Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

abemaciclib (Verzenio)

(Eli Lilly Canada Inc.)

Indication: In combination with endocrine therapy for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of disease recurrence based on clinicopathological features.

September 19, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

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Patient Input

Name of the Drug and Indication	Abemaciclib (Verzenio) in combination with endocrine therapy for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of disease recurrence based on clinicopathological features.
Name of the Patient Group	Canadian Breast Cancer Network
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

The Canadian Breast Cancer Network (CBCN) is a leading, patient-directed, national health charity committed to ensuring the best quality of care for all Canadians affected by breast cancer through the promotion of information, education and advocacy activities. www.cbcn.ca

As a member of the Canadian Cancer Action Network, the Canadian Breast Cancer Network is committed to adhering to the Code of Conduct Governing Corporate Funding.

2. Information Gathering

Information for this submission was collected via:

CBCN's 2022 Triple Negative Breast Cancer Patient Survey: An online survey conducted by the Canadian Breast Cancer Network was distributed to patients living with breast cancer. 981 people completed the English-only survey, of whom 190 had early stage HR-positive, HER2-negative breast cancer. Survey questions comprised of a combination of scoring options. Patients were contacted through the membership databases of CBCN and other patient organizations.

Patients reported that they lived in the following provinces:

- 40.5% from Ontario (77 respondents).
- 11% from Alberta (21 respondents).
- 20.5% from British Columbia (39 respondents).
- 8% from Saskatchewan (15 respondents)
- 7% from Quebec (13 respondents).
- 18% were from Nova Scotia (6 patient), New Brunswick, Newfoundland and Labrador (5 patients from each province), the North West Territories, and Prince Edward Island (1 patient from each province).

They also reported on their age at the time of the survey, and first language:

- 10.5% spoke a first language other than English; 10 patients spoke French as a first language, and ten spoke different languages from one another other than French and English.
- 4.7% were younger than 40 (9 respondents) .
- 35% were between the ages of 41-55 (67 respondents)
- 49.5% were between the ages of 56-70 (94 respondents)
- 14% were older than 71 (26 respondents)

CBCN's 2017 Breast Cancer Patient Survey: An online survey conducted by the Canadian Breast Cancer Network, distributed to patients living with breast cancer. 216 patients participated in the survey, of whom 32 had HR-positive, HER2-negative breast cancer. Survey questions comprised of a combination of scoring options and free form commentary. Patients were contacted through the membership databases of CBCN and other patient organizations.

Patients reported that they lived in the following provinces:

- 12.5% were from British Columbia (4 respondents)
- 9% were from Newfoundland and Labrador (3 respondents)
- 15.5% were from Ontario (5 respondents)
- 19% were from Saskatchewan (6 respondents)
- 19% were from Quebec, Nova Scotia, and Manitoba (2 respondents from each province)
- 9% were from Alberta, New Brunswick, and the Northwest Territories (1 respondent from each province)

They also reported on their age at the time of the survey, and first language:

- 9% spoke a first language other than English; two patients spoke French as a first language, and one spoke Hungarian as a first language.
- 6% were between the ages of 30-40 (2 respondents).
- 25% were between the ages or 41-50 (8 respondents).
- 50% were between the ages of 51-60 (16 respondents).
- 9% were between the ages of 61-70 (3 respondents).
- None of the respondents were 71 or older.

Key informant interviews: CBCN was not able to speak with patients taking abemaciclib for the treatment of HR-positive, HER2-negative breast cancer. We did, however, conducte an interview with someone who has HR-positive, HER2-negative breast cancer but was unable to access abemaciclib due to the requirements that one's Ki-67 score must be 20% or greater at the time that they wanted to access the treatment.

This interview was conducted in November 2023, and discussed treatment goals, choice in treatments, side effects, as well as the social and financial impacts of the treatments.

Printed sources: A review was conducted of current studies and grey literature to identify issues and experiences that are commonly shared among many women living with breast cancer as well as data from the clinical trial related to the treatment in question.

3. Disease Experience

A diagnosis of early stage HR-positive, HER2-negative breast cancer has a significant impact on the life of the patient. Both the diagnosis and treatment of breast cancer have a significant impact on the emotional and physical well-being of patients. Most early stage patients will undergo a variety of treatments that may include surgery, chemotherapy, hormone therapy, targeted therapy and radiation. These treatments cause a significant impact on the lives of patients, not only due to the disruption that attending treatment appointments causes in their daily life; but also due to the many side effects that breast cancer patients experience as a result of treatments.

HR-positive, HER2-negative is a subtype of breast cancer indicated by the presence of either or both the progesterone and estrogen hormone, but not the HER2 protein and accounts for approximately 70% of all breast cancers (Reference: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7903278/#:~:text=The%20majority%20of%20breast%20cancers,%E2%89%A4%2050%20years%20%5B5%5D). HR-positive breast cancer types have a high risk of recurrence, and patients with this subtype want more options to address this increased risk. For HR-positive, HER2-negative patients, there are limited options of targeted therapies. Patients with this subtype of breast cancer can use hormone therapy, however hormone therapies can lose their effectiveness over time. As a result, patients with this subtype of breast cancer must rely more on systemic treatments (such as chemotherapy) which are less effective and have greater side effects than more targeted therapies (Reference: https://www.cbcn.ca/en/subtypes_of_breast_cancer).

4. Experiences With Currently Available Treatments

The Goals of Current Therapy

The goals of current treatment options for early stage breast cancer are to shrink or remove the tumor and prevent recurrence or spreading of the cancer. Treatment options and effectiveness vary by type of cancer, location of cancer, and how symptoms are experienced. People diagnosed with HR-positive, HER2-negative want treatments that eliminate disease, prevent recurrence, and have minimal side effects.

In our 2022 Survey, most of the HR-positive, HER2-negative breast cancer patients had received or were currently receiving surgery (189 patients), hormone therapy (152 patients), and radiation therapy (135 patients). Additional treatments included previous or current treatment with chemotherapy (89 patients), and biologics or targeted therapies (12 patients).

Key Factors for Decision-Making Around Treatment

Respondents in our 2017 Survey indicated that the following key factors influenced their decision-making around treatments:

Effectiveness of the treatment – how well the treatment stabilized their disease and delayed progression of their disease.

Prolonged quality of life – being able to maintain productive, active lives with minimal disruption to daily routines.

Reduced risk of recurrence – reducing the chances that breast cancer will come back or spread

Side effect management – minimizing risk while stabilizing their disease.

Cost and accessibility of treatments – affordability and ease of accessing treatments.

Effectiveness of the treatment:

In both the 2022 Survey and the 2017 survey, efficacy of treatment was a high priority for patients. The 2022 Survey found that 81% of HR-positive, HER2-negative breast cancer patients rated how well a therapy works to treat their cancer as important or very important. In our 2017 Survey, 72 % of HR-positive, HER2-negative breast cancer respondents indicated treatment efficacy to be the most important factor in treatment decision making.

Prolonged quality of life:

In addition to efficacy, quality of life were routinely cited by patients as a key factor in making treatment decisions. In our 2017 Survey, HR-positive, HER2-negative breast cancer patients revealed that improved quality of life (81%) was important or very important to them when considering treatment options. In addition, 72% of HR-positive, HER2-negative breast cancer patients indicated that mobility was an important or very important consideration when making decisions regarding treatment options.

Reducing Risk of Recurrence

In the early stage of breast cancer, reducing the risk of recurrence is routinely cited as a key factor in treatment decision making. In our 2017 Survey, 84% of HR-positive, HER2-negative breast cancer patients revealed that reducing the risk of recurrence was an important or very important consideration when making decisions regarding treatment options.

Side effect management:

In addition to treatment efficacy, prolonged quality of life, and reducing the risk of recurrence, patients have an expectation that these benefits will come with manageable side effects. In our 2017 Survey, 67% of HR-positive, HER2-negative breast cancer respondents indicated that minimal side effect was the most important factor in treatment decision making.

These concern were reiterated anecdotally:

"Making sure I have some quality of life so I can [spend] as much time with my kids and family I don't want them to watch me suffer"

"Trying to balance the most effective treatment regime with the least impact on my day to day living/quality of life. Maintaining a certain level of independence is important to me."

"Definitely the balance of quality of life vs side effects with the [effectiveness]."

Cost and accessibility of treatments:

The financial burden associated with early breast cancer extends far beyond any loss of income during a temporary or permanent absence from employment. In addition to the loss of income during illness, breast cancer patients can incur substantial costs associated with treatment and disease management.

Research on the financial impact of breast cancer on patients identified the following: (Reference: Janet Dunbrack, Breast Cancer: Economic Impact and Labour Force Re-entry. Canadian Breast Cancer Network, 2010)

80% of breast cancer patients report a financial impact due to their illness.

44% of patients have used their savings, and 27% have taken on debt to cover costs.

In our 2017 Survey, the majority of HR-positive, HER2-negative patients reported that their diagnosis had some (47%) or a very large (15.5%) impact on their finances.

Our 2022 Survey indicated that among HR-positive, HER2-negative patients:

28% were prescribed treatments not covered publicly.

41.5% were prescribed support medication not covered publicly.

2% reported that the cost of support medication or treatment medication prevented them from taking the drug.

Need for Personal Choice

Previous discussions with patients have demonstrated the imperative for breast cancer patients to have access to and options regarding what drugs they take. This was evident from respondents in our 2022 survey where 40.5% percent of HR-positive, HER2-negative breast cancer patients expressed being very comfortable making treatment decisions. Most patients are well aware of the adverse effects of treatment up front and they want to make a personal choice that works for them.

5. Improved Outcomes

For early stage breast cancer patients, treatment efficacy and reducing the risk of recurrence is of the greatest concern. Like any other treatment for early stage breast cancer, patients have an expectation that abemaciclib (Verzenio) will effectively treat their cancer, reduce the risk it will return, and offer a good quality of life.

The phase 3 MonarchE trial evaluated and compared adjuvant abemaciclib in combination with endocrine therapy (ET) to adjuvant ET among patients with HR-positive, HER2-negative, high-risk early breast cancer, who had surgery and, as indicated, radiotherapy and/or adjuvant/neoadjuvant chemotherapy. Patients with four or more positive nodes, or one to three nodes and either tumor size ≥ 5 cm, histologic grade 3, or central Ki-67 ≥ 20% were eligible (Reference: https://pubmed.ncbi.nlm.nih.gov/32954927/.)

This study used invasive disease free survival (iDFS) as the primary endpoint, and secondary endpoints of distant relapse-free survival (DFRS), overall survival, and safety, which reflects this patient group's need for more treatment options that delay or prevent recurrence, are effective, and have minimal side effects. The trial found that abemaciclib offered 92% iDFS and 93.6%

DFRS verses 89%, and 90.3% in the control arm respectively. Overall survival data was not yet reported at the time of this submission (Reference: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7768339/)

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Adverse Effects

The data from the phase 3 MonarchE showed that abemaciclib combined with ET had greater side effects than ET alone (any grade 97.9% vs 86.1% respectively) while the safety profile of abemaciclib was consistent with previous studies, and no new safety signals were identified.

Commonly reported side effects of any grade were: diarrhea, neutropenia, fatigue, and leukopenia. Commonly reported side effects of grade 3 or higher were: neutropenia, leukopenia, diarrhea, and lymphopenia. 12.3% of patients treated with abemaciclib reported serious side effects verses 7.2% in the control arm. The number of deaths in both the abemaciclib and control arm was 14 patients (0.5%) (Reference: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7768339/).

Impact of Treatment Options to Patients

Additional treatment options that can reduce the risk of recurrence, relieve cancer-related symptoms, and improve a patient's quality of life have a significant impact on patients. When living with no or with minimal cancer-related symptoms, and with minimal side effects from treatment, patients are able to reduce the impact of cancer on their ability to care for children and dependents, continue with their employment, earn income, spend time with loved ones and participate in their life in a meaningful way by engaging in social activities, travelling, maintaining friendships, and pursuing personal interests.

Value to Patients

The value to patients of reducing the risk of recurrence, offering improved choice in treatments that are effective, and have minimal side effects cannot be over-estimated. For breast cancer patients that have an HR-positive breast cancer, there is an increased risk of disease recurrence which must be addressed by new treatments. Further, the effectiveness of ET alone can diminish over time.

6. Experience With Drug Under Review

CBCN was unable to speak with patients who had experience taking abemaciclib, however we spoke with one patient who wanted to take this treatment but was unable to at the time of the interview because of the recently changed requirement that Ki-67 score must be 20% or greater. This means that the recent Health Canada approval addresses some of the inequities discussed below, but cost remains a barrier while abemaciclib is under funding review.

Patient Profile:

The patient was interviewed in November 2023 and was between the ages of 45-50 at the time of the interview. She was diagnosed with stage III, HR-positive, HER2-negative invasive lobular carcinoma, with a tumour size of 7 cm, and 22 nodes containing cancer in January 2023. She has previously had chemotherapy, radiation, and surgery, and is currently taking hormone therapy. She was unable to access abemaciclib because her Ki-67 score was 18% instead of 20% or greater.

Treatment Goals

The patient indicated that preventing recurrence was the most important treatment goal for her, and spoke about how her current treatments do or do not help her to achieve this goals.

"I guess they are doing what they are supposed to. I just believe everything the medical oncologist is advising. I'm hoping it's working. I'm hoping it does what it is supposed to."

"I know Verzenio has lots of side effects, but if it's helping with the recurrence. I don't think the side effects are to (sic) me, I can go through it."

When asked how effective her current treatment is at controlling her cancer, she had this to say:

"I hope it's working. So I had my surgery, chemotherapy, and radiation. At the moment, they say they don't see any cancer."

Taken together, these statements show the importance this patient places on additional treatment options that prevent a risk of recurrence.

Assessing Efficacy and Risks Associated with Treatment

At the time of the interview, the patient had undergone surgery, radiation, and chemotherapy. She was also taking the hormone therapy anastrozole. She speaks about the side effects of these treatments.

"Chemo was very hard for me. Every treatment [had] some kind of side effects. For nausea, I had some medication proscribed by the oncologist but to me was the joint pain and the muscle pain and the extreme fatigue that took a toll. That was very, very hard."

"Anastrozole is giving me so much joint pain. Day, night, everything is hurting. But some days is harder than other days. If I keep moving and moving, it's not too bad. But as soon as I sit even five minutes and try to get up, everything hurts."

She found joint pain, muscle pain and tiredness to be the three most common side effects, with joint and bone pain the most difficult to tolerate. Here is what she had to say about managing these side effects:

"*I'm trying some supplements. I don't think that it's working. Tart cherry. And also I heard that if you take Claritin, the allergy medication, that can help too. Advil is helping me, but I don't want to take Advil every day. I feel like I have so many medications. My body, I need a break. When it's very painful, I take Advil, but if it's not too, too bad, I try not to take it. And then I am taking my calcium, magnesium, Vitamin D. That was recommended. Those are the supplements. For pain medication, I don't have anything prescribed by the doctors. So I just manage with Advil over the counter."*

She also spoke about whether side effects caused her to discontinue any treatment:

"No. I was lucky. I finish everything."

Alternatives to the Treatment

Although Verzenio is available to some patients, due to the requirement for Ki-67 scores, the patient interviewed shared that she did not have alternative treatment options. Still, she found the treatment she was currently taking effective and chose it for that reason.

"I know it's helping for my cancer not to come back."

She further spoke about what treatments she could use if her current hormone therapy became unavailable.

"From what I heard, there are 3 hormonal blockers, and if mine will be not available anymore, probably they would switch to the other 2."

She also indicated that she wanted to take abemaciclib, but was sad that she was unable to.

"Verzenio is $7000 per month; too expensive. I cannot afford to pay that and my insurance doesn't cover the medication because it's not approved in Canada. But I don't understand why it can be approved in United States or UK and not approved here. That's what's very sad."

"This is strange. Why some women in US, not some women, all of them , like stage I to IV, are using this medication, and here in Canada it's approved just for stage IV. For me, because I'm stage III and so many lymph nodes involved, my oncologist said that medication would be beneficial. For all the criteria for the drug plan and whatever the rules are, the tumour is big, the lymph nodes, there are lots of them, stage III. The only thing I didn't meet was the Ki 67. At the moment for Verzenio, you have to have a Ki67

higher than 20%, and mine is 18%. The US drug plan, this Ki67 criteria, they took it out. So I'm hoping Canada will do that sooner than later. Because all the trials, this medication is working and it's helping. It's helping us. I don't want to get to stage IV and then be offered this medication. Why not be proactive and do the treatment before?"

She was also asked what having just one additional treatment option would mean to her and had this to say:

"Being able to access the additional medication, the one that's called Verzenio, that would mean a lot, especially mentally it's going to help me just relax. Because right now I feel very stressed and I don't know what route to go to access that medication. What do I have to do to be able to take it? That's stressful."

The Social and Financial Impact of the Treatment

Patients expect that treatments will be effective in controlling disease, prevent recurrence, have manageable side effects, be safe, and be affordable to the patients who need it.

The patient spoke about how the efficacy and side effects of her treatment impacted her family, and her quality of life.

"I have my two boys and my husband. They are pretty tough. They are doing okay. My husband, I'm not saying that he's not affected. He is affected. But he's tried to stay positive. We keep doing our everyday routines. School activities, everything."

"So my boys are 14 and 15 and they were able with my husband to be able to pack lunches, go to school, perform afternoon homework activities. They are older kids. They are bigger kids. It was easier that way because the kids are older."

"I took time off from work. I'll be at home until February. So again, I'm very lucky that I could do that. I'm done with my treatments but I'm still tired and I need to sleep during they day. I work as an accounting technician, so I work in an office."

"During my chemotherapy, it was very hard. I felt tired even if I just had to talk with someone. I was sleeping a lot. Not going out. But I try to take one day at a time and do things…I knew better days are going to come and then I try to do things that would make me happy like petting my dog or reading a book or doing something to get out of that."

Overall, the patient had a "very smooth" experience with her current treatments, but felt very strongly that abemaciclib should be available to patients in Canada on the same terms as other jurisdictions. This differential standard of care is "very sad" to her, and she was not able to afford the out of pocket costs associated with this treatment.

"I contacted [the Canadian Breast Cancer Network and asked] how do I have to go about [to access] this medication, Verzenio. What do we need to do, all these people in Canada that have stage I to III? What letters, what emails, what do we have to go through so someone will approve it? It's very sad that patients in different countries are treated differently."

Companion Diagnostic Test

Not applicable

7. Anything Else?

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

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

CBCN connected with the manufacturer, Lilly Canada, to learn about the results of the MonarchE clinical trial.

All other research, interviews and outreach to patients was conducted independently by the Canadian Breast Cancer Network, as was the compilation of information and data for the writing of this submission.

As a member of the Canadian Cancer Action Network, the Canadian Breast Cancer Network is committed to adhering to the Code of Conduct Governing Corporate Funding.

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

No. The Canadian Breast Cancer Network compiled and wrote this submission independently.

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

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.

Name: [redacted]

Position: Health Policy and Advocacy Lead

Patient Group: Canadian Breast Cancer Network (CBCN)

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: abemaciclib (Verzenio)
Indication: Eli Lilly Canada Inc. (Eli Lilly) is requesting reimbursement for Verzenio (abemaciclib), in combination with endocrine therapy for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of disease recurrence based on clinicopathological features.

Name of Patient Group: Rethink Breast Cancer
Author of Submission: [redacted]

1. About Your Patient Group

Rethink Breast Cancer (Rethink) is a Canadian charity known for making positive change. Rethink educates, empowers and advocates for system changes to improve the experience and outcomes of those with breast cancer, focusing on historically underserved groups: people diagnosed at a younger age, those with metastatic breast cancer and people systemically marginalized due to race, income or other factors. We foster spaces to connect, listen, empower and rethink breast cancer, together. Rethink's strategic priorities and organizational direction are guided by the unique, unmet needs identified by breast cancer patients and their families.
Programs and Activities

- • Rethink Breast Cancer builds community, bringing patients with various stages of breast cancer together through our private and public social spaces as well as in-person events
- • Rethink runs patient retreats and facilitates peer-support
- • Rethink creates and runs education forums and conferences
- • Rethink creates support and education tools, resources and content
- • Rethink funds and supports breast cancer research

You can find out more by visiting: Rethink Breast Cancer Instagram; Rethink Breast Cancer Website

2. Information Gathering

For over 20 years, Rethink has been working closely with breast cancer patients in Canada. We learn from and listen to the community to understand their values, priorities and pain points to help drive change and system improvements. Each year, we learn from the patients we serve, survey and collaborate with. We learn from the 40 individuals that we work extremely closely with as key patient advisors; the 100 patients that share their stories on our blog; the 500 patients that participate in our virtual support groups; the 1,600 members of our private peer-support network; the 30,000 people that have joined our Instagram community; and the 150,000 individuals reached each month through the reach of that channel. We listen, learn, engage and have conversations in all these spaces.
Rethink Breast Cancer has several important patient advisory boards and working groups that offer experience-focused insights on issues related to those affected by and concerned about breast cancer, including:

- Metastatic Breast Cancer Advisory Board
- Early Breast Cancer Advisory Board
- Equity, Diversity and Inclusion working group
- Triple Negative Breast Cancer working group (all stages)

For this submission, we have drawn on our general observations and insights gathered through programming and meetings with breast cancer patients as described above. Rethink also conducted in-depth telephone interviews in March 2022 with two patients who have experience with abemaciclib for HR+, HER2- high risk early breast cancer.

3. Disease Experience

Most people in the Rethink community are diagnosed at a younger age. When young people get breast cancer it may be more aggressive, which can lead to tougher treatments. In addition, those diagnosed in their 20s, 30s and early 40s face age-specific issues such as fertility or family-planning challenges, diagnosis during pregnancy, childcare, impact on relationships, body image, dating and sexuality, feeling isolated from peers who don't have cancer, career hiatuses, and financial insecurity. The physical and emotional toll that a breast cancer diagnosis and treatment takes on a young person's life is devastating and traumatic.

When it comes to those in the community who have been told their breast cancer is at a high risk of recurrence, treatment is less about controlling an aspect of the illness and more a deep desire to take on whatever treatment(s) are needed to decrease the chance of recurrence and metastasis. They are facing mortality prematurely and many express a goal to treat aggressively to optimize treatment. Those we interviewed for this submission shared:

"I think when anyone gets a cancer diagnosis, you're always scared of the illness coming back. Especially when I have young kids that I want to be there for, and I have a lot of things I want to do myself. It's not only my kids, but also my life too. I want to be able to enjoy it. Because I feel that I'm doing anything and everything that's available out there to have a lower chance of recurrence, it gives me peace of mind. It gives me less anxiety in my life." –[redacted]
"I am generally a fan of treatment - the more aggressive the better. In fact, after having chemo done, I advocated to have a total axillary LN dissection, and I also had my ovaries out last year. Again, I don't mind treatment at all, even the side effects that come with it - I'm more concerned about the prospect of mortality." [redacted]
"I want to try anything to prevent recurrence, I want to add it to my exercise routine and healthy diet in my bag of tricks[redacted]

4. Experiences With Currently Available Treatments

Current treatment for HR positive HER2 negative early breast cancer depends on the details of the persons diagnosis and the characteristics revealed on their pathology report. It is usually treated with a combination of surgery, chemotherapy, radiation therapy, and hormonal therapy, which can reduce the risk of early-stage breast cancer coming back. Some patients will opt for an oophorectomy. These treatments are all incredibly difficult with both physical and emotional impacts that require a lot of support and care. Peer support is incredibly helpful as is professional support. Being well prepared for what you are about to endure is essential and oncology nurses and a peer community are extremely helpful in this regard both with short term and long-term side effect management. Difficulty coping with the side-effects of hormone therapy is frequently discussed in our community.

4. Improved Outcomes

Each individual patient brings their own personal values and goals to their discussions with their oncology team. Communication and trust in their team is essential. In our experience working closely with many young high risk breast cancer patients, we find most are willing to trade toxicity for confidence in knowing they've "thrown everything they could" at the cancer. In other words, they will choose to endure additional side-effects and impacts on quality of life from the toxicity of a stronger therapy to ensure they are doing everything they can to treat what they know is an aggressive form of breast cancer. That was a take-away from the patients we interviewed for this submission who are on Verzenio.

6. Experience With Drug Under Review

Rethink conducted in depth phone interviews with two patients with high-risk early breast cancer who have experience with abemaciclib (Verzenio).

Patient 1 interview: [redacted]

[redacted] *I'm located in Vancouver, BC. At the end of my pathology report, I was Stage 2B. I was 39 at the time. I had three tumours. I found it myself. We never had any family history. The lump was moving. My family physician was sure that it wasn't cancer, but she just wanted to make sure and have peace of mind, so she sent me for testing and here I am. I did surgery first and then 8 rounds of chemo, 25 rounds of radiation. I did an oophorectomy. At the beginning I was going to do Zoladex, but I talked with my doctors, after 10 years I'll be almost 50 so there was no point for me to stay on Zoladex, so I did an oophorectomy in March. In regards to my treatment path, I wouldn't say hell, although I had days that looked like hell. I was lucky I caught it early. I had node involvement and normally when there's a lymph node involvement it spreads quickly after that. It was a lot of ups and downs; I still have a lot of that. Sometimes I think I came to terms with it, but I don't think I have yet. It was very scary as I have 2 young children. I was working full time. I always say it was my prime time with my kids and my work, but I had to put everything on pause. It's a scary, scary situation to be in because you see so many people that had the same diagnosis, they got the same care, but they had a recurrence. So, when my doctor talked about Verzenio although the side effects are not something that I look forward to, but again it's bringing the possibility of recurrence lower, so I take it.*

I was really lucky that my oncologist referred me – I think the manufacturer is the one paying for me, I'm not paying out of pocket. Here it's $13,000 per month and I definitely cannot afford that. I was very concerned about the cost. Maybe if I didn't have kids, it would be a totally different experience. I had a cousin; she was like my sister. She was 5 years younger than me. She passed away from ovarian cancer in 2019, so we had that scare in our family. Not in a blaming way, but one thing that everyone thought is that she didn't take the cancer seriously. So, from the minute I was diagnosed, I was quite proactive on finding the best solution. When I was talking with my oncologist, I already had done tons of research on breast cancer, what treatments are available, my second opinion from MD Anderson, etc. So, when the Verzenio got approved by Health Canada, I knew about it, I read about it, I did research. I follow quite a few of women with breast cancer on Instagram and I saw them talking about it and the cost of it. So, the cost was something that I was concerned about. $13,000 a month is a lot of money. Both my husband and I are making good money, but this is still a lot of money per month. We thought, we're going to try to do this, and even if we have to remortgage our house to get the money from the equity in our house to pay for the treatments, we're going to do it.

My oncologist was on board for me taking this medication and said there's ways it can be covered. Thankfully I was approved for it. So, I feel very blessed and lucky that this treatment was available to me for free. I understand some provinces don't cover oral chemo and it's scary. Especially with cancer, time is of the essence. You need to be very quick. You cannot wait a year for this to become available because in that year, the cancer might spread and turn metastatic.
I feel so lucky that I have access to it at no cost. But the side effects, I haven't had severe ones yet. I'm very tired, but I'll take being tired rather than the cancer coming back. I think when anyone gets a cancer diagnosis, you're always scared of the illness coming back. Especially when I have young kids that I want to be there for, and I have a lot of things I want to do myself. It's not only my kids, but also my life too. I want to be able to enjoy it. Because I feel that I'm doing anything and everything that's available out there to have a lower chance of recurrence, it gives me peace of mind. It gives me less anxiety in my life.
I would absolutely recommend Verzenio to other patients in my position. This is $13,000 per month. But what if the illness relapses? If you compare the amount of emotional distress and money that they're going to put the family through with loss of life, other chemo, hospice, etc. so many things. When I got diagnosed with breast cancer in Canada, I felt so lucky because finances weren't something I had to worry about. Of course, we were losing my income, but I didn't have any extra costs. But this is the extra cost. If the Canada doesn't fund this, I cannot imagine this stress in having the thought that something was available to me, and I wasn't able to access this because I didn't have the financial resources. It's not fair.

Patient 2 interview: [redacted]

I am 36 years old and was diagnosed with breast cancer when I was 33 years old. I had hormone positive and receptor negative type. I had my double mastectomy first, and my lump was 4.3cm! with 3/4 sentinel lymph nodes positive. I live in Richmond BC. I'm a social worker at a very large long term care home in Richmond. Being sick during the COVID 19 pandemic meant that I wasn't able to be at work during a time when they really needed staff and that was hard. I have a 4-year-old and 6-year-old now.
I didn't mind the treatment because for me, having treatment was taking action. I don't mind treatment at all, even the side effects that come with it - I'm more concerned about the prospect of mortality. My oncologist, who I trust, thought Verzenio would be good for me, so I didn't even hesitate to say yes. As long as it doesn't make my Anastrazole less effective, then I'm game - always.
The Lilley program is paying for my Verzenio. My extended health from work doesn't cover it. The pharmacy that it comes from has been good too. I just don't like that they deliver it monthly because it's a hassle to coordinate, and I'm always worried that something will happen where I don't get my next delivery. I was expecting to get diarrhea my first week, so I took Imodium but then I ended up with constipation for like a week. Now my body has gotten used to it. I still get the occasional cramping or bloating, but nothing I can't tolerate. I would say though, for people just starting on Verzenio that I think once your body adjusts to it, it gets better. The first couple of weeks can be rough.

I would recommend Verzenio. Patients should never have to worry about getting their medications through bureaucratic processes. Please make life easier for patients than they already are. Provinces should fund this medication and make it easy for those who fit the criteria to get it.

7. Companion Diagnostic Test

The removal of the requirement for a Ki-67 score ≥20% will remove a barrier to care for patients. Ther is not equitable access across Canada to Ki-67 testing, creating yet another barrier for access to care. Patients interviewed indicated how critically important it was to them to be able to reduce their risk of recurrence, and by removing this barrier, more people in this patient population will have the choice to make treatment decisions based on their personal priorities and treatment goals.

8. Anything Else?

We'd like to emphasize that young, high-risk breast cancer patients want more effective tools in their toolbox that will help improve their chances against this challenging disease that's turned their life-plans upside-down.
As we ponder "anything else," we think about the MBC community that we know so well—and their loved ones. We think about those we've lost. Too, too many at such a young age over the years. Their families will never be the same. We also think about the MBC community that we see currently thriving. The CDK 4/6 inhibitors have been more of a game-changer in our community than we could have ever imagined. That said, moving the needle on MBC outcomes is still not the same as a cure. Verzenio as an option for those with HR+ HER2- breast cancer that is at a high risk of recurrence can give patients a tangible way to help achieve their goal of a cure.
And, finally, as we have been in the thick of #BitterestPill, an advocacy campaign calling for equal funding for Take Home Cancer Treatments in Ontario, we think about the delays, dollars, distress and discrimination that the current program in Ontario entails, which negatively impacts patient outcomes. Too many are impacted by a policy that's needed updating for over a decade!

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for

participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

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

No.

2. Did you receive help from outside your patient group to collect or analyze data 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 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Eli Lilly 2021			X	
Eli Lily 2022			X	

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.
Name: [redacted]
Position: Lead, Strategic Operations and Engagement
Patient Group: Rethink Breast Cancer

Date: December 7, 2023

Clinician Input

Clinician Group Input

CADTH Project Number: PC0345

Generic Drug Name (Brand Name): abemaciclib (Verzenio)

Indication: In combination with endocrine therapy for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of disease recurrence based on clinicopathological features

Name of Clinician Group: Ontario Health Cancer Care Ontario Breast Cancer Drug Advisory Committee

Author of Submission: Dr. Andrea Eisen, Dr. Orit Freedman, Dr. Haider Samawi, Alaina Charlton, Dr. Ronita Lee

1. About Your Clinician Group

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

Information was gathered at a DAC meeting.

3. Current Treatments and Treatment Goals

Standard treatment varies depending on risk of recurrence but includes combinations of surgery, radiotherapy, adjuvant/ neoadjuvant chemotherapy, and endocrine therapy (ET). Adjuvant ET is standard treatment of HR+, HER2- early breast cancer (EBC) and has been associated with a significant reduction in risk of recurrence and death. The DAC noted in the previous submission, problems with access to Ki-67 testing and supports the inclusion of patients who are similar to Cohort 1 in the MonarchE study. The DAC assumes that patients who are similar to Cohort 2 would continue to be eligible.

Abemaciclib is an oral, continuously dosed, CDK4/6 inhibitor approved for HR+, HER2- advanced breast cancer (ABC). Efficacy and safety of abemaciclib in ABC supported evaluation in the adjuvant setting.

Treatment goals would be improved survival and decrease risk of recurrence.

Reference:

Stephen RDJ t al. Abemaciclib plus endocrine therapy for hormone receptor-positive, HER2-negative, node-positive, high-risk early breast cancer (MonarchE): results from a preplanned interim analysis of a randomised, open-label, phase 3 trial. Lancet Oncol. 2023 Jan;24(1):77-90. doi: 10.1016/S1470-2045(22)00694-5.

Eligible patients were assigned to one of two cohorts.

Cohort 1 included patients with four or more positive pathological axillary lymph nodes or between one and three positive axillary lymph nodes and at least one of the following additional high-risk features: tumour size 5 cm or larger or histological grade 3 disease. Ki-67 was determined centrally in all patients in Cohort 1 with a suitable pretreatment breast tumour tissue sample, but a Ki-67 index was not required for enrolment.

Cohort 2 included patients with between one and three positive axillary lymph nodes, intermediate-risk clinicopathological features (tumour grade <3; tumour size <5 cm) and a centrally determined high Ki-67 index (≥20%) was required as an

additional risk feature. Ki-67 index was centrally assessed in untreated breast tumour tissue sample by means of an investigational Ki-67 immunochemistry assay developed by Agilent Technologies (formerly Dako; Santa Clara, CA, USA).

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.

Despite the advances of treatment in HR+, HER2- BC, up to 30% of patients with high-risk clinical and/or pathologic features may experience distant recurrence. Superior treatment options are needed to prevent early recurrence and development of metastases for this group of patients.

5. Place in Therapy

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

Abemaciclib would be used in addition to ET in high-risk patients following surgery and chemotherapy (if applicable).

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 would be HR+, HER2- early breast cancer (EBC) at high risk of recurrence who are node positive. Patients best suited would align with the inclusion criteria from the clinical trial (i.e. both Cohort 1 and Cohort 2 of the trial).

Patients least suitable would be patients listed in the exclusion criteria from the clinical trial.

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?

No extra imaging is needed but patients would need extra monitoring for hematologic toxicity, diarrhea, and extra visits would be required. Patients should be assessed for toxicity. Additional support from oncology pharmacists and nursing may be required

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

Disease progression and 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]?

Experience with treating breast cancer patients, access to laboratory blood work, and expert pharmacy/nursing support in the management of oral agents.

6. Additional Information

In BRCA1 or BRCA2 carriers, both abemaciclib and Olaparib are adjuvant choices.

There may be downstream effects on subsequent agents when patients relapse. This is addressed in the algorithm.

7. 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.

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 to the group.

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.

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, OH-CCO Breast Cancer Drug Advisory Committee

Date: 15-11-2023

☒ **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, OH-CCO Breast Cancer Drug Advisory Committee

Date: 27-10-2023

☒ 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. Haider Samawi

Position: Member, OH-CCO Breast Cancer Drug Advisory Committee

Date: 27-10-2023

☒ 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: Alaina Charlton

Position: Member, OH-CCO Breast Cancer Drug Advisory Committee

Date: 27-10-2023

☒ 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: Dr. Ronita Lee

Position: Member, OH-CCO Breast Cancer Drug Advisory Committee

Date: 27-10-2023

☒ 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				