CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

trastuzumab deruxtecan (Enhertu)

(AstraZeneca Canada Inc.)

Indication: Enhertu as monotherapy for the treatment of adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior anti-HER2-based regimen.

September 27, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CADTH 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.

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Patient Input for CDA (formerly CADTH) CDR and pCODR Programs

Name of the Drug and Indication	Enhertu as monotherapy for the treatment of adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior anti-HER2-based regimen.
Name of the Patient Group	My Gut Feeling - Stomach Cancer Foundation of Canada
Author of the Submission	Ekaterina Kosyachkova and Teresa Tiano
Name of the Primary Contact for This Submission	Ekaterina Kosyachkova
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

My Gut Feeling – Stomach Cancer Foundation of Canada is the first non-profit organization in Canada, dedicated to providing support, awareness, education, information and advocacy to gastroesophageal cancer patients, survivors and caregivers. My Gut Feeling was founded by two stomach cancer survivors; although the organization was initially developed to help people affected by stomach cancer, people with gastroesophageal (GEJ) and esophageal cancer are included in our service programs and receive ongoing support. Our mission is to improve the quality of life for people affected by gastroesophageal cancers and to make systemic changes to reduce incidence and mortality of GEJ cancers. We strive to give a voice to patients and caregivers, and provide peer mentorship based on lived experience with cancer.

Website: https://mygutfeeling.ca

2. Information Gathering

In order to represent the patient and caregiver voice, My Gut Feeling - Stomach Cancer Foundation of Canada conducted an international online survey to understand the perspective of patients and caregivers affected by gastric, esophageal and/or gastroesophageal (GEJ) cancer including experiences with current treatment and the novel immunotherapy under review. My Gut Feeling launched this survey between September 9 to September 25, 2024. The survey link was posted on My Gut Feelings's social media platforms (including Facebook, Instagram and Twitter) as well as the email distribution list for all members.

In total, thirty people completed the survey, of those, 75% identified as a patient and 25% identified as a caregiver. Specifically, 60% identified as a patient who completed treatment and

15% as a patient in current treatment. The majority, 90% of respondents identified as female and 10% identified as male. Respondents were diagnosed across all ages ranging from 20 to 80 years old: 20-30 years (5%), 31-40 years (5%), 41-50 years (25%), 51 to 70 years (15%), 61 to 70 years (40%), and 71-80 years (10%). Data was gathered internationally with 95% of respondents residing in Canada, 5% in the United States. Of the Canadian respondents, 52.6% resided in Ontario, 15.8% in Alberta, 10.5% in British Columbia, 10.5% in Quebec, 5.3% in Manitoba and 5.3% in Nova Scotia. To ensure unbiased data collection, respondents were asked to refrain from using personal identifiers to preserve anonymity.

Respondents included in this survey had a diagnosis of gastric, esophageal and/or gastroesophageal (GEJ) cancer. The majority of respondents (90%) had gastric cancer and the remainder had GEJ cancer. 85% had adenocarcinoma and 15% were not aware of their cancer type. Of the respondents, 10% were diagnosed with stage one, 10% with stage two, 30% with stage three, 40% with stage four. 10% of patients did not know their cancer stage. When the cancer metastasized, in 20% it had spread to lymph nodes, 10% to peritoneum, 10% to liver and the remainder to other locations including the lungs, brain, bowel and pelvic structures. Most patients were HER-2 negative with only 10% of respondents having HER-2 positive disease. 10% of patients had MSI-high disease and 20% of patients identified that their CPS/PD-L1 score was above 5.

3. Disease Experience

Most respondents (95%), felt that the cancer diagnosis had a *significant* impact on their quality of life, whereas (5%) felt it had a *minimal* impact; nobody (0%) felt it had *no* impact on their quality of life. Areas affected by cancer and its treatment included physical health, mental health, ability to eat, work, finances, social life, identity, and personal image. We received an overwhelming number of direct quotes from patients and caregivers describing their disease experience; we attempted to select direct quotes that best exemplified these challenges. Respondents commented on the physical implications of cancer and its treatment. Symptoms of eating difficulties, poor appetite, reflux, weight loss, nausea, pain and fatigue were mentioned most by respondents. For example, one patient describes their experience: “[after a gastrectomy they experienced] exhaustion, changed relationship with food and eating, muscle aches and pains, muscle spasms, trouble sleeping, gagging, reflux that kept [them] up all night...“[Their] cancer came back after surgery and [they] went back onto chemotherapy. [They were] constantly throwing up and after 6 months, [they reported] no more energy left to fight”. One caregiver replied that “it was hard to watch [their wife] go through treatment. [The wife] lost so much weight and eventually needed total care. Seeing [the wife] suffer was the hardest thing [the caregiver] had to do.

Both patient and caregiver respondents and especially those with metastatic disease, reported a significant impact on their mental health due to the cancer diagnosis and its treatment. For example, one patient commented that “it is a huge adaptation to live with cancer, overwhelming and consuming all aspects of [their] life…Shortly after being told [they] had stage 4 [cancer], [they] were diagnosed with depression and anxiety…No amount of counseling or antidepressants can change the fact that [they] will die….Every day is just a reminder that [they] don’t have long [to live]” This patient questioned, “what’s the point [of living] like this.” Caregiver respondents echoed these feelings. For example, one caregiver described that watching their spouse going through treatment was “traumatic” and that they “still have

nightmares and talk to a therapist…It destroyed [their] life and [they] suffer from PTSD from caregiving". In addition to mental health implications, a cancer diagnosis can lead to changes in identity, relationships with others, social roles and responsibilities. One patient responded that their cancer diagnosis caused them to have to withdraw from relationships with others feeling that they "[didn't] want to go places people just stare because of all the weight loss. People ghost [them] and they don't talk to [them] because they don't know what to say or do"...This patient felt "like a burden to [their] family and [felt] isolated, losing friends, [their] job, now staying home all day, everyday". Another patient described her journey as a mother "[their] daily life is quite different now... [They] do much less because of fatigue and weakness, and struggle more with day to day tasks not only for [themselves] but for [their] kids. [They had to] give up a lot of what [they] used to be able to do and now feel like a bad mother and wife. Changes in identity and family dynamics further impacted psychosocial well-being and exacerbated any pre-existing mental health conditions such as depression and anxiety in both patients and caregivers.

Cancer and its treatments had financial implications on the patient and caregiver. Many respondents had concerns over finances due to inability to work due to the diagnosis and/or treatment for cancer. Many patients took sick leave or stopped working completely due to the physical and mental health side-effects of chemotherapy and/or surgery. Patients and caregivers commented on the time and money lost to attending cancer treatment appointments citing money spent on medications, driving and parking costs, costs of eating at the hospital as financial stressors. For example, one patient wrote that "[they] had to file for bankruptcy" because "[they] were already struggling financially as a single mother before cancer but leaving [their] job to go on disability was the breaking point financially". Other patients commented on the time-toxicity of cancer treatment. One patient states that "there is no time for life, [they] are either getting chemo or spending days feeling lousy after chemo… Weeks off chemo are filled with doctor appointments, blood work and travel to and from the hospital".

Objectively when asked to rank symptom burden, respondents commented that both the cancer itself and the treatments to control the cancer played a major impact on their daily living. Patients and caregivers were asked if any cancer symptoms were experienced *prior* to diagnosis. All (100%) of respondents had experienced at least one symptom *prior* to being diagnosed. Reflux (70%), pain (55%), weight loss (45%), changes in appetite (45%) nausea/vomiting (45%) and painful swallowing (35%) were the most reported symptoms. Other symptoms are outlined in the figure below.

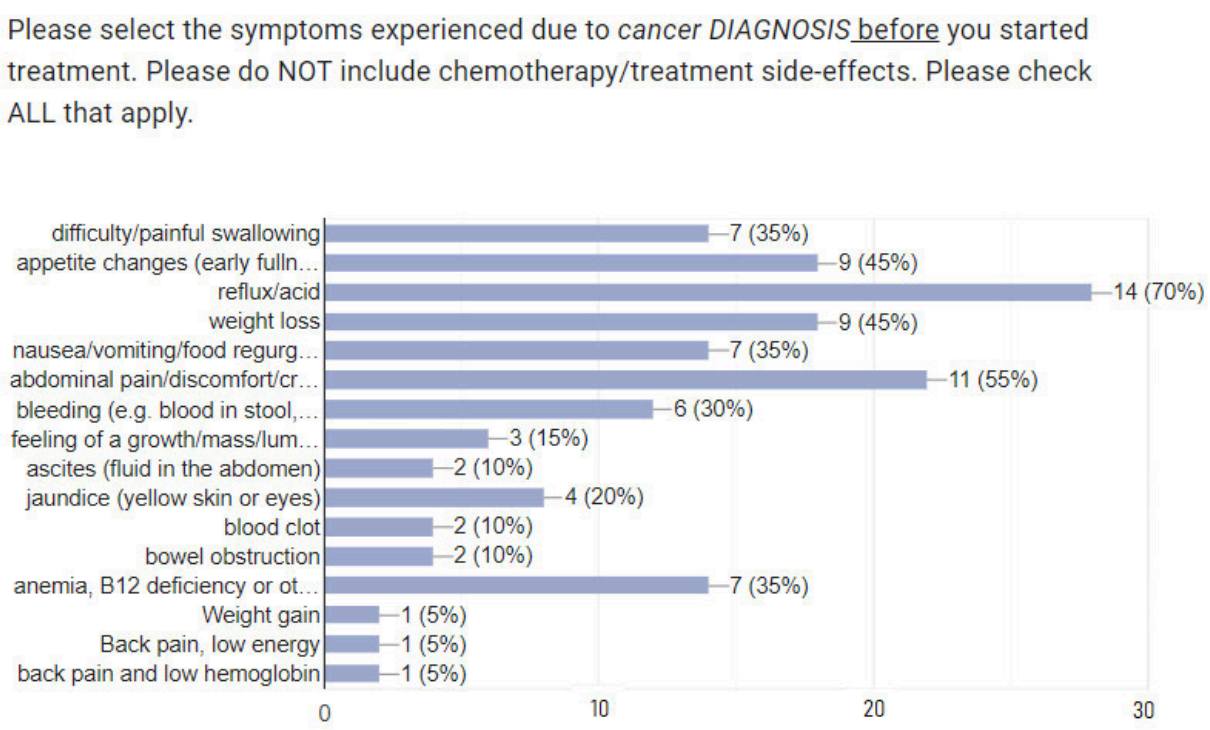

Figure 1. *Patient and caregiver reported symptoms **prior** to diagnosis with gastric, esophageal or gastroesophageal cancer.*

4. Experiences With Currently Available Treatments

Respondents reported that they had experience with a variety of treatment modalities including chemotherapy, immunotherapy, targeted therapy, surgery and radiation. Figure 2 shows the range of therapies that respondents received at the time of this survey.

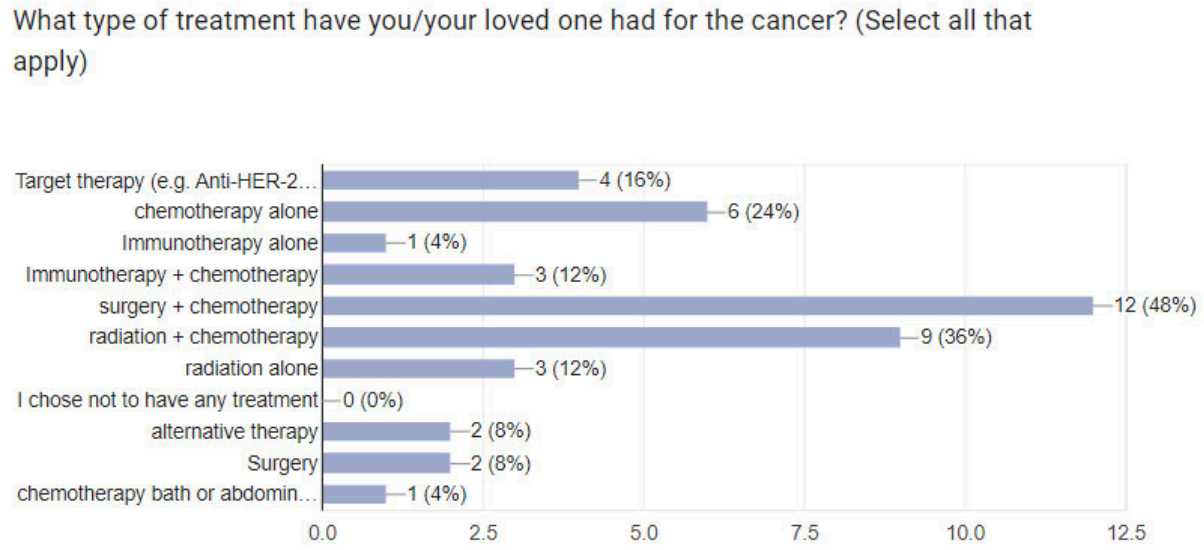

Figure 2. Respondents described the cancer treatment that they or their loved ones received

Participants were asked to evaluate their satisfaction with their current or past treatment on a scale of 1 to 10 (1 = “not satisfied”, 10 = “very satisfied”). The responses are shown in figure 3 below. When asked to expand on their satisfaction rating, participants who were satisfied and gave a score of 5 or above cited treatment response, remission, reduction of cancer associated symptoms (e.g. pain) and cancer control as the primary reasons for their satisfaction. Those that were less satisfied cited recurrence, lack of alternative treatment options, side effect burden or treatment not working as the primary reasons of dissatisfaction. For example, one caregiver gave a score of 0 and expanded on this score by stating “[her] husband died and chemotherapy did not prolong his life…We had no choice in treatment”. Another patient that gave a score of 6 wrote that “[they] developed hepatitis from nivolumbad [Nivolumab immunotherapy], however my body handled it very well and I have had 2 scans showing shrinkage [of their cancer]”.

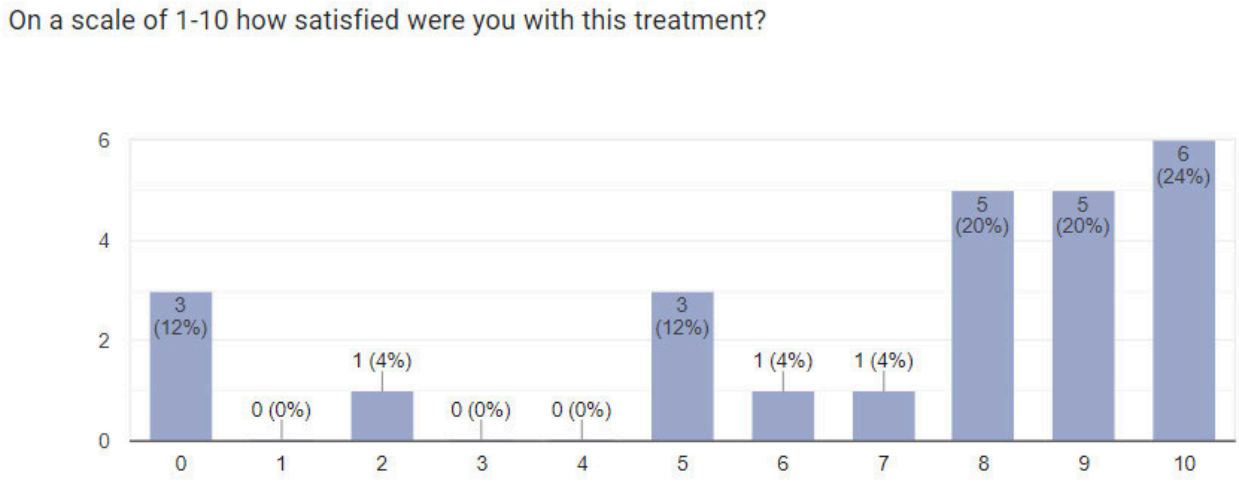

Figure 3. Respondents were asked to rate their degree of satisfaction with current or past treatments

While current therapies lead to mixed satisfaction from respondents in terms of perceived efficacy and cancer control, current treatments have a variety of side effects impacting quality of life. All respondents identified at least one treatment related side effect with 88% reporting fatigue. Other common symptoms included weight loss (80%), appetite changes (80%), nausea/vomiting (76%), chemo brain (64%), diarrhea (60%), taste changes (52%), neuropathy (52%), hair loss (48%), abdominal pain (44%) and insomnia (44%). Less commonly reported symptoms included reflux, constipation, anemia, blood clots, infection, body aches, skin rash, hand-foot syndrome, mucositis, dumping syndrome and blood-work abnormalities (figure 4). Respondents were able to leave additional comments regarding their treatment experiences. We asked respondents to identify the top 3 “worst” symptoms from treatment. Fatigue, appetite changes leading to weight loss and nausea and vomiting were the most commonly reported symptoms, there was no overall consensus regarding the functionally impairing side-effects of treatment.While most were able to tolerate treatment as prescribed (40%), 16% of respondents had their systemic therapy dose-reduced due to side effects, 16% had to delay/skip a cycle of their systemic therapy, 12% had to stop treatment due to side effects and 8% of respondents were hospitalized due to the severity of an adverse event. The analysis from this short survey

demonstrates that current systemic therapy to treat gastro-esophageal cancers has a significant impact on patient morbidity and quality of life.

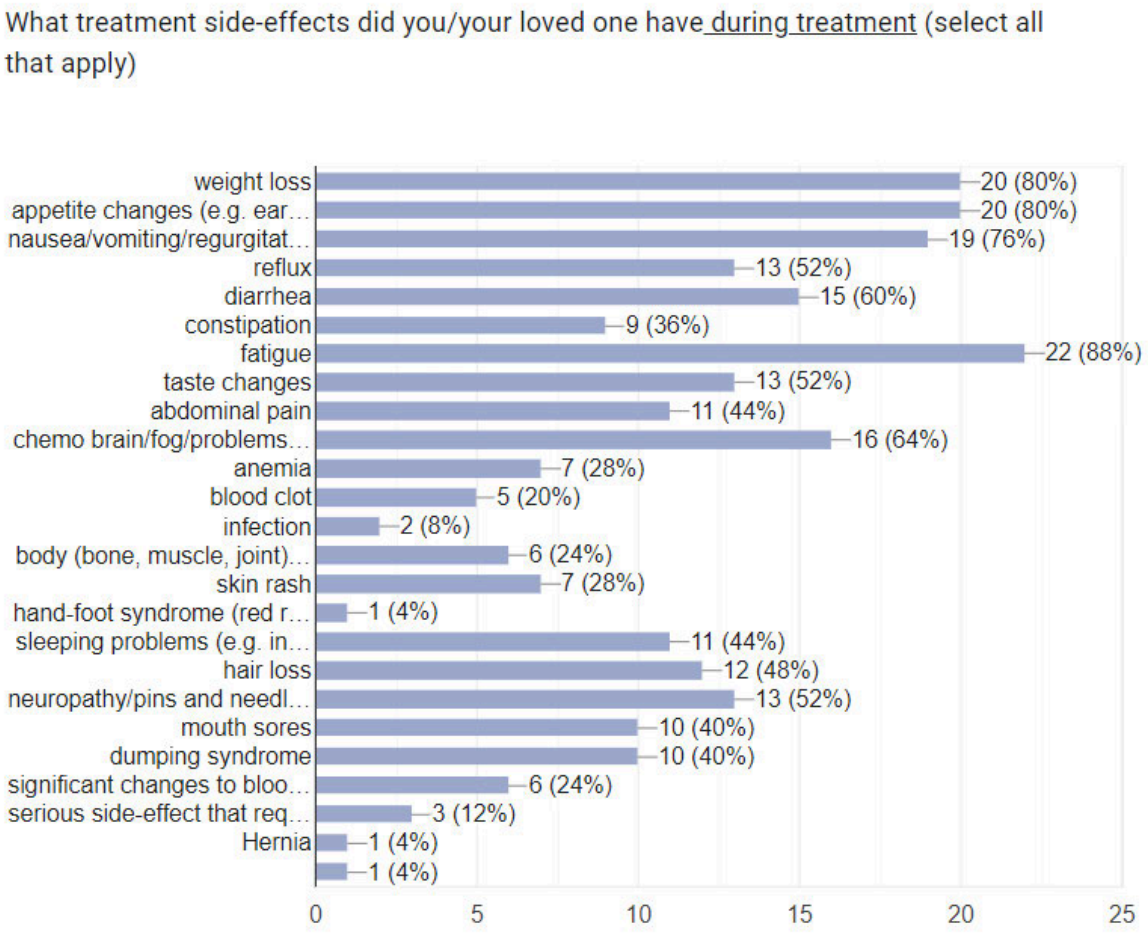

Figure 4. Patient and caregiver reported side effects while on treatment for gastric, esophageal or gastroesophageal cancer.

5. Improved Outcomes

When evaluating their treatment options, patients and caregivers identified multiple factors that are important to them such as quality of life, treatment side effects, cost of treatment, convenience of treatment, duration of treatment and the survival benefits. Respondents recognized that treatments had trade-offs and each respondent placed a different value on these considerations based on their preferences. For example, when asked *"how important is it for you that new therapies bring about improvement in quality of life"*. Almost all respondents (96%) replied with a 10 or "extremely important". When asked "how important is it to advocate for NEW treatment options for gastric, esophageal and gastroesophageal cancer", 96% of respondents replied with a 10 or "extremely important". While cancer control was an important consideration, treatment came at a cost to quality of life which may not be tolerable to all patients. For example, one patient wrote that their "oncologist kept pushing chemotherapy on

me every 2 weeks. It was always about getting to the next CT scan….[They] felt like a number and not a person…Chemo is not easy and it was so hard to push through…eventually it got too hard and [the patient] had to stop chemo to focus less on time being sick and more on time with [their] family". Convenience of treatment was another consideration for patients and caregivers, favouring less invasive systemic therapy, less frequent visits to the hospital and shorter time in the chemo chair. Convenience and the focus on quality of life in the palliative setting can be just as important as longevity when considering treatment options.

We asked respondents if they would pay out of pocket for additional therapies. The majority of respondents were interested in discussing treatment options even if they were not covered by their current healthcare plan or universal healthcare. 48% of respondents replied that they would pay for therapies out of pocket, 49% of patients responded they would "maybe" pay for these treatments if the treatment improved survival (16%), maybe - depending on cost (28%) and maybe - depending on impact on quality of life (5%). This once again demonstrates that while survival is important, respondents place different values on quality versus quantity of life. While our survey found that most people (85%) did not have to pay directly out of pocket for specific treatments, the remainder of respondents (25%) paid for either some targeted therapy or adjunct medications either through private pay or insurance. For example one patient had to pay for biomarker testing out of pocket when this was not covered by the universal healthcare system. Another patient estimated that they spent over $3000 on adjunct medications such as anti-emetics, iron infusions, blood thinner, etc. With the onset of biomarker testing in gastro-esophageal cancers, the universal healthcare system and private insurance lags behind, leaving Canadians with the bill for targeted therapies and adjective medications.

Our survey findings also showed that treatment access varied by geographic location. Clinical trials and novel therapies were more readily available in larger cancer centres that tend to be in Metropolitan areas. Respondents identified that access to first line therapies was "*extremely important"* to them. A patient wrote that for them "there were other possible treatments that [their] oncologist did not raise. [They] had to get second opinions outside the country, by the time [they] explored the options the cancer advanced to a step that it was no longer beneficial.". Barriers to access identified included institutional and health care system barriers, limited availability of treatment and how quickly treatment could be accessed. Respondents had many great suggestions in terms of how to better access treatment. For example, one patient wrote that they wished to have "all the options laid out at the start" to help inform decision making. While current treatments options may improve patient survival, there are clear limitations in available treatment options, access to new therapies and patient centred discussion regarding options. Patients and caregivers want more options from which to choose so that they can make informed decisions based on their values and preferences.

6. Experience With Drug Under Review

Based on our survey, four respondents had experience with Traztuzumab Deruxtecan (Enhertu), the drug under review. Three patients were part of a clinical trial and the fourth patient was not sure how they were able to access this drug. At the time of the survey, three patients were actively on this drug and had been on it for at least one month; the fourth patient discontinued

the drug after disease progression. Participants commented that they were satisfied with this drug primarily because it had fewer side-effects or slowed down their disease. Figure 5 shows the distribution of side-effects with fatigue as the most common response.

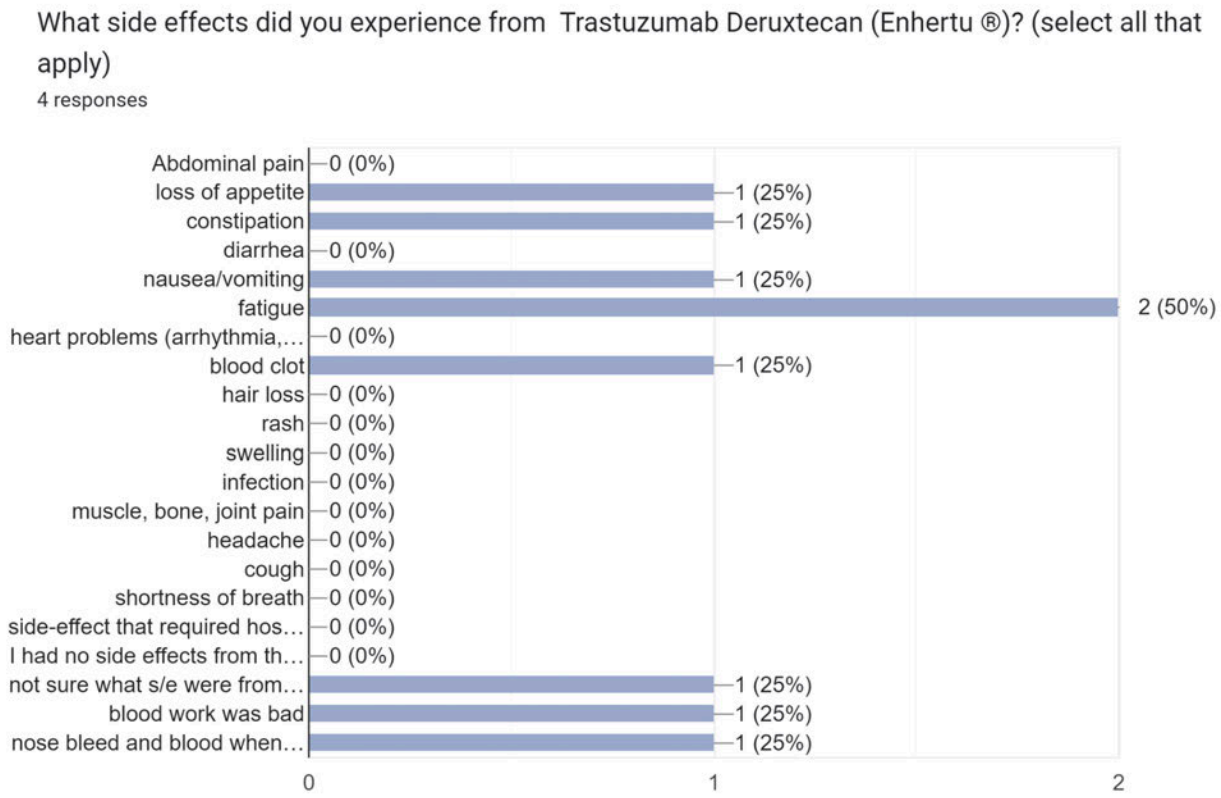

Figure 5. Respondents were asked to select the side-effects they experienced while on Trastuzumab Deruxtacan

When asked to rate the statement *"compared to other previous treatments Trastuzumab Deruxtecan (Enhurthu) was easier to tolerate overall"* (1= "strongly disagree", 10= "strongly agree"), 100% of respondents ranked it a five or above with 75% rating the question as a 10. When asked to rate the statement *"Trastuzumab Deruxtecan (Enhurthu) has improved my quality of life"* on a 1 to 10 scale (1= "strongly disagree", 10 = "strongly agree"), 75% responded with a 10 and 25% with an 8 rating. When asked to elaborate on these ratings, respondents who were satisfied with the drug mentioned disease control and quality of life factors. For example one patient stated "after only a few cycles of treatment, [their] cancer went into complete remission with no evidence of disease on CT scan, PET scan and diagnostic laparoscopy. [They] walked out of the palliative care unit with inability to swallow to then being able to eat and now complete response….[They are] waiting to hear if [they] can now have [curative] surgery." Another patient wrote that they "have been on this drug for over 2.5 years and [they are] still alive! At the start [they were] told to get [their] affairs in order. Chemo

was hard but now [they] are on [Enhurthu] alone and it has been easier to tolerate. [Their] last scan showed [they had] only 1 lymph node with cancer. [They] live [geographically] far so coming to the hospital every 3 weeks for a trial seemed crazy at first, but it worked…[They are] alive and continue to work and be with [their] kids…[They] hope one day the scan will tell me [they] are cured. While we do recognize that our survey has only four respondents on the drug under investigation, these anecdotes do demonstrate the need for patients and caregivers to have options and information on novel therapies that could improve the length and/or quality of life**.**

7. Companion Diagnostic Test

We did not ask questions related to companion diagnostic testing.

8. Anything Else?

Being diagnosed with any cancer is challenging. Gastric, esophageal and gastroesophageal cancers are rare in Canada with few treatment options. Biomarker testing is becoming routine in Canada. Novel biomarker targets are being tested rapidly in this cancer site. Personalized medicine based on biomarkers is on the rise. Drug combinations that attack multiple targets should be studied and the combinations that improve overall survival (OS) and progression free survival (PFS) should be rapidly expedited by CADTH as potential therapeutic options to fill the urgent and unmet need for gastro-esophageal cancers. For those patients and caregivers impacted by this diagnosis, having options brings about a sense of control and hope at a time when cancer strips the patient and family of their identity. This survey administered by My Gut Feeling shows that there is an unmet patient and caregiver need to receive equitable access to therapies that may prolong life, improve symptoms, reduce risk of recurrence and improve treatment tolerability. My Gut Feeling strongly supports the use of Trastuzumab Deruxtecan (Enhertu) as monotherapy for the treatment of adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior anti-HER2-based regimen.

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.

No, My Gut Feeling independently completed this submission

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, My Gut Feeling independently collected and analyzed data used for this submission

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**
Taiho Pharma Canada Inc.		x		
Bristol Myers Squibb			x	
Jazz Pharmaceuticals			x	
Amgen		x		
Astra Zeneca			x	
Astellas			x	
Merk			x	
Daiichi Sankyo			x	
BeiGene Pharma			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: Ekaterina Kosyachkova
Email: [redacted]
Position: Vice-Chair and Co-Founder
Patient Group: My Gut Feeling - Stomach Cancer Foundation of Canada
Date: Sept 27, 2024

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: **PC0367-000**
Generic Drug Name (Brand Name): trastuzumab deruxtecan (Enhertu)
Indication: for the treatment of adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior anti-HER2-based regimen.
Name of Clinician Group ad hoc group of adenocarcinoma-treating physicians & the Canadian Gastrointestinal Oncology Evidence Network (CGOEN)
Author of Submission: Dr. Christine Brezden-Masley, Medical Oncologist, Mount Sinai Hospital
with
Dr. Sharlene Gill, Medical Oncology, BC Cancer Agency
Dr. Eric Chen, Medical Oncologist, Princess Margaret Cancer Centre
Dr. Ravi Ramjeesingh, Medical Oncologist, Dalhousie University, Halifax
Dr. Vincent Tam, Medical Oncologist, Tom Baker Cancer Centre, Calgary
Dr. Rachel Goodwin, Medical Oncologist, The Ottawa Hospital Cancer Center, Ottawa
Dr. Howard Lim, Medical Oncologist, BC Cancer Agency, Vancouver
Dr. Ron Burkes, Medical Oncologist, Mount Sinai Hospital/Princess Margaret Cancer Centre/UHN
Dr. Jennifer Knox, Medical Oncologist, Princess Margaret Cancer Centre, Toronto
Dr. Raymond Jang, Medical Oncologist, University Health Network, Toronto
Dr. Haider Samawi, Medical Oncologist, Juravinski Cancer Center, Hamilton
Dr. Stephanie Snow, Medical Oncologist, QEII Health Sciences Centre, Halifax
Dr. Shaqil Kassam, Medical Oncologist, Southlake Regional Health Centre, Newmarket
Dr. Sukhbinder Dhesy-Thind, Medical Oncologist, Hamilton Health Sciences
Dr. Lucy Ma, Medical Oncologist, University Health Network, Toronto.

1. About Your Clinician Group

The Canadian GI Oncology Evidence Network (CGOEN) is a virtual and inclusive network of Canadian GI Oncology clinicians who contribute to the knowledge of GI cancer and its treatments, including participating in clinical trials, conducting observational research, and involvement in local/provincial and national clinical guideline development and health technology assessment.

2. Information Gathering

Information was gathered using published clinical trial data of DESTINY-Gastric01 (DG-01) and DESTINY-Gastric02 (DG-02) in this disease along with expert clinical experience and published NCCN and ESMO consensus guidelines in treatment of HER2+ metastatic GC/GEJC.

3. Current Treatments and Treatment Goals

Gastric cancer is considered a rare disease, with approximately 4000 cases diagnosed per year in Canada (estimated incidence in 2024) with a 50% associated fatality rate. Many of these diagnoses are in the advanced or metastatic setting. HER2 overexpressing gastric cancer occurs in around 15% of all gastric cancers, leading to only around 600 estimated cases per year in Canada. This is a rare disease.

For metastatic HER2+ GC/GEJC, the median overall survival (mOS) is around 14 months with anti-HER2 targeted therapy and chemotherapy (platinum and 5-FU based: e.g. mFOLFOX6) by the TOGA trial.

Treatment includes anti-HER2 targeted therapy of trastuzumab with standard chemotherapy (mFOLFOX6). Biomarker testing for HER2 is reflex tested on all GC and GEJC tumors, hence treating medical oncologists are aware of the HER2 biomarker and treat accordingly.

More recent clinical trial data in KEYNOTE-811 (KN-811) now has changed the first-line treatment of HER2+ mGC/GEJC disease by adding the anti-PD1 pembrolizumab to standard of care of trastuzumab and FOLFOX in tumors that also have evidence of PD-L1 expression with a combined positive score (CPS)$\geq$1. This CPS biomarker has also been made available on all GC/GEJC biopsies and was evident in 78% of patients in KN-811. Although pembrolizumab is available for many solid tumors, we are awaiting funding for this treatment combination. Currently, there is access to a patient support program through Merck Canada. Goals of treatment are to prolong survival (both OS and PFS) and to also decrease disease burden by improving overall response rate (ORR) as these patients can be very symptomatic with nausea, vomiting, weight loss, abdominal pain, early satiety due to gastric dysmotility, dysphagia and odynophagia. The KN-811 trial demonstrated significant improvements in ORR of 52% with pembrolizumab vs 42% in the control group, in addition to improvements in mPFS HR 0.70 and mOS 20.1 months vs 15.7 months in the control group. Quality of life indicators are important to be maintained with this treatment or improved. Both the TOGA and KN-811 studies have demonstrated no detriment to QoL. It is anticipated that around 15% of patients with HER2+ mGC/GEJC may not be candidates to be treated with pembrolizumab (e.g. CPS<1 or underlying autoimmune disease), thereby using the original TOGA protocol (without pembrolizumab). The KN-811protocol is now considered the new standard of care for HER2+ mGC/GEJC with CPS$\geq$1, as evidenced in NCCN and ESMO guidelines and the final overall survival was recently presented at the 2024 ESMO conference September 14, 2024 continuing to demonstrate survival benefit with the addition of pembrolizumab to trastuzumab + chemotherapy in tumors CPS$\geq$1.

Following disease progression after HER2-targeted therapy in first-line, there is no further targeted therapy available to HER2. Many studies using HER2 targeted therapies have not demonstrated improvements in ORR or OS, thereby leading to standard second-line and third-line systemic therapies. Most recently, the use of trastuzumab deruxtecan (T-DXd), a HER2-targeted antibody drug conjugate, has demonstrated significant clinical efficacy after first-line therapy of trastuzumab and chemotherapy. The randomized open-label Phase 2 clinical trials DESTINY-Gastric01 (DG-01) trial of metastatic HER2+ GC/GEJC following two or more lines of treatment that included the TOGA regimen, clearly showed impressive ORR (the primary endpoint of this study) with T-DXd of 42%, when compared to standard chemotherapy that only demonstrated ORR of 12%. Furthermore, there were 8% of patients in this study that demonstrated a complete response, indicated no evidence of disease! Furthermore, this study

also met its secondary endpoint of an improvement in median OS of 12.5 months compared to SOC chemotherapy of 8.9 months. There was also a doubling in mPFS with T-DXd (5.6 months) compared to 3.5 months with standard of care chemotherapy. This is very effective therapy. DG-02 was a confirmatory single arm study performed in Europe and the United States following disease progression on the TOGA protocol and similar efficacy endpoints were demonstrated, even though this trial was considered second-line. The primary endpoint was ORR by independent central review along with secondary endpoints of PFS and OS – all results very identical to DG-01. The ORR was noted as 42% with 5% achieving a complete radiologic response (that is no evidence of disease!); with a mOS of 12.1 months and a mPFS of 5.6 months. Similar toxicities were noted to DG-01. These two trials confirmed the superior treatment of T-DXd in second line or beyond in HER2+ mGC/GEJC tumors.

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.

T-DXd monotherapy is an extremely effective treatment for HER2+ mGC/GEJC cancer after disease progression following first-line therapy with trastuzumab and chemotherapy. This is a fatal disease that is also a rare disease. Only around 600 HER2+ GC/GEJC cancers are diagnosed per year in Canada with an estimated 400 being metastatic at diagnosis. Of these, it is estimated that only 40% will receive second line therapy following progression on first-line treatment. Therefore, this only estimates around 160 HER2+ mGC/GEJC patients per year in Canada that would be eligible for effective therapy of T-DXd! With the significant benefit of ORR, PFS and OS with T-DXd in the second line setting or beyond, T-DXd should be made available and accessible to our Canadian patients with HER2+ mGC/GEJC where their disease progress after first-line standard therapy (TOGA or KN-811). Furthermore, there may be an opportunity to cure 8% of these patients based on complete responses noted in around 5-8% of patients in both DG-01 and DG-02 clinical studies. There is no effective treatment regimen superior to T-DXd in this clinical setting.

T-DXd is already being used extensively in Canada for metastatic HER2+ and HER2-low breast cancer. There is clinical experience with this compound.

It is also worth noting that the most concerning adverse event is lung toxicity with pneumonitis of around 10-15%. Algorithms and frequent CT imaging has already been implemented with T-DXd in the Canadian oncology setting, specifically as it is used in the metastatic breast cancer setting. Treatment is given every 3 weeks intravenously, and with the use of effective anti-emetic drugs, nausea is effectively managed. Myelosuppression can be mitigated with the use of G-CSF support or by dose reduction. The starting dose is considered a bit higher (6.4 mg/kg) compared to breast cancer (5.4 mg/kg), therefore there is room for dose reductions.

5. Place in Therapy

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

T-DXd is the most effective treatment option for second line or beyond in HER2+ mGC/GEJC.T-DXd is a potent ADC that targets HER2 expressing gastric cancer cells, but also has an effective bystander mechanism where it also is cytotoxic to neighbouring HER2 low or HER2 non-expressing gastric cancer cells. Knowing that gastric cancer can be a heterogenous disease, this makes T-DXd a very potent effective ADC. Hence the efficacy noted with improved ORR including complete responses and an improved 40% survival benefit over standard

chemotherapy in 3rd line treatment or beyond (from the DG-01 clinical study). Furthermore, there continues to be an improved mOS to 12 months in second line (DG-02).

HER2+ mGC/mGEJC is a fatal disease, and T-DXd should be used earlier in second-line therapy for HER2+ mGC/GEJC disease, since these patients do not have effective treatment options, AND the attrition from first to second therapy is estimated at only 40%.Our standard of care currently is paclitaxel (+/- ramucirumab) which only provides an ORR of 16% (28% + ramucirumab) and a mOS of 9.6 months with the combination of paclitaxel + ramucirumab (HR 0.81) demonstrating only a 19% survival benefit to paclitaxel + ramucirumab (this is from the second-line RAINBOW study where HER2+ mGC/GEJC were also enrolled). Even fewer patients received third-line therapy for HER2+ mGC/GEJC, demonstrating the low attrition to third-line therapy and the high fatality rate of this cancer. Therefore, treating patients with effective T-DXd in the second line setting is most appropriate and should be considered the new standard of care based on improved survival, ORR, manageable toxicity and QoL.

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?

All patients with metastatic HER2+ GC/GEJC cancer should be considered for this treatment if their cancer has progressed after first-line trastuzumab (+pembrolizumab if CPS$\geq$1) and chemotherapy (FOLFOX). Patients who have had pneumonitis in the past may not be eligible for T-DXd given this was an exclusion criteria for the use of T-DXd. Furthermore, if the cardiac ejection fraction (EF) is lower than 50%, cardiology would need to be involved to ensure safe treatment of T-DXd given 3% cardiotoxicity rate with a significant drop in EF with T-DXd. Frequent monitoring with a CT scan every 9-12 weeks will assess both treatment response in addition to screening for pneumonitis, which may prematurely halt further treatment of T-DXd. Grade 1 pneumonitis noted on CT imaging requires a hold in treatment until radiologic findings return back to normal, while Grade 2 pneumonitis will permanently discontinue treatment with T-DXd.

With the effective response rate of around 40-50%, most patients will achieve a maximum response with 2 cycles of T-DXd, with treatment lasting up to 8 months (noted in DG-01 and DG-02). Since all GC/GEJC tumors are reflexively tested for HER2, no further testing is required after progression from first line HER2 targeted therapy.

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?

Patients are assessed every 3 weeks prior to treatment with T-DXd. The outcomes from DG-01 and DG-02 are the same clinical parameters used in clinical practice, including efficacy outcomes such as ORR, PFS and OS along with safety and toxicity. Clinically meaningful responses include improvement in symptoms which can correspond to improvements in ORR, tolerability of treatment, improvement in quality of life, duration of response and treatment, PFS and OS – all similar to the clinical trial parameters.

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

Factors to be considered to discontinue treatment would include disease progression, toxicities including severe myelosuppression, liver toxicity, cardiac toxicity (with a significant drop in

ejection fraction) and most notably Grade 2 or worse pneumonitis. Patient choice is also important.

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]?

Treatment with T-DXd should be performed in an outpatient cancer clinic with health care providers having experience in delivery of cytotoxic therapy, including pharmacy, oncology nurses and medical oncologists all who are aware of treatment and side effects (toxicities). Furthermore, access to imaging (CT scan), cardiac imaging (MUGA or echocardiogram) are also important for monitoring of both efficacy and toxicity.

6. Additional Information

Metastatic HER2+ GC/GEJC is a RARE disease – with only a few hundred cases per year. The most efficacious therapy should be considered for this patient population, as median overall survival is less than 2 years. T-DXd provides the opportunity to provide best treatment to this patient population, with improvements in ORR, mPFS and mOS with the chance of a complete response in 5-8% for these patients. It is a remarkable treatment that should be expedited and made available for these patients.

We also urge CDA to apply the recommendations framework that includes Considerations for Significant Unmet Need as described in the Procedures for CDA Reimbursement Reviews section 9.3.1. We also urge CDA to transparently report (in the draft recommendation) how the considerations for significant unmet need contributed to the draft recommendation.

Of importance, pERC should be aware that because T-DXd is so effective in targeting HER2, it has been granted pan-tumour approval by the FDA.

Also, a group of Canadian medical oncologists specializing in the treatment of gastrointestinal cancers (many who are participating in this submission) wrote to the Biotherapeutics and Quality Biologics and Genetic Therapies Directorate of Health Canada to support the NOC/c application of T-DXd for HER2+ GC/GEJC. One of these physicians participated in the clinical trial DESTINY-Gastric03 and had some experience in using T-DXd for HER2+ mGC/GEJC. One of his patients was able to be receive T-DXd as a result of the clinical trial. The patient was diagnosed with Stage IV GEJ adenocarcinoma in July 2021 with metastatic disease to liver. The patient was treated with trastuzumab, cisplatin, capecitabine and pembrolizumab from August 2021 to August 2022. Upon disease progression, the patient required multiple courses of blood transfusion and palliative radiation for tumor associated bleeding. The patient was treated with T-DXd and capecitabine. With this treatment, the patient's tumors disappeared and a complete response to treatment was achieved, and he also significantly improved clinically. As a matter of fact, the patient has returned to full time teaching as a university professor. This is the incredible tumor response that T-DXd is capable of achieving in metastatic HER2+ GC/GEJC disease!

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.

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 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 Dr. Christine Brezden-Masley
Name: Christine Brezden-Masley
Position: Medical Oncologist
Date: September 26, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1 (from last 5 years)

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Novartis				+ Independent Investigator Study "X"
Gilead Sciences				+ Independent Investigator Study "X"
Pfizer				+ Independent Investigator Study "X"
Amgen	x			
Roche	x			
Merck		x		
AstraZeneca				+Institutional Clinical research
Taiho	x			
Knight		x		
Daiichi-Sankyo	x			
Beigene	x			
Eisai	x			
BMS		x		
Astellas		x		
Sanofi	x			

Eli Lilly				+ Independent Investigator Study "X"

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

Declaration for Jennifer Knox

Clinician Information	
Name	*Jennifer Knox*
Position	*Medical Oncologist, Princess Margaret Cancer Centre*
Date	*September 24, 2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Roche (research support)	☐	☐	☐	☒
Ipsen (research support)	☐	☐	☐	☒
Merck (research support)	☐	☐	☐	☒
AZ (research support)	☐	☐	☐	☒
Roche (ad board/consulting)	☒	☐	☐	☐
Ipsen (ad board/consulting)	☒	☐	☐	☐
AZ (ad board/consulting)	☒	☐	☐	☐

Declaration for Vincent Tam

Name: Vincent Tam
Position: Medical Oncologist, Tom Baker Cancer Centre, University of Calgary
Date: 24-09-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca			X	
BMS	X			
Eisai		X		
Incyte	X			
Ipsen		X		
Merck	X			
Roche			X	

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

Declaration for Dr. Haider Samawi

Name: Haider Samawi
Position: Medical Oncologist, Juravinski Cancer Centre
Date: 24-09-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Astra Zeneca	x			
Gilead	x			

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

Declaration for Howard Lim

Name: Howard Lim
Position: Medical Oncologist
Date: September 24, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000

Roche	X			
Bayer	X			
Amgen	x			
Takeda	x			
AstraZeneca		x		
Astellas				
BMS		x		
Lilly	x			
Taiho	x			
Eisai		x		
Ipsen	x			
Incyte		x		

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

Declaration for Lucy Ma

Name: Lucy Ma
Position: Medical Oncologist, Princess Margaret Cancer Centre
Date: 24-09-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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**
Eisai	x			
Bristol Myers Squibb	x			

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

Declaration for Ravi Ramjeesingh

Name: <Ravi Ramjeesingh>
Position: <Medical Oncologist>
Date: September 24, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca		X		
Amgen	X			
Roche	X			
Incyte		X		
Eisai		X		
Ipsen	X			
Merck	X			
Jannsen	X			
Pfizer	X			
Novartis	X			
Knight	X			

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

Declaration for Sharlene Gill

Name: SHARLENE GILL
Position: Medical Oncologist, Professor of Medicine, BC
Date: 24-09-2024

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Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Takeda	X			
Taiho	X			

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

Declaration for Rachel Goodwin

Name: Rachel Goodwin
Position: Medical Oncologist
Date: September 24, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1 (from last 5 years)

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis	x			
Ipsen		x		+Independent Education Grant "X"
Pfizer		x		+Independent Education Grant "X"
Amgen		x		
Roche	x			
Merck	x			
AstraZeneca	x			
Taiho	x			
Apo	x			
Eisai	x			
BMS		x		
Astellas	x			

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

Declaration for Ronald Burkes

Name: Ronald Burkes
Position: Medical Oncologist Mount Sinai Hospital
Date: 23/09/2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Amgen	x			
Takeda	x			

Add or remove rows as required				

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

Declaration for Sukhbinder Dhesy-Thind

Name: Sukhbinder Dhesy-Thind
Position: Medical Oncologist, Juravinski Cancer Centre, Hamilton
Date: 23-09-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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**
Novartis Canada	X			
X				
Add or remove rows as required				

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

Declaration for Stephanie Snow

Name: Stephanie Snow
Position: Medical Oncologist
Date: September 26, 2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1 (from last 5 years)

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Pfizer		x		
Takeda	x			
Taiho	x			
GSK	x			

Roche	x			
J&J	x			
Knight	x			
Astellas	x			
Beigene	x			
Lily	x			
Sanofi	x			
EMD Serono	x			

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

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0367-000
Generic Drug Name (Brand Name): trastuzumab deruxtecan (Enhertu)
Indication: For the treatment of adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior anti-HER2-based regimen.
Name of Clinician Group: OH (CCO) Gastrointestinal Cancer Drug Advisory Committee
Author of Submission: Dr. Erin Kennedy, Dr. Suneil Khanna, Dr. Tim Asmis, Dr. Rachel Goodwin, Dr. Michael Raphael

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 in a videocall.

3. Current Treatments and Treatment Goals

Current treatments include clinical trials, chemotherapy (i.e. ramucirumab+ paclitaxel, FOLFIRI), and single agent irinotecan.

The goals include to improve symptoms, quality of life and overall survival.

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.

Very few patients respond to second line therapy. Currently, there are no HER2 specific agents available as second line therapy.

5. Place in Therapy

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

This treatment would be used in the second line setting.

Although rare, trastuzumab deruxtecan should also be available for use in esophageal cancer in the second line setting.

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 include those with HER2+ gastric/GEJ cancers.

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?

History, physical, labs, CT scans with response assessed every 2 to 3 months.

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

Disease progression, intolerance.

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]?

Outpatient setting under the care of a healthcare provider with training in oncology.

6. Additional Information

This drug should be approved in the interim until the results for the phase 3 trial is available.

7. Conflict of Interest Declarations

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

   OH (CCO) provided a secretariat function to the group.

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

   No.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Erin Kennedy
Position: Lead, OH (CCO) Gastrointestinal Cancer Drug Advisory Committee
Date: 06-09-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
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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. Suneil Khanna
Position: Member, OH (CCO) Gastrointestinal Cancer Drug Advisory Committee
Date: 06-09-2024

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Table 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
AstraZeneca	X			
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. Tim Asmis
Position: Member, OH (CCO) Gastrointestinal Cancer Drug Advisory Committee
Date: 06-09-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 3

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000

AstraZeneca		X		
Add company name				
Add or remove rows as required				

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

Declaration for Clinician 4

Name: Dr. Rachel Goodwin
Position: Member, OH (CCO) Gastrointestinal Cancer Drug Advisory Committee
Date: 06-09-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

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**
AstraZeneca	X			
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. Michael Raphael
Position: Member, OH (CCO) Gastrointestinal Cancer Drug Advisory Committee
Date: 06-09-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 5

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Add company name				
Add company name				
Add or remove rows as required				

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