CADTH | pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review
Final Economic Guidance Report

Neratinib (Nerlynx) for Early Breast Cancer

December 5, 2019

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1 ECONOMIC GUIDANCE IN BRIEF

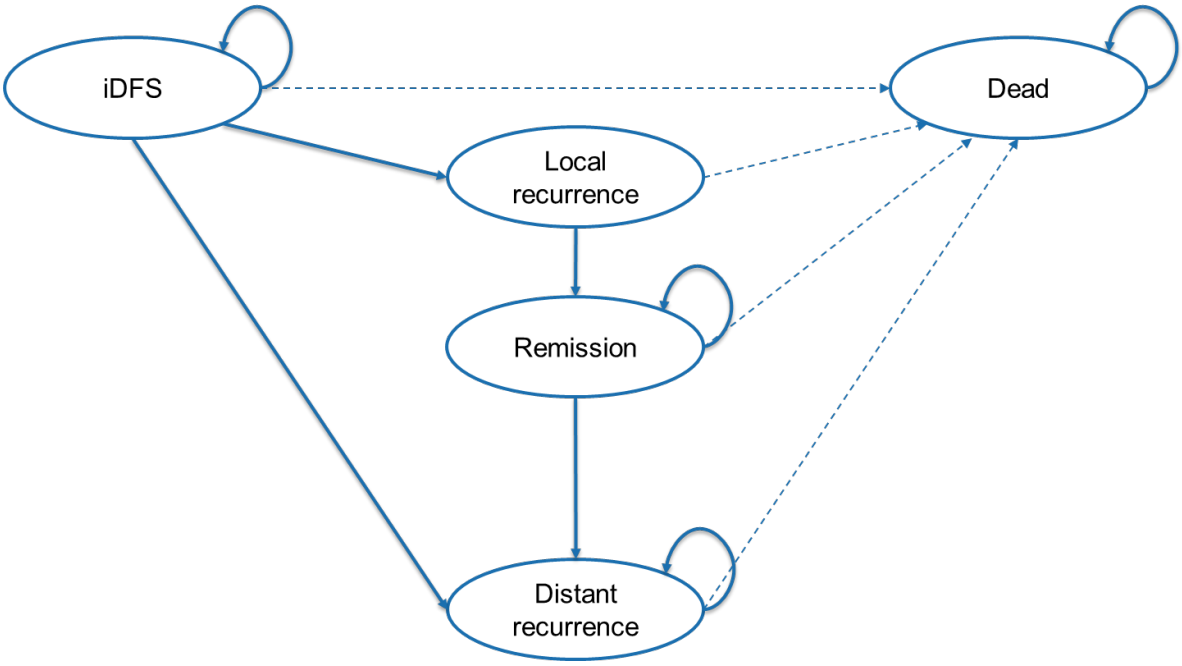
1.1 Submitted Economic Evaluation

The economic analysis submitted to pCODR by **Knight Therapeutics** compared neratinib to best supportive care (BSC) for patients with early-stage hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-overexpressed/amplified breast cancer. The sponsor's reimbursement request is in line with the Health Canada indication.

Table 1. Submitted Economic Model

Funding Request/Patient Population Modelled	Knight Therapeutics is requesting neratinib be reimbursed for the following indication: for the extended adjuvant treatment of adult patients with early-stage HER2-positive, HR-positive breast cancer who are less than 1 year from the completion of adjuvant trastuzumab-based therapy. The funding request aligns with the patient population that the economic model is built on.
Type of Analysis	CUA, CEA
Type of Model	Markov model
Comparator	BSC (defined as no active treatment)
Year of costs	2018
Time Horizon	Lifetime (55 years)
Perspective	Government/Third-party payer
Cost of neratinib	• $45 per 40 mg tablet • $270 per day • $7,560 per 28-day course • $98,550 over 1 year
Cost of BSC/ no treatment	• No active treatment costs (health state/disease recurrence costs)
Model Structure	Markov model comprised of five health states: invasive disease-free survival (iDFS), local recurrence, remission, distant recurrence, and death.
Key Data Sources	Clinical efficacy and adverse event (AE) data were sourced from a subgroup of patients from the ExteNET trial[1,2] to align with the funding request population. Data were based on the 5-year data cut (analyses using the 2-year data cut were also provided by the sponsor during the review). Utility values were sourced from the ExteNET trial and multiple international publications in healthy people (Lloyd et al.)[3] and breast cancer patients (Lidgren et al.).[4] Cost inputs were derived from the Ontario Schedule of Benefits, as well as the published literature[5-9] and other HTA reviews.[10]

Figure 1. Model Structure.



Source: Pharmacoeconomic submission[11]

1.2 Clinical Considerations

According to the pCODR Clinical Guidance Panel (CGP), there may be a small net clinically meaningful benefit with the addition of extended adjuvant neratinib following trastuzumab-based therapy for patients with early-stage, HER2-positive, HR-positive breast cancer.

- Relevant issues identified included:
    - The CGP noted that the patient population indicated in the reimbursement request is based on a post-hoc subgroup analysis of patients (as opposed to a subgroup pre-specified in the trial protocol/statistical analysis plan) from the ExteNET trial, which had numerous limitations (e.g. protocol amendments, losses to patient follow-up, etc.).
    - The CGP indicated the trial is limited by a short duration of follow-up and the lack of mature OS data; therefore, use of iDFS as a surrogate outcome for OS increases uncertainty.
    - The CGP questioned the external validity of the ExteNET trial given the evolving landscape for HER2-targeted treatment and recent results (likely practice changing) of the KATHERINE trial, which evaluated trastuzumab-emtansine (T-DM1) in the adjuvant setting.
    - The CGP noted caution is needed in extrapolating the ExteNET trial data to patients treated with adjuvant pertuzumab or T-DM1.

Summary of registered clinician input relevant to the economic analysis
Two registered clinician inputs were provided for the drug under review.

- Registered clinician input identified a lack of treatments available for patients with early breast cancer and highlighted a need to improve clinical outcomes for these patients. The responses also indicated that neratinib would not take the place of any current therapy; instead, neratinib would be an addition to the current treatment pathway for patients.
- Registered clinicians agreed that node negative patients would likely not be considered for neratinib.
- sponsorThere was disagreement between the two registered clinician inputs regarding generalizability of neratinib to other subgroup populations (i.e. stage I disease; completed trastuzumab within the last 2 years; treated with (neo)adjuvant pertuzumab plus trastuzumab).
- Registered clinician input noted that the drug under review was most likely to be used in patients with a higher risk of relapse, as the absolute benefit for the overall population is low. The same clinicians indicated there is preference to use T-DM1 following neoadjuvant treatment versus the drug under review.
    - Feedback from the CGP agreed with the registered clinical input, also noting that treatment of HER2-targeted breast cancer was an evolving landscape.
- Registered clinicians considered the toxicity profile and management of AEs for the drug under review to be similar to those for lapatinib, for which clinicians have extensive experience.
- Registered clinicians disagreed as to whether the drug under review should be used in patients who received pertuzumab plus trastuzumab in the neoadjuvant/adjuvant setting given the available data.

- Companion diagnostic testing would be required to identify HER2-positive patients, though this testing is already currently funded.
    - This was acknowledged in the sponsor's economic submission, and thus no costs or impacts were assumed with the introduction of neratinib.

Summary of patient input relevant to the economic analysis
Two patient groups provided feedback for the drug under review.

- Key concerns for patients with breast cancer are the risk of recurrence and death. Patients reported that current therapies (monotherapy or combination) were effective, manageable and/or tolerable. However, quality of life was found to have been impacted by current therapies; citing fatigue, inability to work, inconvenience of accessing treatment, and the financial burden of treatment.
    - Survival and recurrence were incorporated in the sponsor's model, as were quality of life measures (utility values). In line with CADTH economic evaluation guidelines,[12] the perspective was that of the public payer and not a societal perspective.
- Patients who had experience with neratinib reported experiencing side effects either immediately upon starting neratinib or up to two weeks after receiving the first dose. The most common side effect was diarrhea.
    - Diarrhea and other adverse events were considered in the sponsor's model, as was the cost of prophylaxis treatment for diarrhea.

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

PAG identified the following as factors that could impact the implementation of neratinib:

- Clinical factors: Clarity on eligible patient population, appropriate timeframe from completion of adjuvant trastuzumab-based therapy, and duration of therapy beyond 12 months.
    - The submitted economic evaluation did not consider the potential for extended use of neratinib. The CGP did not consider use beyond 12 months likely in Canadian clinical practice.
- Economic factors: Large pill burden of six tablets per day for a year, additional healthcare resources for monitoring and management of adverse events.
    - The submitted economic evaluation did not consider the impact of pill burden. Additional healthcare resources for monitoring and management of adverse events were incorporated in the model.

1.3 Submitted and EGP Reanalysis Estimates

The sponsor's probabilistic base case analysis reported that over the 55-year (lifetime) time horizon, neratinib was associated with an incremental cost of $55,779 and generated, on average, an additional 1.19 QALYs compared to BSC over the modeled time horizon, resulting in a sequential ICUR of $46,936 per QALY gained for neratinib compared to BSC (Table 2). The sponsor reported that neratinib had a 52% probability of being considered cost-effective at a willingness-to-pay threshold of $50,000 per QALY. The deterministic results were consistent with the probabilistic results.[11]

The main cost drivers were the cost and duration of treatment and the probability of recurrence.

The main drivers of benefit were the age at treatment initiation, the distribution used for iDFS, duration of benefit, and utility values.

The EGP noted that based on the sponsor's economic model, the majority (80%) of the neratinib costs were accrued within the first year of the model time horizon, while within the first year fewer QALYs were generated relative to the comparator. Based on the submitted analysis, less than 3% of the incremental benefits were accrued over the trial duration, while 146% of the incremental costs were accrued during that period of time.

Based on reanalysis of the sponsor's probabilistic base case, the EGP found that neratinib was associated with an incremental cost of $60,759 and generated, on average, an additional 0.72 QALYs compared to BSC over the 55-year (lifetime) time horizon, resulting in a sequential ICUR of $82,326 per QALY gained for neratinib compared to BSC (Table 3).

Table 2. Submitted and EGP Estimates (probabilistic analysis).

Estimates (range/point)	Submitted	EGP Reanalysis
ΔE (LY)[a]	1.34	0.97
ΔE (QALY)	1.19	0.74
ΔC ($)	55,779	60,759
ICUR estimate ($/QALY)	46,936	82,326

ΔC = incremental costs; ΔE = incremental effects; ICUR = incremental cost-utility ratio; LY = life-year; QALY = quality-adjusted life-year.
Source: Pharmacoeconomic submission[11]

Table 3. Submitted and EGP Estimates (deterministic analysis).

Estimates (range/point)	Submitted	EGP Reanalysis
ΔE (LY)[a]	1.32	0.99
iDFS	2.00	1.51
Local recurrence	-0.05	-0.03
Remission	-0.32	-0.26
Distant recurrence	-0.32	-0.22
ΔE (QALY)	1.19	0.77
iDFS	1.67	1.18
Local recurrence	-0.03	-0.02
Remission	-0.26	-0.20
Distant recurrence	-0.17	-0.15
Adverse events	-0.02	-0.03
ΔC ($)	55,857	60,569
ICUR estimate ($/QALY)	46,912	78,626

ΔC = incremental costs; ΔE = incremental effects; ICUR = incremental cost-utility ratio; iDFS = invasive disease-free survival; LY = life-year; QALY = quality-adjusted life-year.
[a] Not reported by sponsor, calculated by EGP
Note: breakdown reported for deterministic results as this was not reported by the sponsor for the probabilistic analysis.
Source: Pharmacoeconomic submission[11]

The EGP requested that the sponsor provide an analysis that presented data from the ExteNET trial using the 2-year data cut (primary efficacy analysis), based on feedback from the pCODR Methods Team and CGP highlighting limitations with the 5-year data cut (sensitivity analysis). The sponsor provided an abridged version of the model that incorporated this request; however, the results of this analysis were not flexible to allow testing of alternate assumptions and did not align with the results of the 5-year analysis, appearing to overestimate the long-term incremental

benefit of neratinib based on the extrapolation approach taken. As such, given the limitations highlighted, the EGP did not undertake any reanalyses based on the 2-year data cut.

The key limitations with the submitted economic evaluation were:

- **Duration of treatment effect was overestimated:** The sponsor assumed treatment effect would continue for up to 12 years for neratinib and 16 years for the comparator group (based on extrapolation of ExteNET data) until transitioning to general population mortality estimates. In a scenario analysis, the sponsor tested tapering the treatment effect over a period of 8.65 years after the end of the trial period (i.e. 13.9 years post-neratinib initiation), based on linear extrapolation of the hazard ratio in ExteNET for patients regardless of HR status (i.e. full ITT population). Feedback from the CGP suggested the duration of treatment benefit assumed in the sponsor's base case was overestimated, and tapering the treatment effect a shorter duration, in line with the duration of HERA trial, was more likely to be appropriate (~10 years post-neratinib initiation). Incorporating the duration of the ExteNET trial, the tapering period in the model was set to 5 years. Despite this reduction in the duration of the treatment effect, the CGP considered this may still overestimate the benefit of neratinib, given their reservations regarding the clinical findings from the trial as highlighted in section 1.2.
- **Model fit for iDFS appeared to overestimate the benefit of neratinib:** The sponsor claimed that the modelled distribution used was the most appropriate distribution based on the Akaike information criterion (AIC), Bayesian information criterion (BIC) and visual fit over the entire modelled period. The EGP disagrees with the sponsor's assertion. The flexible spline-based (1-knot) Weibull distribution chosen by the sponsor appeared to overestimate the incremental hazard ratio over time for neratinib compared to BSC. This overestimation of effect may be mitigated, in part, by the incorporation of a tapering of effect over time. However, the EGP identified the stratified generalised gamma distribution as an appropriate distribution that should have been given greater consideration, based on the AIC, BIC and visual fit. Feedback from the CGP considered either the spline-based Weibull or stratified generalised gamma distributions to be generally appropriate but suggested that the stratified generalised gamma distribution may provide a more appropriate fit compared to the flexible spline-based (1-knot) Weibull distribution, particularly in light of the CGP's reservations regarding the clinical findings, the lack of mature OS data for neratinib, and the trajectory of patients based on the 2-year and 5-year data analyses. As >95% of the incremental benefit occurs in the period after the 5-year trial duration, the extrapolation assumption is a key factor in assessing the cost-effectiveness of neratinib.
- **Several utility values informing the base case were highly uncertain:** Utility values were sourced from several different sources: iDFS values were sourced from the ExteNET trial,[11] remission was assumed equivalent to iDFS, local recurrence was sourced from Lidgren et al.[4], and distant recurrence was sourced from Lloyd et al.[3] The use of data from Lloyd et al.[3] to inform the base health states was not well justified given the availability and use of inputs for other health states from Lidgren et al.[4]; particularly as the values from Lloyd et al.[3] were generated from a vignette study of healthy patients, while data from Lidgren et al.[4] were based on EQ-5D derived values from Swedish breast cancer patients. The utility value derived from the ExteNET trial for iDFS was sourced from the EQ-5D-3L questionnaire administered at various time points during the 12-month treatment period and used a UK value set. This value was slightly higher than the utility value for healthy Canadians aged 50-59 (0.83),[13] which suggests the sponsor-derived value for iDFS likely overestimated the quality of life in that patient cohort in the Canadian context. Furthermore, limited information was provided by the sponsor[11] regarding the methodology used for the trial-

based utility analysis and information reported in the NICE economic evaluation of neratinib[14] identified concerns with the amount of missing data apparent in this analysis.

Other limitations that were identified with the submitted economic evaluation were:

- **Cost and resource use estimates may not reflect Canadian practice:** Feedback from the CGP suggested that fewer patients in Canadian practice receive second-line therapy post-recurrence (80%) than assumed by the sponsor (90%), and that the estimated usage of treatments incorporated for patients experiencing recurrence differed to what has been observed in Canadian practice (greater IV trastuzumab use in non-metastatic recurrence patients, greater pertuzumab plus trastuzumab use in first-line early metastatic breast cancer, and limited use of docetaxel alone).
- **Age at treatment initiation may be underestimated:** The mean age at treatment initiation in the model was 51 years. Feedback from the CGP suggested that in Canadian practice, patients on average are likely to be older (55 to 60 years of age).
- **Results of the ExteNET trial are associated with some uncertainty:** The population of interest was based on a post-hoc subgroup analysis of patients from the ExteNET trial. Further, the ExteNET trial had several protocol amendments which impacted the methodological rigour of the analyses undertaken. Limitations with the 5-year analysis (losses to patient follow-up) identified by the pCODR Methods Team and the CGP suggested the 2-year data analysis may be preferred. However, the analysis provided by the sponsor using data from the 2-year analysis lacked methodological rigour, was not flexible to test alternate assumptions, and appeared to overestimate the long-term incremental treatment effect of neratinib. Feedback from the CGP suggested the clinical benefit of neratinib was overestimated in the ExteNET trial, particularly for the subgroup of patients for whom the sponsor has requested reimbursement.

1.4 Detailed Highlights of the EGP Reanalysis

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

- Corrections were applied to address data input errors: The EGP revised the duration of impact of AEs based on identified differences between the submitted model and pharmacoeconomic (PE) report.
- Duration of effect was overestimated: The sponsor assumed that treatment effect was maintained after the trial period. The EGP applied a tapering of effect which assumed that after 10 years the hazard ratio was equal to 1 (as suggested by the CGP and similar to the follow-up period in the HERA trial).[15]
- Model fit for iDFS is uncertain and likely overestimates the benefit of neratinib: The sponsor used a flexible spline-based (1-knot) Weibull distribution. The EGP applied the use of the stratified general gamma distribution.
- Utility values are associated with limitations and likely overestimate the benefit of neratinib: The sponsor's utility value sources and values were associated with uncertainty. The EGP applied utility values in line with the sponsor's scenario analysis (using data from Lidgren et al. for all base health states).
- Proportion of patients receiving treatment in the second-line setting: The sponsor overestimated the proportion of patients who would receive second-line treatment, based on feedback from both the sponsor's clinical expert input[11] and the CGP for this review. The EGP conducted reanalyses based on the alternate values provided by the CGP that were considered more representative of Canadian clinical practice (80% of

patients would receive second-line treatment post-recurrence compared with sponsor's assumption of 90%).

- Resource use in the post-recurrence setting was considered to be different in Canadian practice: The sponsor's assumptions regarding the use of different treatments in the post-recurrence setting was seen as incorrect based on feedback from the CGP: IV trastuzumab was used for non-metastatic recurrence (100%, as opposed to a 50/50 split with subcutaneous trastuzumab), and the use of pertuzumab plus trastuzumab was increased (from 52% to 75%) with reduced docetaxel alone use (from 25% to 5%). The EGP conducted reanalyses based on the alternate values provided by the CGP.

These revisions comprised the EGP base case, as reported in Table 4.

Table 4. Detailed Description of EGP Reanalysis (probabilistic results).

Description of Reanalysis	ΔC	ΔE QALYs	ΔE LYs	ICUR (QALY)	Δ from submitted ICUR
Baseline (sponsor's best case)	55,779	1.19	1.34	46,936	--
#1. Correction of errors identified with submitted model	55,614	1.18	1.34	47,146	0.4%
#2. Treatment effect: hazard ratio = 1 at 10 years post initiation of neratinib treatment	61,465	0.92	1.04	66,764	42.2%
#3. Model fit: stratified generalised gamma distribution for iDFS	61,171	0.93	1.06	65,501	39.6%
#4. Utilities: All utilities based on Lidgren et al.	55,691	1.04	1.34	53,303	13.6%
#5. Resource use: Proportion receiving 2nd line treatment	56,635	1.19	1.33	47,716	1.7%
#6. Resource use: Revised treatment assumptions post-recurrence	51,765	1.19	1.34	43,440	-7.4%
EGP's Reanalysis for the Base Case					
Description of Reanalysis	**ΔC**	**ΔE QALYs**	**ΔE LYs**	**ICUR (QALY)**	**Δ from submitted ICUR**
#7. EGP Base Case (#1+#2+#3+#4+#5+#6)	60,759	0.74	0.97	82,326	75.4%

ΔC = incremental costs; ΔE = incremental effects; ICUR = incremental cost-utility ratio; iDFS = invasive disease-free survival; LY = life-year; QALY = quality-adjusted life-year.

The EGP's base case results were stable across multiple model runs and have reasonable congruence with the deterministic results. If a decision maker's willingness-to-pay threshold is $50,000 per QALY, neratinib has a 21% probability of being considered cost-effective based on the EGP base case. If a decision maker's willing ness to pay is $100,000 per QALY, neratinib has a 63% probability of being considered cost-effective based on the EGP base case.

The EGP also conducted the following scenario analyses on the EGP base case:

- Tapering of effect to a hazard ratio of 1 after 13.9 years.
- Use of the sponsor's flexible spline-based (1-knot) Weibull distribution.
- Dose intensity set to 100%

- Duration of treatment with neratinib set to 12 months
- Age at model entry/treatment initiation set to 55 years
- Time horizon set to 40 years
- iDFS utility value based on the sponsor's utility value

Table 5. EGP Scenario Analysis (probabilistic results).

Description of Reanalysis	ΔC	ΔE QALYs	ΔE LYs	ICUR (QALY)	Δ from EGP base case ICUR
Scenario analyses on the EGP Base Case					
#7a. Treatment effect: hazard ratio = 1 at 13.9 years post initiation of neratinib treatment	59,454	0.79	1.03	75,519	-8.3%
#7b. Model fit: spline-based (1-knot) Weibull distribution	54,447	0.80	1.05	73,806	-10.3%
#7c. Dose intensity: 100%	71,332	0.74	0.97	96,457	17.2%
#7d. Treatment duration: 12 months	69,883	0.72	0.95	97,548	18.5%
#7e. Age at model entry: 55 years	60,597	0.66	0.88	91,650	11.3%
#7f. Time horizon: 40 years	60,817	0.71	0.94	85,338	3.7%
#7g. Utility value for iDFS: 0.837	60,727	0.81	0.97	75,122	-8.8%

ΔC = incremental costs; ΔE = incremental effects; ICUR = incremental cost-utility ratio; iDFS = invasive disease-free survival; LY = life-year; QALY = quality-adjusted life-year.
Note: results are presented for the probabilistic analysis

Over the trial duration of 62 months, patients receiving neratinib accrued no additional QALYs, while 111% of the incremental costs were accrued over the same time period.

The EGP also undertook price reduction analyses based on both the sponsor's base case analysis and the EGP reanalysis base case (Table 6). Based on the EGP's base case, a price reduction of nearly 35% was required to achieve an ICUR of $50,000 per QALY for neratinib compared to BSC, while a price reduction of more than 5% was required to achieve an ICUR of $75,000 per QALY.

Table 6. EGP Price Reduction Scenario Analysis.

Incremental Cost ($) per QALY Gained for neratinib compared with BSC		
Price	**Sponsor's base-case analysis**	**Re-analysis by EGP**
Submitted	46,936	82,326
25% reduction	30,424	57,141
50% reduction	15,319	31,638

Note: results are presented for the probabilistic analysis

A key consideration that was not able to be assessed was that no evidence was provided (or identified) for the use of neratinib in patients who have used trastuzumab in combination with pertuzumab; only in patients who have used trastuzumab monotherapy. While trastuzumab in

combination with pertuzumab was not recommended by pERC for the treatment of HER+ EBC patients at high risk of recurrence, feedback from the CGP was that this treatment may still be used in Canada in some patients.

1.5 Evaluation of Submitted Budget Impact Analysis

The factors that most influence the budget impact analysis (BIA) include the drug acquisition cost of neratinib, the duration of treatment with neratinib and dose intensity, the size of the eligible patient population, and the market share. Increases in each of these assumptions from baseline increase the budget impact of neratinib.[16]

Key limitations of the BIA model include uncertainty in the derivation of the patient population. The EGP also noted the uncertainty surrounding the duration of treatment with neratinib and dose intensity. The EGP undertook exploratory analyses in addition to the scenario analyses undertaken by the sponsor to highlight the uncertainty associated with the budget impact of neratinib for Canadian public drug plans.

1.6 Conclusions

The EGP's best estimate of ΔC and ΔE for neratinib when compared to BSC is:

- $82,326/QALY gained
- The EGP undertook scenario analyses that indicated using alternate treatment effect and utility assumptions resulted in a lower ICUR, while applying conservative dosing assumptions and population assumptions that may be more generalizable to the Canadian setting resulted in a higher ICUR.
- The extra cost of neratinib is approximately $60,000 over the assumed lifetime time horizon. 110% of the incremental costs were observed over the trial duration (62 months); and fewer costs were accrued by neratinib patients beyond the trial period. The EGP noted that 75% of the total neratinib costs are accrued within the first year of treatment. The main cost drivers were the acquisition cost of neratinib and cost to treat recurrence.
- The extra clinical effect of neratinib is approximately 0.70 QALYs over the assumed time horizon (ΔE). Over the trial duration (62 months), patients derive less than 2% of the total incremental QALYs; 98% of the benefit is derived in the extrapolation period. Within the first year of treatment of the trial (the period in which patients receive neratinib), patients derived fewer QALYs than the comparator treatment. Key drivers of the incremental benefit were the duration and magnitude of the treatment effect.

Overall conclusions of the submitted model:

- There is substantial uncertainty surrounding the cost-effectiveness estimate presented by the EGP. A price reduction would improve the cost-effectiveness of neratinib.
- The cost-effectiveness of neratinib is driven by the extrapolated results beyond the 5-year trial period, while the majority of the incremental costs are accrued within the first year.
- Feedback from the CGP relayed concerns that the use of data from a post-hoc subgroup analysis of patients from the ExteNET trial (which had methodological limitations) may overestimate the benefit associated with neratinib, and therefore the ICUR presented by the EGP is likely to be underestimated.

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. Pursuant to the *pCODR Disclosure of Information Guidelines*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations.

3 ABOUT THIS DOCUMENT

This Economic Guidance Report was prepared by the pCODR Economic Guidance Panel and supported by the pCODR Breast 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 neratinib for early breast cancer. A full assessment of the clinical evidence of neratinib for early breast cancer 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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