CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

sacituzumab govitecan (Trodelvy)

(Gilead Sciences Canada, Inc.)

Indication: Trodelvy (sacituzumab govitecan) is indicated for the treatment of adult patients with unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+, or IHC 2+/ISH-) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting.

January 18, 2024

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0323-000
Brand name (generic)	Sacituzumab govitecan
Indication(s)	HR+, HER2-advanced or metastatic breast cancer
Organization	Breast Medical Oncologists Across Canada
Contact information[a]	Name: Mita Manna Title: Assistant Prof, UofS and provincial lead for breast disease site, Saskatchewan Cancer Agency, Saskatoon Cancer Centre Email: [redacted]

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

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	☒

1) Section 2: Regarding ECOG performance status (PS) for patient selection: While registration trials commonly require ECOG PS of 0-1, in the real world settings clinicians should be permitted to use judgement to consider therapy for ECOG PS2 patients who are likely to benefit. Performance status may be affected by very long term chronic unrelated illnesses not unrelated to cancer prognosis and not limiting to lifespan. While the experts had recommended use in ECOG PS2 patients where appropriate, this is not specified in the Implementation Guidance column of Table 1. This is in agreement with the clinician input from experts consulted by CADTH.

2) Section 7: Regarding the pricing column, CADTH and PERC commonly do not find new cancer drugs cost effective at the sponsor submitted prices, and often note that price reduction is required. However, it is inappropriate to specify a threshold of $50,000/QALY gained — this number was arbitrary, developed for renal disease treatments and never inflation adjusted since the 1980s. It is widely acknowledged to be unreasonable and out of date, even by PCPA and heath economics experts. This threshold number should not be referred to in this recommendation.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☒

1) Section 3.2: Recommend including mention of utilizing Sacituzumab Govitecan in the event of intolerance or severe toxicity to prior Topoisomerase inhibitor antibody drug-conjugate (ie discontinuation of Trastuzumab Deruxtecan due to Interstitial lung disease).

2) Section 5: As in most trials, the TROPICS-02 did scans every 6 weeks. The Implementation Guidance column should specify scans "as per standard of care", since the clinician guidance in the narrative section explains that scans in practice are done every 3 months.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒

1) Section 1.3: Regarding lines of systemic therapy: The recommendation mentions patients must have received 2-4 lines of prior chemotherapy. It is exceptionally rare for patients to receive more than 4 lines of chemotherapy in the clinical setting often due to decline in performance status, increased toxicities (specifically bone marrow toxicity), as well as exhaustion of therapy options. Therefore, the recommendation could be modified to >/= to 2 lines of prior chemotherapy.

2) Section 1.0: The qualifying use of chemotherapy in the early stage setting in patients with early relapse should be mentioned under "Reimbursement condition".

[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		
2. 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.		
3. 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		
4. 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. Anil Joy		

C. New or Updated Conflict of Interest Declarations

Updated Declaration for Clinician 1	
Name	*Dr. Mita Manna*
Position	*Medical Oncologist, Saskatchewan Cancer Centre, Saskatchewan Cancer Agency*
Date	*Please add the date form was completed (05-01-2024)*
☒	**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**
Seagen	☒	☐	☐	☐
Daiichi Sankyo	☒	☐	☐	☐
Gilead Sciences	☐	☐	☒	☐
AstraZeneca			☒	

New or Updated Declaration for Clinician 2	
Name	*Dr. Sandeep Sehdev*
Position	*Medical Oncologist, The Ottawa Hospital Cancer Centre. Assistant Prof, U of Ottawa*
Date	*January 7 2024*
☒	**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**
Gilead	☐	☐	☒	☐
AstraZeneca	☐	☐	☒	☐
Daiichi Sankyo	☒	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Karen Gelmon*
Position	*Professor of Medicine, University of British Columbia*
Date	*Please add the date form was completed (09-01-2024)*
☒	**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**
Gilead	☐	☒	☐	☐
Astra Zeneca	☐	☐	☒	☐

New or Updated Declaration for Clinician 4	
Name	*Dr. Nathalie LeVasseur*
Position	*Medical Oncologist, BC Cancer, Vancouver Centre*
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**
Astra Zeneca	☐	☒	☐	☐
Gilead	☐	☐	☒	☐
Seagen	☒	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Dr. Christine Brezden-Masley*
Position	*Medical Oncologist and Associate Professor of Medicine, University of Toronto*
Date	*January 11, 2024*
☒	**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**
Astellas	☐	☐	☒	☐
Eli Lilly	☐	☐	☒	☐
Astra Zeneca	☐	☐	☒	☐
Pfizer	☐	☐	☒	☐
Merck	☒	☐	☐	☐
BMS	☐	☒	☐	☐
Amgen	☒	☐	☐	☐
Gilead Sciences	☐	☒	☐	☐
Novartis	☐	☐	☒	☐

Seagen	☐	☒	☐	☐
Hoffman La Roche	☒	☐	☐	☐

New or Updated Declaration for Clinician 6	
Name	*Jan-Willem Henning*
Position	*Medical Oncologist, Clinical Associate Professor*
Date	*Please add the date form was completed 12/01/2024*
☒	**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**
Astra-Zeneca, Novartis	☐	☒	☐	☐
Pfizer, Gilead, Seagen, University of Toronto, ReThink Breast Cancer	☒	☐	☐	☐
	☐	☐	☐	☐

New or Updated Declaration for Clinician 7	
Name	*Geoffrey Watson*
Position	*Staff Medical Oncologist*
Date	*14-01-2024*
☒	**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**
AstraZeneca	☒	☐	☐	☐
Pfizer	☒	☐	☐	☐
Gilead	☒	☐	☐	☐
Knight Therapeutics	☒	☐	☐	☐
Novartis	☒	☐	☐	☐

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0323-000
Generic Drug Name (Brand Name): Sacituzumab govitecan (Trodelvy)
Indication: The treatment of adult patients with unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+, or IHC 2+/ISH-) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting.
Name of Clinician Group: Ontario Health (Cancer Care Ontario) Breast Cancer Drug Advisory Committee
Author of Submission: Dr. Andrea Eisen, Dr. Orit Freedman, Dr. Phillip Blanchette, Dr. Haider Samawi, Alaina Charlton

1. About Your Clinician Group

OH-CCO's Cancer Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

2. Information Gathering

Information was gathered via videoconferencing.

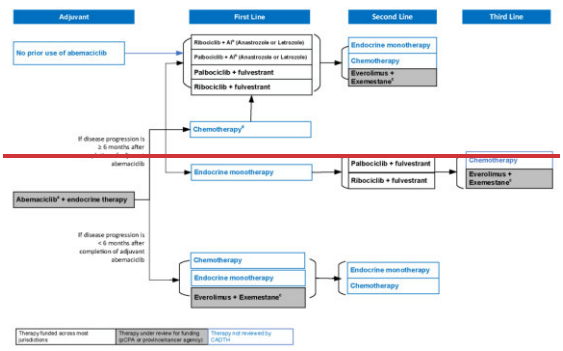
3. Current Treatments and Treatment Goals

The current treatments that are used in HR+/HER- breast cancer in third line and beyond include eribulin, capecitabine, gemcitabine, and vinorelbine. The goals to address are to delay disease progression, improve progression free survival, and prolong life.

Health-related quality of life data is missing from the trial which is an important goal to consider.

Figure 1: Provisional Funding Algorithm Diagram for HR+ HER2– Breast Cancer

Hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative breast cancer



4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Metastatic breast cancer remains an incurable illness and thus better treatments are needed. This treatment is applicable to patients who are HR+/HER2 low or HR+/HER2-0. Sacituzumab govitecan provides an unmet need for patients who are HR+/HER2-0.

Patients who are ER low positive do not meet the strict criteria of triple negative. ER low (ER 1-10%) patients would typically not be prescribed endocrine therapy however they should still be considered for Sacituzumab govitecan.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

In the TROPiCS trial, the median number of prior treatments was three and many patients in the trial had 8+ prior treatments. Sacituzumab govitecan would be an additional line of therapy to consider for 3rd line and beyond in patients with HR+/HER2- metastatic breast cancer.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

Patients best suited for this drug would be as per the proposed indication.

The DAC reviewed the eligibility criteria for the TROPiCS 02 trial. We note that there could be some patients in this group who have been on treatment for a very long time such that they never received a CDK 4/6 inhibitor. That is, some patients have become endocrine resistant before CDK4/6 inhibitors became available. There are also patients that are intolerant to CDK 4/6 inhibitors. Therefore, patients should not be required to have had a prior CDK 4/6 inhibitor before starting this drug. However ideally, the patients eligible for treatment should have received an endocrine therapy otherwise.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

The trial endpoints are OS, objective response, clinical benefit rate, duration of response, patient-reported outcomes, and safety. These are meaningful in the clinical setting as well.

The trial assessed response every 6 weeks for the first year and then every 12 weeks thereafter. In clinical practice, if patients are doing well and do not have undue toxicity, then the assessment of response in the first year may have a slightly reduced frequency. Patients are typically assessed every cycle of treatment for toxicity.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Treatment is typically discontinued upon disease progression or undue toxicity.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Settings with clinicians who have expertise in the administration of systemic therapy to patients with advanced disease.

6. Additional Information

The DAC is aware that an update to the survival analysis was recently available at the ASCO meeting.[1]

"SG continues to demonstrate improved OS versus TPC (median, 14.5 vs 11.2 mo; HR, 0.79 [95% CI, 0.65-0.95]; nominal P=0.01). The OS rates (95% CI) for SG versus TPC were 60.9% (54.8-66.4) and 47.1% (41.0-53.0) at 12 months, 39.2% (33.4-45.0) and 31.7% (26.2-37.4) at 18 months, and 25.6% (20.4-31.1) and 21.1% (16.3-26.3) at 24 months."

The DAC notes that an improvement in the 12-month overall survival as seen in this study is clinically significant in this heavily pretreated population.

1. Sara T., Aditya B., Frederik M., et al. Final overall survival (OS) analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan (SG) in patients (pts) with hormone receptor–positive/HER2-negative (HR+/HER2–) metastatic breast cancer (mBC). *Journal of Clinical Oncology* 2023 41:16_suppl, 1003-1003. DOI: 10.1200/JCO.2023.41.16_suppl.1003

7. Conflict of Interest Declarations

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1. Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

   OH-CCO provided secretariat function.

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No.

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. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Andrea Eisen
Position: Lead, Ontario Health (Cancer Care Ontario) Breast Cancer Drug Advisory Committee
Date: 26-07-2023

☒ **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.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$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				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Orit Freedman
Position: Member, Ontario Health (Cancer Care Ontario) Breast Cancer Drug Advisory Committee
Date: 21-07-2023

☒ 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.

Table 2: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	**$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				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Dr. Phillip Blanchette
Position: Member, Ontario Health (Cancer Care Ontario) Breast Cancer Drug Advisory Committee
Date: 21-07-2023

☒ 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.

Table 3: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$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				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Dr. Haider Samawi
Position: Member, Ontario Health (Cancer Care Ontario) Breast Cancer Drug Advisory Committee
Date: 21-07-2023

☒ 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.

Table 4: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$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				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: Alaina Charlton
Position: Member, Ontario Health (Cancer Care Ontario) Breast Cancer Drug Advisory Committee
Date: 21-07-2023

☒ 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.

Table 5: Conflict of Interest Declaration for Clinician 5

	Check appropriate dollar range*			
Company	**$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				

* Place an X in the appropriate dollar range cells for each company.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0323
Brand name (generic)	Trodelvy (sacituzumab govitecan)
Indication(s)	The treatment of adult patients with unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+, or IHC 2+/ISH-) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting.
Organization	Ontario Health (Cancer Care Ontario) Breast Cancer Drug Advisory Committee
Contact information[a]	Name: Dr. Andrea Eisen

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?		

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. Clarification is required for the HR-low subgroup. If a patient with HR-low disease is treated with CDK 4/6 inhibitor and then does not respond, does this mean that they require treatment as per HR positive pathway? That is, they would need 2 additional lines of chemo before receiving Sacituzumab govitecan (SG). Or, if they do not respond to CDK 4/6 inhibitor, can they move on to SG after only 1 line of chemo (as per TNBC algorithm). The DAC strongly recommends that patients with a good performance status who have received more than 4 lines of prior chemotherapy, be deemed eligible to receive Sacituzumab govitecan, as a grandparented patient group.		
	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. See above.		

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

Appendix 2. Conflict of Interest Declarations for Clinician Groups

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- For conflict of interest declarations:
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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		
2. 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. OH-CCO provided a secretariat function to the group.		
3. 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		
4. 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. Andrea Eisen • Dr. Haider Samawi		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	Dr. Ronita Lee
Position	Member, Ontario Health (Cancer Care Ontario) Breast Cancer Drug Advisory Committee
Date	*14-01-2024*
☒	**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**
Gilead	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	Alaina Charlton
Position	Member, Ontario Health (Cancer Care Ontario) Breast Cancer Drug Advisory Committee
Date	14-01-2024
☒	**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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Gilead	☒	☐	☐	☐
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

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	PC0323
Name of the drug and Indication(s)	Sacituzumab govitecan for the treatment of adult patients with unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH–) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting
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
Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
Please provide details regarding the information that requires clarification.
b) Reimbursement conditions and related reasons
Please provide details regarding the information that requires clarification.
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.

- Under considerations for initiation of therapy – b) Prior therapies required for eligibility, PAG suggests removing this statement: "The clinical experts indicated that the only caveat may be in patients who are considered HR low, where they suspect the response to endocrine therapy and CDK4/6 inhibitor is low. In which case, the clinicians believed that it may be reasonable for these patients to only receive chemotherapy".
- Under Generalizability, PAG would like to confirm pERC's opinion on the clinical experts' statement on patients who cannot tolerate a CDK4/6 inhibitor or are not able to take it due to medical contraindications and whether this only referred to the time-limited considerations.

Outstanding Implementation Issues

In the event of a positive draft recommendation, drug programs can request further implementation support from CADTH on topics that cannot be addressed in the reimbursement review (e.g., concerning other drugs, without sufficient evidence to support a recommendation, etc.). Note that outstanding implementation questions can also be posed to the expert committee in Feedback section 4c.

Algorithm and implementation questions
1. Please specify sequencing questions or issues that should be addressed by CADTH (oncology only)
1. An update to the algorithm is needed (rapid algorithm) 2.
2. Please specify other implementation questions or issues that should be addressed by CADTH
1. 2.
Support strategy
3. Do you have any preferences or suggestions on how CADTH should address these issues?
May include implementation advice panel, evidence review, provisional algorithm (oncology), etc.

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0323-000
Brand name (generic)	sacituzumab govitecan
Indication(s)	The treatment of adult patients with unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+, or IHC 2+/ISH-) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting.
Organization	The Canadian Breast Cancer Network (CBCN)
Contact information	Name: JK Harris

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

CBCN agrees with the recommendation to reimburse with conditions because of the unmet need for more treatments in this setting, as discussed in our patient submission. We also recognize the importance of evidence-based recommendations.

In light of sacituzumab govitecan's performance as compared to chemotherapy and the small population of HR+ CNS metastatic patients who may be otherwise eligible for this medicine, we would welcome a review of the decision to exclude those with CNS metastasis on the basis that TROPiCS-02 excluded patients with their characteristic (pg 4, #3.1). We are seeking a review of this exclusion because other chemotherapies that are standard of care were approved without this exclusion despite not having specific evidence for CNS. While there may be sufficient reason to exclude CNS metastatic patients who may otherwise be eligible for trastuzumab deruxtecan (Enhertu), there will be a gap created for those patients who are not. Sacituzumab govitecan has been shown to a better choice than many standard of care chemotherapies and cancer is know to have blood-brain barrier activities so it is important to ensure that inequity isn't created by excluding patients with CNS

metastatic breast cancer, a relatively small population that would benefit from being eligible without there being large financial impacts.

Finally, some patients will take 3 lines of hormone therapy when the disease was previously slow growing, and hormone therapy is also considered systemic. Therefore, we seek clarity on the recommendation to fund only when the patient has received 2-4 lines of previous systemic chemotherapy, plus a clear distinction between systemic chemotherapies or other forms of systemic therapies as discussed on pages 4 (#1.3) and page 6.

Specific text:

Page 4: reimbursement condition: Patients must not have: 3.1. active CNS metastases and/or carcinomatous meningitis. Reason: The TROPiCS-02 trial excluded patients with these characteristics.

Reimbursement condition: Refractory to or relapsed after 2 to 4 prior systemic chemotherapy regimens for metastatic disease. Reason: Evidence from the TROPiCS-02 trial demonstrated that treatment with sacituzumab govitecan resulted in a survival benefit in patients with these characteristics.

Page 6: …The committee noted that the CADTH analysis was conducted in the Health Canada indicated population, which allows use in patients who have received an endocrine-based therapy and at least two additional systemic therapies. To align with the TROPiCS-02 trial, pERC noted patients should only be considered for sacituzumab govitecan if they received an endocrine-based therapy, including a hormone and a CDK4/6 inhibitor, and have failed two systemic chemotherapies. This

population is narrower than the Health Canada indication and therefore it was noted that the budget impact in this population will be smaller than the CADTH estimate.

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?

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	☒

CBCN appreciate the need for responsive funding algorithms that reflects the changing drug landscape, but this presents adoption issues at the provincial level because of inconsistencies between some provincial TNBC criteria (ER <1%) as compared to CADTH criteria (ER <10%), and we seek clarity on how such inconsistencies will be addressed when implementing this recommendation. Further, there is a significant discrepancy between the quality adjusted life years estimate submitted by the sponsor (pg. 3), and CADTH economic impact analysis (pg. 24). Clearer details are needed about how these varied estimates are expected to impact implementation of CADTH's recommendation, and timely pCPA negotiations.

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.

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	*JK Harris*
Position	*Health Policy and Advocacy Lead*
Date	*17/01/2024*
☐	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	☐
Yes – CBCN sought the input of our medical advisory board in preparation for our feedback.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
No. 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**
Lilly Canada				X
Roche				X
Pfizer				X
AstraZeneca				X

CADTH

CADTH Provisional Funding Algorithm
Feedback on Draft Provisional Funding Algorithm

CADTH Provisional Funding Algorithm
Feedback on Draft Report

Stakeholder information	
CADTH project number	PC0323-000-000
Condition under review	HR, HER2- advanced or metastatic breast cancer
Organization	Rethink Breast Cancer
Contact information[a]	Name: Jenn Gordon Title: Lead, Strategic Operations and Engagement [redacted] [redacted]

[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.

SECTION 1: IMPLEMENTATION ADVICE For reports without implementation advice, skip to Section 2		
Stakeholder agreement with the draft provisional funding algorithm		
1. Please indicate if the stakeholder agrees with the implementation advice.	Yes	☐
	No	☒
Rethink Breast Cancer agrees with the majority of the implementation advice with the exception of Table 1 point 3.2. Consideration should be given to patients who <u>have</u> previously been treated with a topoisomerase1 inhibitor who <u>cannot tolerate</u> a ropoisomerase1 inhibitor. There is an unmet need for this particularly small patient population who have not experienced disease progression, but rather intolerable side effects.		
Implementation advice panel consideration of the stakeholder input		
2. Does the draft advice demonstrate that the panel has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
Clarity of the draft implementation advice		
3. Are the reasons for the panel's advice clearly stated in the draft report?	Yes	☒
	No	☐
4. Have the implementation issues been clearly articulated and adequately addressed in the draft report?	Yes	☒
	No	☐

SECTION 2: PROVISIONAL FUNDING ALGORITHM		
Stakeholder agreement with the draft provisional funding algorithm		
5. Please indicate if the stakeholder agrees with the draft provisional funding algorithm.	Yes	☒
	No	☐
Please explain why the stakeholder agrees or disagrees with the draft algorithm. Whenever possible, please identify the specific element from the algorithm and the rationale. Note that algorithms are based on CADTH pERC recommendations, CADTH implementation advice, and the historical jurisdictional funding context.		
Clarity of the draft provisional funding algorithm		
6. Is the proposed provisional algorithm clearly represented and described in the draft report?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

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.

A. Patient Group Information	
Name	*Jenn Gordon*
Position	*Lead, Strategic Operations and Engagement*
Date	*January 18, 2024*
☒	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**
Gilead	☐	☐	☐	☒

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	PC0323
Brand name (generic)	TRODELVY® (sacituzumab govitecan)
Indication(s)	Treatment of adult patients with unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+, or IHC 2+/ISH-) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting.
Organization	Gilead Sciences Canada, Inc.
Contact information[a]	Name: [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.

Gilead agrees with the draft recommendation that Trodelvy be reimbursed for the treatment of adult patients with unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH–) breast cancer who have received endocrine-based therapy and at least two additional systemic chemotherapies in the metastatic setting based on the added survival benefit demonstrated by the TROPiCS-02 trial.

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?

Reimbursement Condition 1.3 does not reflect the feedback provided by stakeholders that Trodelvy would be a valuable option for patients "3rd line and beyond" or after "at least 2 lines" of prior therapy.

To reflect this feedback, Reimbursement Condition 1.3 should be modified to "Refractory or relapsed after 2 or more prior systemic chemotherapy regimens for metastatic disease".

Alternatively, a time-limited opportunity for access should be available for those few patients who did not to have the opportunity previously to use Trodevly earlier on their treatment journey and remain fit enough to receive treatment.

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.

	Yes	☐

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	No	☒
If not, please provide details regarding the information that requires clarification. Table 1, Reimbursement Condition 3.2. To be consistent with the recently updated CADTH Provisional Funding Algorithm (PH0033-000), this criteria should include implementation guidance in Table 1 similar to the mTNBC setting. Specifically, implementation guidance should include allowance for patients to switch between trastuzumab deruxtecan and sacituzumab govitecan due to intolerance or toxicities.		
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.