

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: trastuzumab deruxtecan (Enhertu)

Indication: Anticipated indication as filed with Health Canada: for the treatment of adult patients with unresectable or metastatic HER2 (human epidermal growth factor receptor 2)-positive breast cancer who have received a prior treatment with an anti-HER2-based regimen in the metastatic setting or developed disease recurrence during or within 6 months of completing neoadjuvant or adjuvant therapy

Name of Patient Group: Rethink Breast Cancer

Author of Submission: MJ DeCoteau

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 all 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. 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 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)

Rethink also benefits from regular knowledge exchange with our Scientific Advisory Committee, which includes some of the leading clinician scientists in Canada who treat breast cancer.

For this submission, we have drawn on our general observations and insights regarding the experience of metastatic HER2 positive breast cancer patients gathered through programming and meetings as described above. Rethink has a long history of developing resources for the HER2 positive breast cancer community, including producing an award-winning documentary *About Her* screened at film festivals along with a television broadcast on W Network. Our information gathering for this survey includes focused conversations with our Metastatic Breast Cancer Advisory Board, which includes three HER2 positive members. Rethink also conducted email interviews this March with three patients who have experience with Enhertu through AstraZeneca's patient support program. Finally, we have revisited written correspondence from fall 2020 with a patient involved in our organization who was desperately asking Rethink to collaborate on advocacy to make Enhertu available faster in Canada. Our hearts went out to her but knowing where Enhertu was in the HTA progress, we knew that effective advocacy options did not exist. She decided to go the Go Fund Me route and hoped to raise enough to travel

across the border in the height of a global pandemic to pay for treatment with Enhertu in Buffalo, NY.

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.

Of all breast cancers diagnosed in Canada, up to 15% will have a subtype known as HER2 positive breast cancer that is a more aggressive form, often occurring in young people, and has a high risk of recurrence or presentation as Stage IV at diagnosis. While anti-HER2 treatments in the early setting means fewer people are relapsing, there are still many in our community with recurrent HER2 positive metastatic breast cancer or de novo HER2 positive metastatic disease who need treatment. This stage of disease is not curable, and the median life expectancy following a diagnosis of metastatic HER2 positive breast cancer is 5 years once metastases have been diagnosed.

Processing this reality of a life-limiting diagnosis is extremely difficult, especially for the young patients in our community and the emotional impacts on quality of life cannot be understated. Moreover, many develop brain metastasis, which is difficult to treat and has a heavy symptom burden with both physical impacts and often changes in mood, personality and thinking. These cognitive and psychosocial challenges negatively impact both the patients and their caregivers who often have to take on an overwhelming number of responsibilities. Other symptoms of advanced HER2 positive metastatic breast cancer depend on the sites of the metastasis and include fatigue, shortness of breath for lung metastasis, pain and bone fractures for bone mets as well as nausea, headache and of course challenges doing normal daily activity. Our MBC Advisory Board strongly believes in the benefit of metastatic patients accessing palliative/supportive care services early to help address these symptoms.

4. Experiences With Currently Available Treatments

Metastatic HER2 positive breast cancer is usually treated with pertuzumab, trastuzumab and a taxane. One of the patients we interviewed who recently started Enhertu received her metastatic diagnosis in 2016. At that time, treatment started with having her ovaries removed and taking letrozole. Her tumors reduced and were stable for around 3 years. With progression in 2019, she received Perjeta and Herceptin, then Herceptin, then Kadcylla. She had this to say about the regimen of treatments she received from the time of her initial MBC diagnosis in 2016 to having progression in 2021:

“I was able to improve and be stable for a good time and have received one chemo and two immunotherapies in this time. I was very scared because the very advanced stage of the mets, but fortunately they stayed in the lungs and have not gone anywhere else so far. Chemo treatments are very scary, and I was very nervous about how much I would not been able to do for my family because of treatment. The first chemo was ok, no big side effects apart from thinning of the hair, I think all the work to stay strong paid, I kept being me despite the chemo. Immunotherapies were easy on me.” –Mary F.

5. 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. It’s important that patients have a clear understanding of trade-offs and are well prepared for common side-effects of a given treatment. One of the patients we interviewed who was on Enhertu did not know hair loss was a factor with Enhertu until treatment was underway. While she expressed that the trade-off to shrink the tumour is worth it, she would have coped better with that side effect had she been prepared and could have explored cold capping to try and minimize hair loss.

In our experience working closely with many young metastatic breast cancer patients, we find most are willing to trade toxicity to control their 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. Rachel M., a patient in our community who was raising funds to pay out of pocket to access Enhertu in Buffalo in 2020 had this to say at that time regarding trade-offs:

"I've learned that there is no 'worst'. There is no 'nothing left'. I used to think that when I would start needing oxygen tanks carted around with me or attached to me 24/7 in my home that it would be the worst. It's not, since it allows me to keep breathing and living.

I thought that when I heard the words, "it has metastasized to your brain", it would be game over. It wasn't. It isn't. I had two spots in my brain this time last year that we resolved with a special radiation. I thought when I heard the words, 'you have three to six months and there's only a few drug options available that have a 10% chance', that I would just curl into a ball and pray I heard wrong. I didn't. I took those words, one year ago. The meds I decided to take that had a 10% efficacy rate were working. The lung disease is heavily burdensome and I now have about fifty per cent of both lungs covered in tumors. We are buying time. There's also tumors in my lymph nodes, liver and spine, all of which are small, asymptomatic and don't require radiation.

I have continued to live a pretty normal life. As my mantra goes, I'm the healthiest I can be. I'm not that girl with cancer even though my face and body have started to betray me due to some medication I am forced to take in order to help me breathe. While depressing to watch at first, I now say that I don't care what I look like, just keep me here, Lord. Every night, I give thanks for making it through, pray to wake up in the morning, and ask so humbly, for another day.

So long as I can move and get around, I will wash Marin's hair in the bath, I will help prepare meals, I will make 60 jars of jam."

6. Experience With Drug Under Review

Rethink conducted email interviews in March 2022 with three patients with metastatic HER2 positive breast cancer who have experience with Enhertu. All three expressed gratitude that they had access through a patient support program.

Patient 1: Mary F.

I am 48 years old, was diagnosed at 38 with stage 2b, P+, E+ and Her2- (I think it was kind of border line). There was no lymph nodes involved and further testing determined that my risk for recurrence was low so I went with lumpectomy and radiotherapy only. At 42 my lung mets were discovered, I don't think my doctors were very optimistic, but they did not say so. With lots of

patient, a great healthcare team and God's help I was able to improve and be stable for a good time and have received one chemo and two immunotherapies in this time. When December 2021 brought news of some met advance my doctor recommended Enhertu. He has mentioned before that he was excited about this new treatment.

The diagnosis of MBC gave my life a due date, it became very real. I was super afraid since my kids aged 9 and 13 at that time still needed time with me. I have had 4 treatments of Enhertu so far, apart some Nausea, which was stronger the first 2 treatments and some fatigue, I have had no side effects. I keep working full time, today I went to my dance class 4 hours after finished my Enhertu infusion! I read the latest data on Enhertu and I am very optimistic that I will live long enough to try the new big thing coming to help me live with cancer as we do with other chronic diseases. I am looking forward to seeing my daughter graduate from High School and son from College. I believe Enhertu will help me get there!

I was very scared to not be able to access this med. Was not sure if insurance would cover it, and for sure did not have the resources for paying for it. I hope that Canada starts paying for it very soon.

This medication side effects have been very mild to none. It is probably too early to say, but I think the benefits will greatly surpass the negative side effects. I would definitely say you should try. The mechanism of action is very smart, making sure the medication enters where it should enter.

Patient 2: Liz B

I have had breast cancer for about 7 years. I had one breast removed, followed by chemo and radiation. A few years later it had metastasized to my liver. That was a very difficult moment. That led to a new round of chemo with all the dreadful side effects. About a year later I had a lesion in my hip bone which was successfully radiated and a year later a lesion in my brain again successfully radiated (cyber knife). Each time there is the dreadful progression, the chemo is changed. Before Enhertu I was on a trial drug for about a year before I had 'progression'. The Ontario Health System has given me outstanding treatment, for which I am very, very, thankful.

I have only been on Enhertu for a short time. I have yet to have tests to evaluate the effectiveness of the drug for me. I am very grateful to the company for providing me with the drug and I am obviously hopeful it works for me. I will know better in the coming weeks/months. My oncologist has a lot of faith in this drug, so I have my fingers crossed that it is as good as he thinks it is.

Patient 3: Debbie B

I was diagnosed in 2016 and I'm 66 years old..

I started out with surgery on my breast, just the tumor removal. Then another surgery about a month later, on my axillary lymph nodes. The cancer metastasized and spread into my brain, liver and again into my left breast and lymph nodes. I had a tumor removal surgery on my brain in 2017. Since then, I have been on various different chemos, blockers and radiation as the cancer has now spread to my spine as well.

I wanted to try Enhertu because my Oncologist Dr. had read and heard about it and she felt it might be a good fit for me. I had heard nothing about it myself, but she had and told me it had a good success rate in the trials. So I decided to try it. There was a lack of communication and some problems though between the Enhertu booking dept., which resulted in a delay of 6 weeks. At that time I could feel my left breast increased and hardened by quite a bit as well as, a tumor in my left arm pit also grew.

Since being on the treatment, which I take every 3 weeks now, the tumors have definitely decreased. I am waiting to find out from my Dr. as to how much but I can see and feel, they have gone down by quite a bit. So the drug does seem to be working. The side effects are terrible though. I did not know when I started it would cause me to lose my hair again, and I am unfortunately losing it. Also approximately a week after each treatment I am really sick. I didn't expect this for the first dosage and I was vomiting several times a day for around three days. Even had to go to the hospital. Since that time, I have been working with my Dr. who has prescribed a few different anti-nausea medications, so I am prepared. They are working. Another terrible side effect during that time is Fatigue. I find it is very, very hard to do anything. I end up, basically in bed for a few days. Unable to work or do anything. My Dr. has since decreased my dosage. The first treatment didn't seem to make much of a difference, but I just had another treatment and the fatigue this time was definitely there, but not as severe.

I would recommend the Enhertu to other patients. Especially because I can see and feel the shrinking in a couple of my tumors and without the drug they had increased quite a bit. So I am able to see it is working. I would definitely let the other patients know about the bad side effects though.

I do feel all patients should have access from the Gov. to this treatment. I feel very fortunate to be able to try it and would hope the same for anybody in my situation. It would be absolutely impossible for me to have access through my own finances and I can't imagine there are too many people who could afford it themselves. Which is so unfair already.

7. Companion Diagnostic Test

Nothing to report on this topic.

8. Anything Else?

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 and those who are running out of options. We also think about the MBC community that we see currently thriving. We want more Canadians with HER2 positive metastatic breast cancer to have the opportunity to thrive for longer by having access to the most effective treatment as a second line option. It’s hard to re-read Rachel M.’s emails, knowing that she’d run out of time to benefit from Enhertu. Rachel was diagnosed with Stage 1 HER2 positive breast cancer in 2013, when she was eight months pregnant. She became metastatic in 2017 and got involved in our education and advocacy campaigns. Unfortunately, she progressed and in late 2020, out of options in Canada, she and her husband travelled to Roswell Park in Buffalo, NY to line up treatment with Enhertu. They were raising funds to pay for it, but she died before reaching her fundraising goal. A young mom gone too soon. But that’s the unmet need. And that’s why two members of our MBC Advisory Board currently on their first line of treatment are advocating hard for Enhertu – they want a second line treatment that gives them, and others like them, the best possible outcome. Suzanne has young kids and was diagnosed de novo; Margaret, diagnosed with MBC early in pregnancy, has a toddler. These women need treatments that will keep their cancer stable for as long as possible. The stakes are incredibly high.

We ask a few more minutes of your time to read their stories, which are included as Appendix B.
Appendix A: 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
<Enter Name Here>				
AstraZeneca 2022				X
AstraZeneca 2021				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: MJ DeCoteau

Position: Founder and Executive Director

Patient Group: Rethink Breast Cancer

Date: April 14, 2022

Appendix B: Testimonials of the Unmet Need

Margaret Loniewska:

I am currently 42 (43 in May). I was diagnosed at 40 with Stage 1 Triple Positive breast cancer while pregnant but before I could start chemotherapy, it was discovered that the cancer was already well metastasized to my bones. I am 3+ her2 positive based on the initial biopsy. I live in Toronto with my husband and 2 year old daughter. I was working on getting a regulatory affairs certification when diagnosed. I currently work part time as a tutor at a private girls school teaching math and science.

After my lump was diagnosed as cancer, I had the lumpectomy, and this was followed by A/C chemo (4 rounds) and after my daughter was born, I was able to finally get on targeted treatment (Herceptin + Perjeta) and hormone blocking treatment. In terms of health, I would say that so far after the diagnosis my health has very slowly been improving with the current treatment. This means that my pain slowly disappeared and other side effects are slowly being dealt with (thanks to the palliative care team).

Enhertu has been on my radar from the very beginning of my diagnosis. From what I know from different MBC groups, this is a very effective treatment for many patients. Many patients share that this treatment has allowed them to be NED or NEAD. Even though so far my treatment has been working, I feel much more confident about my health knowing that at least there is an effective line of treatment coming up. I am most interested in the effectiveness of Enhertu to work in her2 low patients. I am very anxious about the cancer changing to less her2+ which happens quite often. I understand that there are some more potential side effects with Enhertu (diarrhea, etc) but this is something I already deal with in my current treatment. Patients on Enhertu really describe it as miracle drug and I would definitely like to have access to effective treatment the same as in the US. I also mentally am not prepared for weekly chemo which will absolutely destroy my QoL.

I think if how it stands now, my next line of treatment would be TDMI (Kadcyla) but this doesn't have much success for many patients (OS improvement is short). After TDMI, normally Enhertu is given (in the US). This is very real looming anxiety for all MBC patients. And this is only two lines away. Knowing that Kadcyla isn't so effective especially after long Herceptin use, the next line really comes up quick. If this isn't covered, I would definitely figure out a way to get this paid for as this would be my best chance at an effective response.

I think Enhertu should be funded because it is proven to be an extremely effective treatment for her2+ and even for her2 low patients and currently there isn't anything else on the market other than very harsh chemotherapies that extremely reduce the quality of life for MBC patients.

RJ Pauloski, Margaret's husband:

MBC is a difficult diagnosis to receive and a difficult disease to live with. The uncertainty of whether or not your treatment will work, what the side effects may be and what your quality of life is all cause a great amount of anxiety for the patient and the patient's family. Fortunately Margaret has responded well to targeted therapy which has allowed us to have precious time together as a family with her quality of life being reasonably good (all things considered). The biggest worry is the dreaded moment that we have progression and the disease no longer responds to the current line of therapy. The unknowns here are terrifying.

Enhertu is such an important treatment option for HER2+ MBC patients as other therapies (such as TDM1) are not as effective and non-targeted therapies have a very negative impact on quality of life (and survival). I am a member of an Enhertu clinical trial group on Facebook. The experiences of the women in this group are dramatic. Most of the women have had 2nd and 3rd line treatments fail, have had recurrence and have exhausted other targeted treatment modalities. For these women Enhertu is one of the final options to effectively stave off progression of their disease. Enhertu for the most part seems to be well tolerated (as well tolerated as treatment can be) and the response from treatment for the most part seems incredible (tumor reductions, total regression, etc.). I think if you were to ask the women on Enhertu in this group they would all agree that the treatment has been a life saver. If Enhertu is not funded by the government we would try to pay out-of-pocket or travel to the US to participate in a clinical trial. Not all women would be in a position to do this - making government funding all the more important. We would not be able to sustain out-of-pocket costs for long, as the treatment is expensive (\$10k+ per month) - but what is the value of a life? It would be a significant hardship but we would have to try and make it work. It is imperative that the government fund this treatment NOW. Enhertu is a life-extending drug for HER2+ MBC patients who have had other lines of treatment fail. It is highly effective and allows women to have a reasonable quality of life while on treatment; it literally keeps HER2+ MBC patients alive and there is no other treatment like it. HER2+ MBC patients need more FUNDED tools to manage their disease and Enhertu is one of the gold standards of late-line treatment.

Suzanne Horvath

I was diagnosed in December 2016 with HER2+ metastatic breast cancer de novo at 47. I live in Toronto, Ontario and worked for 20+ years as an educator and administrator in the public school board.

A diagnosis with MBC means living with cancer for the rest of my life. There is a constant worry that the current treatment I am on will stop working one day. As an MBC patient every treatment line is vital for my survival. The goal is to stay on whatever treatment that works for as long as possible. Enhertu is another possible lifeline of treatment for me. I have heard that many in the US have had success with it. I would like it to be a part of my future treatment plan when I need it. I would also like further drug support for all of us living with Her2+ MBC. We are the group currently dying from cancer. If this treatment can prolong my life, then I want it. I want to see my children grow and live the best life that I can. While I understand that everyone reacts to treatment differently, another chance to live with a good quality of life is important to me. I want to be given the chance to try Enhertu and hopefully live as long and as well as possible with my family and friends. I will continue to advocate for myself and others. People with Her2+ metastatic breast cancer deserve more. I can safely say that most Canadians, including myself, want to support those with cancer. As we learn how to treat cancer better, we also need to support that need for all Canadians. Safe and good treatments should be available to all who are eligible regardless of age, gender, race and socioeconomic status.

Rachel M (Written in 2020)

Rob and I travelled to Roswell Park 2 weeks ago to learn about it and I wrote about it in my blog and go fund me page. The drug is called Enhertu. The cost for me as a Canadian is \$26,000 per infusion with a minimum of 3 if not 6 infusions to gather any meaningful response results. I'm not sure if we will entertain the total of over \$300,000 (no way really my god, I could by a house), but maybe just 3 and see how that works. We are taking it day by day on that front with a great go fund me campaign and will cross the Buffalo bridge (literally) when it's right.

In the meantime, I am starting some radiation for some side effects I am finally starting to feel with my breathing, as the lungs are the pesky buggers (along with 11 spots in the brain that I just had Gamma Knife radiation on in October. They were almost undetectable so I'm hopeful there. It wiped the two I had in the brain last year so everyone feels this will be the same.

Tucatinib worked for about six months for me. Shrunk the lung tumours and bought more time. Then we switched when we saw resistance and I've been going down the lines ever since. One year ago exactly, Dr. B. gave me 3-6 months and I said well that's not going to happen and what other drugs are there? There were only 3 he suggested and had a 10% chance of working. I chose an old treatment of oral chemo call Cyclophosphamide and Methotrexate. That has worked until my last scans in late Aug where things showed some growth and some stability. We opted to stay on these meds while he told me about Enhertu and Roswell. So off on that mission, we went. The doctors there are supportive of my candidacy for the drug and were ready to start that day (of course when you're a golden egg of CDN cash).

Now I am doing some radiation on my spine thinking some small tumours are pressing on the nerves of the airway that's causing pressure and side effects in my chest and back. I've been asymptomatic for so long that this is all new for me. My breathing started getting tougher in May, hence starting the Dexamethasone and gaining 50 lbs.

I will also switch to a new chemo that is by infusion called Carboplatin that I have not had before. Combined with Herceptin again which I will be paying for although the wonderful insurance liaisons have been wonderful with finding compassionate programs or working through my insurance to help with the costs at the private clinic).

We are going to keep fundraising for Enhertu - it's going overwhelmingly well so far. I want to be the first person on the list the second Health Canada approves Enhertu and we can start the bridging program.

Tell me what I can do now or in the near future to stay as close to this as possible. I will do anything you suggest as will my family and network.