouring PLUVICTO™. The key driver of dropout in the control arms of both the VISION and TheraP trials was reported as "patient disappointment at not having access to $^{177}$Lu vipivotide tetraxetan" (as stated in the Critical appraisal, internal validity subsection, on page

20). Therefore, the results of the CADTH's reanalysis (i.e., adjustments to utility values in the economic analyses) underestimate the true value of PLUVICTO™ when compared to BSC/BSoC.

Lastly, the sponsor has reservations around the $50,000/QALY willingness-to-pay (WTP) threshold used for an end-of-life therapy, such as PLUVICTO™. There is sufficient evidence provided by the sponsor that demonstrates that PLUVICTO™ extends life, while also preserving quality of life, in an indication that is characterized by a short life expectancy. Therefore, the sponsor believes that a higher WTP threshold that is more reflective of end-of-life care should be considered.

Notwithstanding the economic comments, AAA supports the conversion of the draft recommendation to a final recommendation. Further, AAA is committed to working with the pCODR participating jurisdictions via the pCPA process to ensure that patients have timely access to this new and innovative targeted 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 | ☐ |
| 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. | | |

The sponsor would like to add additional clarity to the implementation guidance surrounding PSMA testing found in Table 1, on page 4 of the draft recommendation. Although $^{68}$Ga-PSMA-11 was used in the VISION trial, other PSMA imaging tracers (e.g., $^{18}$F-DCFPyL, and $^{18}$F-PSMA-1007) can be used to ascertain PSMA status in prostate cancer. Therefore, the sponsor kindly requests that the implementation guidance clarify that PSMA-positivity should be assessed using a validated tracer combined with PET-CT imaging.

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