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PAN-CANADIAN
ONCOLOGY DRUG REVIEW

**pan-Canadian Oncology Drug Review
Final Economic Guidance Report**

Trifluridine-Tipiracil (Lonsurf) for Gastric Cancer

March 24, 2020

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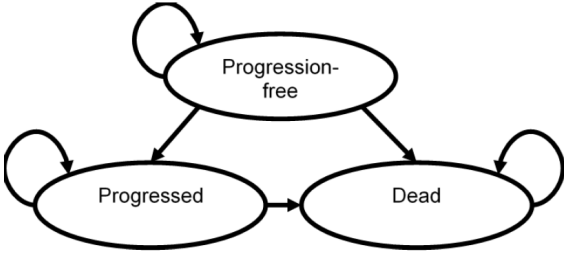
1 ECONOMIC GUIDANCE IN BRIEF

1.1 Submitted Economic Evaluation

The economic analysis submitted to pCODR by Taiho Pharma Canada Inc. compared trifluridine-tipiracil with best supportive care to placebo plus best supportive care as per the inclusion criteria of the pivotal study for third-line treatment of adult patients with metastatic gastric cancer who have been previously treated with at least two prior lines of chemotherapy including a fluoropyrimidine, a platinum, and either a taxane or irinotecan and if appropriate with HER2/neu-targeted therapy. The economic model is consistent with the funding request.

Table 1. Submitted Economic Model

Funding Request/Patient Population Modelled	Trifluridine-tipiracil versus best supportive care alone for the treatment of adult patients with metastatic gastric cancer or adenocarcinoma of the gastroesophageal junction, who have been previously treated with at least two prior lines of chemotherapy including a fluoropyrimidine, a platinum, and either a taxane or irinotecan and if appropriate with HER2/neu-targeted therapy. The economic model is consistent with the funding request.
Type of Analysis	Cost Effectiveness Analysis (\$/Life Years), Cost Utility Analysis (\$/QALYs)
Type of Model	Markov cohort, partitioned-survival
Comparator	Best supportive care
Year of costs	2019
Time Horizon	10 years
Perspective	Canadian public health care payer perspective
Cost of Trifluridine-tipiracil	Drug dosage for adults is 35 mg/m ² administered orally, twice daily, on Days 1 to 5 and Days 8 to 12 of each 28-day cycle (10 total days). Average patient BSA (TAGS trial): 1.749 m ² . Price per tablet (currently approved): 15mg tablet: \$76.25 20mg tablet: \$78.53 At 100% dose intensity, based on average BSA, average 28-day cycle cost is \$4,711.80; \$471.18 per treatment day; \$168.28 per day over 28 days. At dose intensity 89.6%, 28-day cost \$4,221.78.
Cost of best supportive care	Best supportive care considered to be placebo, with zero comparative cost.
Model Structure	Partitioned survival model (PSM) with escalating health states: Progression-free, Progressed, and Death.

	 <pre> graph TD PF([Progression-free]) --> PF PF --> P([Progressed]) PF --> D([Dead]) P --> P P --> D D --> D </pre>
Key Data Sources	<p>Data informing overall survival (OS), progression-free survival (PFS), and (Grade 3+) treatment-emergent adverse events were derived from the TAS-102 Gastric Study (TAGS) trial (Shitara 2018). Extrapolation of the OS and PFS long term survival was extrapolated from the TAGS trial, with progressed disease being the residual difference.</p> <p>Unit costs were from Ontario public plan sources. Utilities for health states were obtained from literature for second-line metastatic gastric cancer (UK HTA 378), utilities for adverse events were obtained from a literature review, and duration/rates of occurrence were obtained from the TAGS trial.</p>

1.2 Clinical Considerations

According to the pCODR Clinical Guidance Panel (CGP), the comparison of trifluridine-tipiracil to placebo is appropriate. The clinical guidance panel concluded there is a net overall clinical benefit to trifluridine-tipiracil in the treatment of advanced gastric adenocarcinoma after progression on 2 prior lines of therapy based on one high-quality randomized controlled trial that demonstrated a clinically and statistically significant benefit in overall survival for trifluridine-tipiracil compared with placebo. The adverse event profile for trifluridine-tipiracil was manageable and there was no difference in quality of life compared to placebo.

Burden of Illness and Need

After progression on first and second line systemic therapy, there is no standard third line treatment for gastric cancer. The prognosis in this setting is poor and median survival is just over 3 months with best supportive care. At the Royal Marsden, a quaternary referral centre in the United Kingdom, only 14% of gastroesophageal cancer patients received third line therapy. Thus, there is significant unmet need in this very small population of patients who are fit for third line therapy. The oral route of administration is preferred by patients and reduces resource utilization in cancer centres. It is also advantageous for patients who live outside major urban centres.

Effectiveness

The primary endpoint of OS was significantly improved with trifluridine-tipiracil compared to placebo (median OS 5.7 months vs 3.6 months, HR 0.69; 95% CI: 0.56, 0.86; p=0.0006). One-year OS was significantly improved from 21% in the trifluridine-tipiracil arm compared to 13% in the placebo arm. There were no pertinent imbalances in baseline factors or co-interventions that would have influenced overall survival. Survival is the most clinically relevant outcome for trials evaluating third line treatments

for metastatic gastric cancer. Input from patient groups emphasized the importance of survival and quality of life.

In terms of quality of life, no differences were observed between patients treated with trifluridine-tipiracil and placebo. The mean baseline GHS based on the EORTC QLQ-C30 was 58.4 for both treatment arms. There were no clinically relevant changes (≥ 10 points) in GHS from baseline to up to cycle 3 in each treatment arm. Additionally, there were no clinically relevant differences in the mean change in score from baseline for most of the functioning and symptom scales of the EORTC QLQ-C30, except for role functioning at cycle 3, where there was a difference of 10 points favouring placebo, and the pain scale at cycle 2, where there was a difference of 11.3 points favouring trifluridine-tipiracil. There were no clinically relevant changes in mean scores from baseline in the QLQ-STO22 scores.

The improvement in median PFS in the trifluridine-tipiracil arm was 2.0 months and in the placebo arm it was 1.8 months (HR: 0.57; 95% CI: 1.7, 1.9; $p < 0.0001$). The efficacy of trifluridine-tipiracil is largely driven by stable disease (ORR 4.5% with trifluridine-tipiracil vs 2.1% in the placebo; DCR 44.1% with trifluridine-tipiracil vs 14.5% with placebo). European patients would be expected to have similar outcomes to Canadian patients. Overall, the TAGS data should be generalizable to the Canadian population.

Safety

The most common \geq grade 3 treatment related AEs in the trifluridine-tipiracil arm were anemia ($n=63$; 18.8%) and neutropenia ($n=78$; 23.3%), which are common side effects that oncologists are very familiar with managing. These laboratory values are often asymptomatic, as reflected by neutral effect on quality of life for patients treated with trifluridine-tipiracil compared to placebo, and do not impact the patient's experience. The proportion of patients who discontinued treatment due to any AE was similar in the two arms (12.8% of patients treated with trifluridine-tipiracil arm vs 16.7% with placebo). SAEs occurred in a similar proportion between treatment arm, occurring in 42.7% of patients in the trifluridine-tipiracil arm and in 41.7% of patients in the placebo arm. Clinical experience in the real-world setting supports tolerability of trifluridine-tipiracil in heavily pre-treated patients.

Summary of registered clinician input relevant to the economic analysis:

Current Treatment for the Indication Under Review:

There is no standard third line treatment in this setting. Irinotecan based treatment can be considered if not received in earlier lines of therapy.

EGP comment: *The cost-effectiveness model was based on trifluridine-tipiracil versus no standard third line (i.e., best supportive care).*

Eligible Patient Population

The inclusion/exclusion criteria of the TAGS trial are realistic when applied in real life clinical practice.

In addition:

- Trifluridine-tipiracil is an option for patients who have contraindications to chemotherapy in earlier lines or for patients who want a low intensity treatment such as elderly patients.
- It is reasonable to extend the use of trifluridine-tipiracil to patients with ECOG Performance Status of 2, because of a predictable toxicity profile.
- There is no evidence to extend the use of trifluridine-tipiracil to patients with CNS metastases

- It is reasonable to extend the use of trifluridine-tipiracil to patients who have had prior immunotherapy.
EGP comment: *The cost-effectiveness model was based solely on the inclusion/exclusion criteria of the TAGS trial and does not provide evidence for indication creep or introduction to earlier lines of therapy.*

Relevance to Clinical Practice

Patients with metastatic gastric cancer have very limited treatment options available once their condition has become refractory to first line treatment, and no options if their condition has become refractory to second line treatment. The observed OS benefit of the trifluridine-tipiracil combination therapy in the TAGS trial is clinically meaningful, and the adverse events are preventable and manageable as out-patients.

EGP comment: *The cost-effectiveness model was based solely on the inclusion/exclusion criteria of the TAGS trial which provides evidenced for third-line therapy.*

Sequencing and Priority of Treatments

As per the TAGS study design, patients who previously received immunotherapy (anti-PD-1 or anti-PD-L1) as first or second line of treatment were included. MSI-high metastatic gastric or GEJ adenocarcinomas should receive immunotherapy in earlier systemic lines, if there are not contraindications, as previous evidence along with MMR confirmed a benefit in overall survival in this limited group of patients. However, outside of clinical trials, immunotherapy (pembrolizumab) is currently not available to most Canadian patients with gastric cancer.

Therefore, treatment sequencing should be reviewed case-by-case.

EGP comment: *The cost-effectiveness model does not investigate sequencing.*

Implementation Considerations:

As an oral medication, implementation of trifluridine-tipiracil into practice would mainly affect pharmacy resources. Trifluridine-tipiracil is well tolerated with limited toxicities but could possibly increase drug related visits either to clinic or the emergency department. It is anticipated that the implementation of trifluridine-tipiracil into clinical practice would be straight forward.

EGP comment: *The submitter's cost-effectiveness model does not include dispensing fees, but was included in EGP reanalysis. The cost of the most common adverse events was included in the cost-effectiveness model: neutropenia, anemia, neutrophil count decreased, decreased appetite, fatigue, leukopenia, general physical health deterioration, asthenia, abdominal pain, and ascites.*

Summary of patient input relevant to the economic analysis

Patients considered:

Disease Experience

Side effects of gastric cancer are many and include anemia, B12 deficiency, and dumping syndrome, and the most common are fatigue (85%), weight loss (77%), and loss of appetite (70%).

Quality of life was substantially impacted in 66% of patients, 40% of them are no longer able to work, and a quarter of them feel they can no longer fulfill family obligations. Psychologically, 96.5% of patients suffer from anxiety or depression, and 56% noted that fatigue makes it difficult for them to function at any kind of normal level.

EGP comment: *The cost effectiveness model included the impact on quality of life for 10 different adverse events, and the decrease in quality of life when changing from the progressive-free health state to the palliative progressed health state.*

Experiences with Currently Available Treatments

Current treatments are able to manage patient's gastric cancer symptoms for 73% of patients, meanwhile 28% did not have any drug therapy for their gastric cancer, all of whom were at very early stages. All patients who had drug treatments experienced side effects from these drugs, including diarrhea, nausea, hair loss, vomiting, loss of appetite, weight loss, mouth sores, anemia, low white blood cell count, fatigue, general body pain, skin rash, hand and foot syndrome, abdominal cramping. The three side effects that were the most difficult to manage were fatigue, nausea and weight loss.

EGP comment: *The cost effectiveness model included the impact on quality of life for 10 different adverse events, which included most of the survey patients reported side effects (anemia, low white blood cell count, fatigue, loss of appetite, weight loss) but were often reported differently in the trial (survey: general body pain, versus trial: ascites).*

Improved Outcomes

100% of patients think it is important that new therapies improve quality of life, such as a sense of wellness and relief from side effect. Meanwhile, 97% patients said that overall survival was important. 86% of patients responded they would take a drug that has been proven to provide better quality of life even if it did not extend overall survival. For patients the three most important side effects that they would expect a new drug to manage were nausea, fatigue and vomiting.

EGP comment: *The cost effectiveness model included the estimation of the benefit to overall survival and quality of life as the incremental cost per life year gained and the incremental cost per quality of life years gained, respectively.*

Experience with Drug Under Review

In the survey, 0 patients and 2 caregivers had experience with trifluridine-tipiracil, both for patients with trifluridine-tipiracil as a 4th line treatment. The caregiver-reported experience of the 2 patients was reported favourably: increased rest, recovery from weight loss, and increased energy.

Summary of Provincial Advisory Group (PAG) input relevant to the economic analysis

PAG considered the following factors (enablers or barriers) important to consider if implementing a funding recommendation for trifluridine-tipiracil which are relevant to the economic analysis:

Currently Funded Treatments

PAG noted that for patients with metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction, who have been previously treated with at least two prior systemic treatment regimens for advanced disease, there is no standard of care and patients may receive best supportive care (BSC).

EGP comment: *The cost-effectiveness model was consistent with lack of available therapies and compared trifluridine-tipiracil to best supportive care.*

Eligible Patient Population

PAG is seeking guidance on whether the following subgroups of patients would be eligible for trifluridine-tipiracil:

- ECOG PS of 2
- CNS metastases
- In earlier lines if patients have contraindication to chemotherapy
- Prior immunotherapy

There is a potential for indication creep to first- or second-line treatment or other GI cancers.

EGP comment: *The cost-effectiveness model was modelled based on the inclusion/exclusion criteria of the TAGS study, and does not address indication creep including to earlier lines of therapy.*

Implementation Factors

PAG had concerns with the demand for additional resources:

- Increased dispensing fees for complex dosing, although blister packaging of the tablets is an enabler,
- drug wastage can also occur if patients develop adverse events and need to discontinue treatment
- introducing two dispensing fees because trifluridine-tipiracil being available in two strengths
- to treat toxicity, monitor complete blood count, and for supportive therapy
- additional financial barriers, since oral medications are not funded in the same mechanism as intravenous cancer medications, and may require co-payments and deductibles.

EGP comment: *The cost-effectiveness model includes the cost of drug wastage, adverse events, and monitoring. The sponsor's model did not include the cost of dispensing but the dispensing fees were included in the EGP reanalysis. The personal expenditures for copayments and deductibles were not included consistent with CADTH guidelines which includes only government payer costs.*

Sequencing and Priority of Treatments

Trifluridine-tipiracil would be an additional line of therapy. PAG noted that trifluridine-tipiracil provides an option for patients who are fit enough to receive therapy and fills the treatment gap where BSC would be the alternate option.

PAG noted that for patients with MSI-high metastatic gastric or GEJ adenocarcinomas and with private drug insurance, pembrolizumab is an option. PAG is seeking guidance on sequencing pembrolizumab with trifluridine-tipiracil.

EGP comment: *The cost-effectiveness model does not address sequencing and includes average characteristics only.*

Companion Diagnostic Testing: None required.

1.3 Submitted and EGP Reanalysis Estimates

Of the total incremental 0.19 Life Years (or 2.3 months), 60% occur in PFS, and 40% occur in the progressed state. Of the total incremental cost of \$21,266, 90% of that costs were driven by the cost of the drug \$19,252. Adverse events generated a relatively small additional \$1,044 per patient, and an estimated zero difference in QALYs.

Compared to the submission, the EGP reanalysis increased the extra cost of trifluridine-tipiracil versus placebo by \$1,898 (from \$19,349 to \$12,247), which contributed to the increased ICER +\$23,936/QALY (from \$150,529 to \$174,465).

Table 2. Submitted and EGP Reanalysis Estimates (Probabilistic, 5,000 iterations)

	Submission			EGP Reanalysis			Change
	trifluridine/ tipiracil	BSC	Δ	trifluridine/ tipiracil	BSc	Δ	
QALYs	0.47	0.34	0.13	0.45	0.33	0.12	-0.01
PFS	0.21	0.13	0.08	0.21	0.13	0.08	0.00
progression	0.26	0.22	0.04	0.24	0.21	0.04	-0.01
Life Years*	0.73	0.54	0.19	0.70	0.52	0.18	-0.01
PFS	0.29	0.17	0.11	0.28	0.17	0.11	0.00
Progressed	0.44	0.37	0.08	0.42	0.35	0.07	-0.01
Costs	\$55,608	\$36,259	\$19,349	\$56,436	\$35,189	\$21,247	\$1,898
Drug	\$17,355	\$0	\$17,355	\$19,288	\$0	\$19,288	\$1,934
Medical	\$4,472	\$3,389	\$1,082	\$3,537	\$2,353	\$1,184	\$102
AE	\$1,238	\$198	\$1,041	\$1,355	\$350	\$1,005	-\$36
Palliative	\$32,543	\$32,672	-\$129	\$32,256	\$32,486	-\$230	-\$101
ICER (cost/QALYs)			\$150,529			\$174,465	\$23,936
ICER (cost/LYs)			\$101,403			\$118,374	\$16,971

*Deterministic value only available

The main assumptions and limitations with the submitted economic evaluation were:

The economic model was built upon the relevant comparative analysis of the TAGS trial (trifluridine-tipiracil versus placebo) (Shitara 2018). The economic model projected PFS and OS beyond the trial period for up to 10-years and relies little on extrapolation since a large majority of PFS and OS events occurred during the trial period with a median duration of follow-up for trifluridine-tipiracil of 10.5 months and 10.7 months for placebo. Resource utilization for each health state and for each adverse events was estimated based on a Canadian clinical survey, while unit costs were based on Ontario unit prices for physician services, laboratory testing and drug costs (OSB-PS 2019, ODB-Labs 2019, ODB 2019). Rates of adverse events were taken from the TAGS trial. Quality of life for adverse events and for health states (progressive-free, progressed) were taken from literature (pCODR Submission, Taiho Pharma Canada Inc 2019).

The TAGS trial was evaluated trifluridine-tipiracil plus best supportive versus best supportive care alone. Best supportive care was assumed to be similar between placebo and treatment groups, although this assumption would be hard to test because of the long varied list of concomitant medications, with an approximate average of 5 different ATC level IV drug (chemical/therapeutic/pharmacological subgroup) per person.

Incremental costs and ICER were most sensitive to planned dosage (based on BSA), dose intensity, and duration of therapy.

The benefit to quality of life is less certain. The lifetime quality of life benefit was driven mostly by extrapolated longer survival, while adverse events had little impact. Quality of life (such as EQ-5D) was not captured during the trial relying on literature values. In addition, utilities of health states were taken from patients with 2nd line gastric cancer, which may be different than the values for patients with 3rd line gastric cancer. UK weights for EQ-5D were

used instead of Canadian weights, whereas Canadian utilities are often non-statistically different from UK weights, but the direction varies by disease and AEs.

Detailed Highlights of the EGP Reanalysis

The most influential parameters are those that define the average BSA (and thus in turn the cost of treatment for the trifluridine-tipiracil arm), parameters around the cost of the progressed disease health state, and the choice of PFS survival curve.

EGP investigated different PFS and OS survival curve extrapolations, and the choice of PFS survival curve was the most consistent with the trial evidence, and the OS survival curve was the most conservative choice. No EGP reanalysis based on survival curves was required.

Other parameters were less influential: age of cohort, female (%), choice of OS survival curve, utility values of pre-progression and progressed health states, utility decrements for each adverse event, proportion of each adverse events, adverse event duration, and palliative cost.

The EGP made the following changes to the submitted economic model:

1. The dose intensity for trifluridine-tipiracil during the trial was 89.6% (i.e., the actual dose received versus the planned dose). In EGP reanalysis, the dose intensity was set to 100% to capture the full cost of the dosage.
2. In the sponsor's economic model, there was incomplete unit costs applied to resource utilization, where only physician billing fees were included. For diagnostic tests in Canada, the total cost includes physician billing fees and additionally includes institutional costs. The institutional costs for CT scans and ultrasounds were obtained from the Ontario Case Costing Initiative (OCCI) cost calculator (\$701 for CT scans abdomen and \$129 for abdominal ultrasounds in the ambulatory setting; CIHI intervention codes 30T20 and 30T30 for ICD-10-CA code C16) (OCCP 2017). In addition, in EGP reanalysis, the Ontario dispensing fee (\$8.83 was added) for each cycle of the oral medication.
3. The sponsor's economic model used a 10-year time horizon. Since the expected OS duration for 99% of the patients treated with trifluridine-tipiracil is 5-years, EGP reanalysis used a 5-time horizon, consistent with previous submissions for gastric cancer and noted as an appropriate approach by the CGP. In the EGP reanalysis final model, the 5-year overall survival rate for Trifluridine Tipiracil was approximately 1% for trifluridine tipiracil and for BSC was less than 1%.
4. In the sponsor's economic model, the patient's cancer is aggressively monitored until the progressed state (1 oncology visit per month, 1 CT scan every other month), and after the progressed state (2 oncology visits per month, 1 CT scan every other month). However, once the progressed state is reached and therapy is discontinued, the CGP suggested that the patient's health state is purely palliative with no subsequent therapies available. In EGP reanalysis, frequent oncology visits and CT scans were replaced by annual visits and diagnostic testing.

Table 3: Detailed Description of EGP Reanalysis (Probabilistic, 5000 iterations)

EGP reanalysis					
Description of Reanalysis	ΔC	ΔE QALYs	ΔE LYs	ICUR (/QALY)	Δ from baseline submitted ICER
Submitter's base case	\$19,349	0.13	0.19	\$150,529	
[1] Dose intensity 100%	\$21,336	0.13	0.18	\$166,268	\$15,739
[2] Missing costs	\$20,137	0.13	0.18	\$157,493	\$6,964
[3] 5 year time horizon	\$19,139	0.12	0.18	\$156,759	\$6,230
[4] Progressed state care	\$18,907	0.13	0.18	\$147,587	-\$2,942
Best case estimate of above [1,2,3,4] parameters					
EGP reanalysis best case	\$21,247	0.12	0.18	\$174,465	\$23,936

1.4 Evaluation of Submitted Budget Impact Analysis

The factors that most likely increase the budget impact include increased duration of therapy since treatment is to be given until disease progression, unacceptable toxicity occurs or patient withdrawal, increased BSA resulting in higher dosage, increased future market share, and increased prevalence of gastric cancer.

Key limitations of the BIA model include the unknown potential of indication creep moving into the larger first or second line therapy stages, and unknown market share because of the absence of a currently available active comparator. The market share, duration of therapy, and prevalence of cancer were explored in the sponsor's sensitivity analysis. The BIA only includes the cost of the drug and does not include costs for screening for and treatment of adverse events thus leading to an underestimated BIA.

1.5 Conclusions

The EGP's best estimate of ΔC and ΔE for trifluridine-tipiracil when compared to best supportive care is:

- \$174,465/QALY
- The ICER is higher for increased BSA.
- The extra cost of trifluridine-tipiracil is \$21,247. The extra cost is driven by drug costs (duration of therapy, dosage based on BSA, and dose intensity).
- The extra clinical effect of trifluridine-tipiracil is 0.12 QALYs (or equivalently 1.46 quality adjusted months). Improvements in quality of life is driven by increased overall survival (0.18 life years or equivalently 2.2 additional months).

Overall conclusions of the submitted model:

- The economic model was built upon the relevant comparative analysis of the TAGS trial. A projected lifetime model relies little on extrapolation since a large majority of PFS and OS events occurred during the trial period.
- Incremental costs and ICER were sensitive to planned dosage (based on BSA), dose intensity (discontinuation due to toxicity and adverse events), and duration of therapy.
- The benefit to quality of life is less certain. The lifetime quality of life benefit was driven mostly by extrapolated longer survival (which was a conservative estimate), while quality of life from adverse events had little impact. Quality of life was not captured during the trial relying on literature values.

2 DETAILED TECHNICAL REPORT

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in Section 1. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

3 ABOUT THIS DOCUMENT

This Economic Guidance Report was prepared by the pCODR Economic Guidance Panel and supported by the pCODR Gastrointestinal Clinical Guidance Panel and the pCODR Methods Team. This document is intended to advise the pCODR Expert Review Committee (pERC) regarding resource implications and the cost-effectiveness of trifluridine-tipiracil (Lonsurf) for gastric cancer. A full assessment of the clinical evidence of [drug name and indication] is beyond the scope of this report and is addressed by the relevant pCODR Clinical Guidance Report. Details of the pCODR review process can be found on the pCODR website (www.cadth.ca/pcodr).

pCODR considers it essential that pERC recommendations be based on information that can be publicly disclosed. Information included in the Economic Guidance Report was handled in accordance with the *pCODR Disclosure of Information Guidelines*. There was no non-disclosable information in the Economic Guidance Report provided to pERC for their deliberations.

This Final Economic Guidance Report is publicly posted at the same time that a pERC Final Recommendation is issued. The Final Economic Guidance Report supersedes the Initial Economic Guidance Report. Note that no revisions were made in between posting of the Initial and Final Guidance Reports.

The Economic Guidance Panel is comprised of economists selected from a pool of panel members established by the pCODR Secretariat. The panel members were selected by the pCODR secretariat, as outlined in the pCODR Nomination/Application Information Package and the Economic Guidance Panel Terms of Reference, which are available on the pCODR website (www.cadth.ca/pcodr). Final selection of the pool of Economic Guidance Panel members was made by the pERC Chair in consultation with the pCODR Executive Director. The Economic Guidance Panel is editorially independent of the provincial and territorial Ministries of Health and the provincial cancer agencies.

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