CADTH

CADTH REIMBURSEMENT REVIEW

Clinician Input

Pertuzumab (Perjeta)

(Hoffman-La Roche Limited)

Indication: Early stage breast cancer

May 7, 2021

CADTH Reimbursement Review
Clinician Group Input Template

CADTH Project Number	**PC0241-000**
Generic Drug Name (Brand Name)	**Pertuzumab**
Indication	**Neoadjuvant pertuzumab in combination with 4-6 cycles of neoadjuvant taxane and trastuzumab in Stage II-III HER2+ breast cancer**
Name of the Clinician Group	**BC Cancer Breast Tumour Group**
Author of the Submission	**Dr. Stephen Chia**
Contact information	Name: Dr. Stephen Chia Title: Medical Oncologist, Chair – BC Cancer Breast Tumour Group Email: schia@bccancer.bc.ca Phone:604-877-6098 ext 2734

1. About Your Clinician Group

Please describe the purpose of your organization. Include a link to your website (if applicable).

The British Columbia Breast Tumour Group is a multi-disciplinary group that exists and operates within BC Cancer and has the mandate to sets the standards of care, treatment options and pathways from screening to pathology to surgery to radiation oncology to systemic treatments across the spectrum of breast cancer care in British Columbia.

www.bccancer.bc.ca

2. Information Gathering

Please describe how you gathered the information included in the submission.

Review of pertinent literature.

The author of this submission has previously written the Clinical Guidance document for neoadjuvant pertuzumab in HER2+ breast cancer when it was first submitted years ago. A lot of the information was gathered from that document.

There was no assistance provided by Hoffmann LaRoche in the creation of this document.

3. Current treatments

3.1. Describe the current treatment paradigm for the disease

Focus on the Canadian context.

Please include drug and non-drug treatments.

Drugs without Health Canada approval for use in the management of the indication of interest may be relevant if they are routinely used in Canadian clinical practice. Are such treatments supported by clinical practice guidelines?

Treatments available through special access programs are relevant.

Do current treatments modify the underlying disease mechanism? Target symptoms?

Response:

For HER2+ stage II-III breast cancer the current treatment pathway in Canada is for the consideration of neoadjuvant chemotherapy (taxane +/- anthracycline) concurrent with neoadjuvant trastuzumab (for the taxane component) for 6-8 cycles prior to surgery. The two main clinical reasons for this neoadjuvant approach is for down staging of the primary tumour and axillary nodes to improve the surgical approach (lumpectomy rather than mastectomy and/or sentinel lymph node biopsy versus axillary lymph node dissection) and to use pathological response determination (pCR versus no pCR) to decide adjuvant treatment (trastuzumab for pCR cohort versus T-DM1 for non-pCR cohort).

Pertuzumab delivered in the neoadjuvant setting concurrent with the taxane and trastuzumab has been demonstrated in randomized clinical trials (e.g. NeoSphere and PEONY) to improve pCR rates from approximately 21% to 40% - and almost doubling of pCR rates. This comes with limited added toxicity. Furthermore in the NeoSphere trial the pertuzumab was only given in the neoadjuvant setting for 4 cycles. Despite being underpowered (n=107 per arm) as a secondary analysis – disease free survival (DFS) trended to be better in the pertuzumab arm. Furthermore in the intent to treat population – those patients overall that achieved a pCR had a significantly improved DFS versus those that did not achieve a pCR. Confirming the strong prognostic effect of achieving a pCR. The intent of the treatment is complete eradication of disease (both gross disease in breast/nodes and potential microscopic metastases) to improve cure rates.

Pertuzumab is not publically funded as a standard regimen in eligible Stage II-III HER2+ breast cancer patients concurrent with the taxane and trastuzumab in Canada. There is a patient assistance program (OncoCare) supported by Roche for assistance in insurance navigation, co-pay assistance and infusion centre coordination. There is no compassionate or free pertuzumab in the program. Thus at present there is significant inequity and access to this agent in this setting across Canada.

4. Treatment goals

4.1. What are the most important goals that an ideal treatment would address?

Examples: Prolong life, delay disease progression, improve lung function, prevent the need for organ transplant, prevent infection or transmission of disease, reduce loss of cognition, reduce the severity of symptoms, minimize adverse effects, improve health-related quality of life, increase the ability to maintain employment, maintain independence, reduce burden on caregivers.

Response:

Induce tumour clinical response for both enhanced breast cancer surgery (e.g. down-staging for breast conservation surgery) and pathological response (hopefully pCR) such that adjuvant treatment is NOT escalated to T-DM1. Achievement of pCR has consistently been associated with improved clinical outcome in both clinical trials, meta-analyses of trials (e.g. FDA) and in real world data analyses (e.g. BC population data from BC Cancer Breast Cancer Outcomes Unit).

5. Treatment gaps (unmet needs)

5.1. Considering the treatment goals in Section 4, please describe goals (needs) that are not being met by currently available treatments.

Examples:

- *Not all patients respond to available treatments*
- *Patients become refractory to current treatment options*
- *No treatments are available to reverse the course of disease*
- *No treatments are available to address key outcomes*
- *Treatments are needed that are better tolerated*
- *Treatment are needed to improve compliance*
- *Formulations are needed to improve convenience*

Response:

The international standard of care is for the delivery of neoadjuvant pertuzumab and trastuzumab concurrent with the taxane in Stage II-III HER2+ breast cancer. The gap is a significantly lower pCR rate (about 50% lower) with the pertuzumab. This not only translates to a potentially lower long term clinical outcome, but also exposes more patients to more toxic adjuvant treatment (T-DM1) rather than adjuvant trastuzumab alone.

5.2. Which patients have the greatest unmet need for an intervention such as the drug under review?

Would these patients be considered a subpopulation or niche population?

Describe characteristics of this patient population.

Would the drug under review address the unmet need in this patient population?

Response:

There does appear to a be a greater pCR effect in the estrogen receptor negative (ER-) HER2+ cohort relative to the ER+/HER2+ cohort. Otherwise the benefit is regardless of T (tumour) size or N (nodal) status. Perhaps the greatest need is in the inflammatory breast cancer population and the inoperable stage IIIC breast cancers to downstage to get to primary surgery.

6. Place in therapy

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

Is there a mechanism of action that would complement other available treatments, and would it be added to other treatments?

Is the drug under review the first treatment approved that will address the underlying disease process rather than being a symptomatic management therapy?

Would the drug under review be used as a first-line treatment, in combination with other treatments, or as a later (or last) line of treatment?

Is the drug under review expected to cause a shift in the current treatment paradigm?

Response:

Pertuzumab would fit into the current treatment pathways of neoadjuvant taxane/trastuzumab +/- anthracycline. It would align as per the current pCODR submission of 4-6 cycles concurrent the taxane (e.g. TCHP x 6 or AC x 4 followed by paclitaxel/pertuzumab/trastuzumab x 4.

6.2. Please indicate whether or not it would be appropriate to recommend that patients try other treatments before initiating treatment with the drug under review. Please provide a rationale from your perspective.

If so, please describe which treatments should be tried, in what order, and include a brief rationale.

Response:

No it would not be appropriate to try other treatment options. This is a curative intent setting. Clinical and radiological imaging is not accurate to predict pCR. Thus as long as the treatment is tolerated, the goal it to deliver the chemotherapy and anti-HER2 antibodies upfront before surgery.

6.3. How would this drug affect the sequencing of therapies for the target condition?

If appropriate for this condition, please indicate which treatments would be given after the therapy has failed and specify whether this is a significant departure from the sequence employed in current practice.

Would there be opportunity to treat patients with this same drug in a subsequent line of therapy? If so, according to what parameters?

Response:

The use of neoadjuvant pertuzumab may impact the use of pertuzumab in the metastatic setting. Not based on randomized trials, but based on prior assumptions, it would be reasonable to still consider pertuzumab, trastuzumab and a taxane as 1st line treatment (the current standard of care) for metastatic HER2+ breast cancer if there is 12 months or longer since last dose of neoadjuvant pertuzumab.

6.4. Which patients would be best suited for treatment with the drug under review?

Which patients are most likely to respond to treatment with the drug under review?

Which patients are most in need of an intervention?

Would this differ based on any disease characteristics (e.g., presence or absence of certain symptoms, stage of disease)?

Response:

Stage II-III HER2+ breast cancer in patients medically fit to receive neoadjuvant chemotherapy and dual anti-HER 2 directed therapies.

6.5. How would patients best suited for treatment with the drug under review be identified?

Examples: *Clinician examination or judgement, laboratory tests (specify), diagnostic tools (specify)*

Is the condition challenging to diagnose in routine clinical practice?

Are there any issues related to diagnosis? (e.g., tests may not be widely available, tests may be available at a cost, uncertainty in testing, unclear whether a scale is accurate or the scale may be subjective, variability in expert opinion.)

Is it likely that misdiagnosis occurs in clinical practice (e.g., under-diagnosis)?

Should patients who are pre-symptomatic be treated considering the mechanism of action of the drug under review?

Response:

HER 2 testing is standardized by the ASCO/CAP guidelines. Most pathology labs participate in a QA program. Patients are identified by the surgeon for referral to Medical Oncology for consideration of neoadjuvant systemic therapies. The future direction is for greater neoadjuvant treatment in primary operable breast cancer. Breast surgeons across the country are very aware and familiar with this approach and this treatment strategy.

6.6. Which patients would be least suitable for treatment with the drug under review?

Response:

Not medically fit for chemotherapy or anti-HER 2 antibodies. Multiple co-morbidities. Has poor LVEF.

6.7. Is it possible to identify those patients who are most likely to exhibit a response to treatment with the drug under review?

If so, how would these patients be identified?

Response:

There is currently no predictive clinical factor or a biomarker that has been validated as predictive of benefit to neoadjuvant anti-HER 2 directed therapy other an HER-2 positivity (IHC 3+ and/or FISH positive as per ASCO/CAP guidelines). There is emerging data that stromal TILs (tumour infiltrating lymphocytes) is predictive of a higher pCR to both chemotherapy and to the HER-2 directed antibodies (pertuzumab and trastuzumab). This biomarker is not standardly reported or used in clinical decision making today.

6.8. What outcomes are used to determine whether a patient is responding to treatment in clinical practice?

Are the outcomes used in clinical practice aligned with the outcomes typically used in clinical trials?

Response:

Pathological complete response (pCR) – defined as no invasive disease in breast and lymph nodes. Residual DCIS is permissible in the definition.

6.9. What would be considered a clinically meaningful response to treatment?

Examples:

- *Reduction in the frequency or severity of symptoms (provide specifics regarding changes in frequency, severity, and so forth)*
- *Attainment of major motor milestones*
- *Ability to perform activities of daily living*
- *Improvement in symptoms*
- *Stabilization (no deterioration) of symptoms*

Consider the magnitude of the response to treatment. Is this likely to vary across physicians?

Response:

Enhanced breast cancer surgery such as down-staging from mastectomy to breast conserving surgery and/or axillary node dissection to sentinel node biopsy. The most clinically meaningful response is the achievement of a pCR. This is associated with significantly improved long term clinical outcomes (DFS and OS). This also abrogates the recommendation for adjuvant T-DM1.

6.10. How often should treatment response be assessed?

Response:

Pathologically.

6.11. What factors should be considered when deciding to discontinue treatment?

Examples:

- *Disease progression (specify; e.g., loss of lower limb mobility)*
- *Certain adverse events occur (specify type, frequency, and severity)*
- *Additional treatment becomes necessary (specify)*

Response:

Clinical progression of disease as documented by physical exam and/or radiological imaging or significant adverse event (such as clinically significant cardiotoxicity) or diarrhea.

6.12. What settings are appropriate for treatment with the drug under review?

Examples: Community setting, hospital (outpatient clinic), specialty clinic

Response:

Delivery is concurrent with taxane and trastuzumab – thus in outpatient chemotherapy unit.

6.13. For non-oncology drugs, is a specialist required to diagnose, treat, and monitor patients who might receive the drug under review?

If so, which specialties would be relevant?

Response:

N/A.

7. Additional information

7.1. Is there any additional information you feel is pertinent to this review?

Response:

No.

8. Conflict of Interest Declarations

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 clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

No

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 <u>each clinician</u> that 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

Clinician Information	
Name	*Dr. Stephen Chia*
Position	*Chair – BC Cancer Breast Tumour Group*
Date	*Please add the date form was completed (06-05-2021)*
☒	**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				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Hoffmann LaRoche	☐	☒	☐	☐
Novartis	☐	☒	☐	☐
Pfizer	☒	☐	☐	☐

Eli Lilly	X			
AstraZeneca	X			

Declaration for Clinician 2

Clinician Information	
Name	*Dr. Daniel Rayson*
Position	*Division Chief Medical Oncology- Dalhousie University and QE II Health Sciences Centre, Halifax NS*
Date	*May/7/2021*
☒	**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				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Pfizer	☐	☒	☐	☐
Astra Zeneca	☒	☐	☐	☐
Roche	☒	☐	☐	☐
Eli Lilly	X			

Declaration for Clinician 3

Clinician Information	
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				
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	☐	☐	☐	☐

Declaration for Clinician 4

Clinician Information	
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

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	☐	☐	☐	☐

Declaration for Clinician 5

Clinician Information	
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

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

CADTH Reimbursement Review
Clinician Group Input Template

CADTH Project Number	PC0241-000
Generic Drug Name (Brand Name)	Pertuzumab/Brand: Perjeta (Roche)
Indication	**Indications:** Perjeta in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either 2 cm in diameter or node positive). **Manufacturer Requested Reimbursement Criteria[1]:** Pertuzumab in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either 2 cm in diameter or node positive). Patients should receive neoadjuvant treatment with pertuzumab in combination with trastuzumab and chemotherapy for three to six cycles depending on the regimen chosen. Patients who start pertuzumab in combination with trastuzumab and chemotherapy in the neoadjuvant setting and do not have residual disease following surgery should continue to receive adjuvant trastuzumab to complete one year of HER2-directed therapy.
Name of the Clinician Group	**Ontario Health (Cancer Care Ontario) Breast Cancer Drug Advisory Committee (DAC)**
Author of the Submission	**Dr. Andrea Eisen, Dr. Orit Freedman, Dr. Phillip Blanchette, Annie Ngan (pharmacist)**
Contact information	Name: Dr. Andrea Eisen Title: Ontario Cancer Lead – Breast Cancer DAC Email: andrea.eisen@sunnybrook.ca Phone: NA

1. About Your Clinician Group

Please describe the purpose of your organization. Include a link to your website (if applicable).

OH-CCO's 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

Please describe how you gathered the information included in the submission.

Discussed jointly via email and at a DAC meeting.

3. Current treatments

3.1. Describe the current treatment paradigm for the disease

Focus on the Canadian context.

Please include drug and non-drug treatments.

Drugs without Health Canada approval for use in the management of the indication of interest may be relevant if they are routinely used in Canadian clinical practice. Are such treatments supported by clinical practice guidelines?

Treatments available through special access programs are relevant.

Do current treatments modify the underlying disease mechanism? Target symptoms?

Response:

Current standard of care for T1c or greater (if N0) or any node positive disease is neoadjuvant trastuzumab and chemo. If there is residual disease post surgery, patients would be offered adjuvant TDM1.

4. Treatment goals

4.1. What are the most important goals that an ideal treatment would address?

Examples: Prolong life, delay disease progression, improve lung function, prevent the need for organ transplant, prevent infection or transmission of disease, reduce loss of cognition, reduce the severity of symptoms, minimize adverse effects, improve health-related quality of life, increase the ability to maintain employment, maintain independence, reduce burden on caregivers.

Response:

Survival, recurrence, acceptable toxicities, improve health-related QoL

5. Treatment gaps (unmet needs)

5.1. Considering the treatment goals in Section 4, please describe goals (needs) that are not being met by currently available treatments.

Examples:

- *Not all patients respond to available treatments*
- *Patients become refractory to current treatment options*
- *No treatments are available to reverse the course of disease*
- *No treatments are available to address key outcomes*
- *Treatments are needed that are better tolerated*
- *Treatment are needed to improve compliance*
- *Formulations are needed to improve convenience*

Response:

Despite optimal systemic and local therapy, approximately 25% to 30% of HER2-positive patients still experience disease recurrence. Better/improved treatments are needed.

5.2. Which patients have the greatest unmet need for an intervention such as the drug under review?

Would these patients be considered a subpopulation or niche population?

Describe characteristics of this patient population.

Would the drug under review address the unmet need in this patient population?

Response:

Those at greatest risk of recurrence include higher stage disease.

6. Place in therapy

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

Is there a mechanism of action that would complement other available treatments, and would it be added to other treatments?

Is the drug under review the first treatment approved that will address the underlying disease process rather than being a symptomatic management therapy?

Would the drug under review be used as a first-line treatment, in combination with other treatments, or as a later (or last) line of treatment?

Is the drug under review expected to cause a shift in the current treatment paradigm?

Response:

Pertuzumab will be added to neoadjuvant trastuzumab.

6.2. Please indicate whether or not it would be appropriate to recommend that patients try other treatments before initiating treatment with the drug under review. Please provide a rationale from your perspective.

If so, please describe which treatments should be tried, in what order, and include a brief rationale.

Response:

Not applicable. This is a neoadjuvant therapy.

6.3. How would this drug affect the sequencing of therapies for the target condition?

If appropriate for this condition, please indicate which treatments would be given after the therapy has failed and specify whether this is a significant departure from the sequence employed in current practice.

Would there be opportunity to treat patients with this same drug in a subsequent line of therapy? If so, according to what parameters?

Response:

Pertuzumab will be an additional drug to existing neoadjuvant trastuzumab. If patients development recurrence, consideration will need to be given to the downstream sequencing and HER2-directed therapy as pertuzumab-trastuzumab are funded in the first-line metastatic setting.

6.4. Which patients would be best suited for treatment with the drug under review?

Which patients are most likely to respond to treatment with the drug under review?

Which patients are most in need of an intervention?

Would this differ based on any disease characteristics (e.g., presence or absence of certain symptoms, stage of disease)?

Response:

The DAC notes that the manufacturer's funding request is as follows: *Pertuzumab in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either 2 cm in diameter or node positive).*

The DAC notes that when selecting patients who may potentially be candidates for adjuvant TDM1, patients with either 1cm in diameter or node-positive disease were eligible in the KATHERINE trial.

In Ontario's Evidence Building Program, approximately 100 patients per year has T1a-b N0 HER2-positive disease.

6.5. How would patients best suited for treatment with the drug under review be identified?

Examples: *Clinician examination or judgement, laboratory tests (specify), diagnostic tools (specify)*

Is the condition challenging to diagnose in routine clinical practice?

Are there any issues related to diagnosis? (e.g., tests may not be widely available, tests may be available at a cost, uncertainty in testing, unclear whether a scale is accurate or the scale may be subjective, variability in expert opinion.)

Is it likely that misdiagnosis occurs in clinical practice (e.g., underdiagnosis)?

Should patients who are pre-symptomatic be treated considering the mechanism of action of the drug under review?

Response:

All newly diagnosed invasive breast cancer patients have HER2 status tested.

6.6. Which patients would be least suitable for treatment with the drug under review?

Response:

Patients who are not suited for neoadjuvant chemo therapy or HER2-directed therapy based on comorbidities (e.g., low LVEF).

6.7. Is it possible to identify those patients who are most likely to exhibit a response to treatment with the drug under review?

If so, how would these patients be identified?

Response:

This drug will only be used in breast cancer patients who are HER2-positive.

6.8. What outcomes are used to determine whether a patient is responding to treatment in clinical practice?

Are the outcomes used in clinical practice aligned with the outcomes typically used in clinical trials?

Response:

Not applicable – this is neoadjuvant therapy.

6.9. What would be considered a clinically meaningful response to treatment?

Examples:

- *Reduction in the frequency or severity of symptoms (provide specifics regarding changes in frequency, severity, and so forth)*
- *Attainment of major motor milestones*
- *Ability to perform activities of daily living*
- *Improvement in symptoms*
- *Stabilization (no deterioration) of symptoms*

Consider the magnitude of the response to treatment. Is this likely to vary across physicians?

Response:

Increased pCR and improved disease-free survival and overall survival.

6.10. How often should treatment response be assessed?

Response:

Patients are monitored routinely during neoadjuvant therapy to evaluate response to treatment.

6.11. What factors should be considered when deciding to discontinue treatment?

Examples:

- *Disease progression (specify; e.g., loss of lower limb mobility)*
- *Certain adverse events occur (specify type, frequency, and severity)*
- *Additional treatment becomes necessary (specify)*

Response:

Disease progression on treatment (rare), toxicities.

6.12. What settings are appropriate for treatment with the drug under review?
Examples: Community setting, hospital (outpatient clinic), specialty clinic ***Response:*** Outpatient clinic.
6.13. For non-oncology drugs, is a specialist required to diagnose, treat, and monitor patients who might receive the drug under review?
If so, which specialties would be relevant? ***Response:*** NA
7. Additional information
7.1. Is there any additional information you feel is pertinent to this review?
Response: The DAC notes that the strategy proposed is not specifically evaluated in any clinical trial.

8. Conflict of Interest Declarations

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 clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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 support to the DAC in completing this input.

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 <u>each clinician</u> that 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

Clinician Information	
Name	*Dr. Andrea Eisen*
Position	*Ontario Cancer Lead; Medical oncologist*
Date	*28-April-2021*
☒	**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

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	☐	☐	☐	☐

Declaration for Clinician 2

Clinician Information	
Name	*Dr. Orit Freedman*
Position	*Medical oncologist*
Date	*29-April-2021*
☒	**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

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	☐	☐	☐	☐

Declaration for Clinician 3

Clinician Information	
Name	*Dr. Phillip Blanchette*
Position	*Medical Oncologist*
Date	*30-April-2021*
☒	**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				
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	☐	☐	☐	☐

Declaration for Clinician 4

Clinician Information	
Name	*Annie Ngan*
Position	*Pharmacist*
Date	*29-April-2021*
☒	**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				
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	☐	☐	☐	☐

Declaration for Clinician 5

Clinician Information	
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				
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	☐	☐	☐	☐