Reimbursement Review

Provisional Funding Algorithm

Indication: Advanced or metastatic non–small cell lung cancer with activating epidermal growth factor receptor mutations

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Publication date: June 2023

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Background

Following a request from jurisdictions, CADTH may design or update an algorithm depicting the sequence of funded treatments for a particular tumour type. These algorithms are proposals for the jurisdictions to implement and adapt to the local context. As such, they are termed "provisional." Publishing of provisional algorithms is meant to improve transparency of the oncology drug funding process and promote consistency across jurisdictions.

Provisional funding algorithms are based on 3 principal sources of information:

- CADTH pCODR Expert Review Committee (pERC) reimbursement recommendations and/or implementation guidance regarding drug place in therapy and sequencing
- implementation advice from panels of clinicians convened by CADTH concerning sequencing of drugs in the therapeutic space of interest
- existing oncology drug reimbursement criteria and legacy funding algorithms adopted by jurisdictional drug plans and cancer agencies.

Note that provisional funding algorithms are not treatment algorithms; they are neither meant to detail the full clinical management of each patient nor the provision of each drug regimen. The diagrams may not contain a comprehensive list of all available treatments, and some drugs may not be funded in certain jurisdictions. All drugs are subject to explicit funding criteria, which may also vary between jurisdictions. Readers are invited to refer to the cited sources of information on the CADTH website for more details.

Provisional funding algorithms also delineate treatment sequences available to patients who were never treated for the condition of interest (i.e., incident population). Time-limited funding of new options for previously or currently treated patients (i.e., prevalent population) is not detailed in the algorithm.

Provisional funding algorithms may contain drugs that are under consideration for funding. Algorithms will not be dynamically updated by CADTH following changes to drug funding statuses. Revisions and updates will occur only upon request by jurisdictions.

Jurisdictional cancer drug programs requested a CADTH provisional funding algorithm on advanced or metastatic non–small cell lung cancer (NSCLC) with activating *EGFR* mutations. However, no outstanding implementation issues were identified, and no additional implementation advice is provided in this report. The algorithm depicted herein is meant to reflect the current and anticipated funding landscape based on the previously mentioned sources of information.

History and Development of the Provisional Funding Algorithm

This will be the first rapid provisional funding algorithm report for *EGFR*-positive NSCLC to incorporate CADTH recommendations for the following drugs: afatinib (Giotrif), amivantamab (Rybrevant), atezolizumab (Tecentriq), erlotinib (Tarceva), gefitinib (Iressa), nivolumab (Opdivo), osimertinib (Tagrisso), pembrolizumab (Keytruda), and pemetrexed (Alimta).

All of the previously listed drugs have received a positive reimbursement recommendation from CADTH, with the exception of gefitinib (Iressa), for which the Canadian Expert Drug Advisory Committee (CEDAC) issued a do not list recommendation in 2004; however, subsequent evidence became available following the publication of findings from the IPASS trial, which resulted in a few jurisdictions now funding gefitinib in the first-line setting.

Table 1: Relevant CADTH Recommendations

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
Amivantamab (Rybrevant)	March 20, 2023	pERC recommends that amivantamab be reimbursed for the treatment of adult patients with locally advanced or metastatic NSCLC with activating *EGFR* exon 20 insertion mutations whose disease has progressed on, or after platinum-based chemotherapy only if the following conditions are met: **Initiation:** 1. Treatment with amivantamab should be reimbursed when initiated in adult patients with *EGFR* exon 20 insertion–positive metastatic or unresectable NSCLC who progressed on or after prior platinum-based chemotherapy for metastatic disease. 2. Patient must have good performance status. 3. Patients must not have any of the following: a. untreated brain metastases b. been previously treated with a TKI with known activity against exon 20 insertion disease. **Discontinuation:** 4. Amivantamab should be discontinued for patients who do not exhibit a response to treatment as per physician discretion or for whom treatment is intolerable. 5. Patients should be assessed for treatment response every 9 to 12 weeks.

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		Prescribing: 6. Amivantamab should be prescribed by clinicians with expertise in the management of NSCLC. 7. Amivantamab should not be given or reimbursed in combination with other systemic anti-cancer drugs. **Pricing:** 8. A reduction in price. **Feasibility of adoption:** 9. Access to *EGFR* exon 20 insertion mutation testing. **Guidance on sequencing:** The clinical experts noted that patients with advanced lung cancer generally do not experience complete response to treatment. In the CHYRSALIS trial, 3 patients experienced a complete response, per BICR, with amivantamab. pERC agreed with the clinical experts that patients with confirmed complete response, for whom treatment is stopped, amivantamab can be restarted at the time of disease progression providing there are no contraindications. In the CHRYSALIS trial, patients with untreated brain metastases were excluded. In total, 23.5% of patients had treated brain metastases at baseline. pERC agreed with the clinical experts that patients with stable or treated metastases should be eligible for amivantamab. However, patients with new or unstable CNS metastases should not be eligible to receive therapy with amivantamab prior to receiving treatment for the CNS metastases. The clinical experts noted that assessment of disease every 6 weeks is a clinical trial-imposed period. pERC agreed with the clinical experts that in clinical practice, patients should be assessed for response every 9 to 12 weeks, depending on disease stability (for example, initial imaging may be at 6 to 9 weeks and responding patients may be assessed every 12 weeks as per the discretion of the treating clinician). pERC agreed with the clinical experts that patients who missed 2 consecutive doses due to toxicity should be eligible to continue treatment with amivantamab, provided that there is continued response, and toxicity experienced was not life-threatening and has resolved.

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		Clinical judgement should be used as to the appropriateness of continuing vs. discontinuing treatment in these circumstances. The clinical experts suggested that patients who have failed platinum-based chemotherapy and are being treated with other agents even if they have not experienced disease progression should be eligible to switch to amivantamab as the currently available treatments are generally less effective. pERC discussed and agreed that switching should only be allowed for toxicity reasons if the patient has not progressed on the previous treatment, or if the patient cannot tolerate an adequate dose of a regimen. Clinician judgement should be exercised. pERC agreed with the clinical experts that genetic testing for EGFR mutations is standard across Canada, most commonly through PCR or NGS. Patients with NSCLC should receive testing for genetic mutations at diagnosis using either PCR or NGS.
Osimertinib (Tagrisso)	January 10, 2022	pERC recommends that osimertinib should be reimbursed as adjuvant therapy after tumour resection in patients with stage IB-IIIA (American Joint Committee on Cancer [AJCC] 7th edition staging system) non–small cell lung cancer (NSCLC) whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations only if the following conditions are met: **Initiation:** 1. Adult patients (≥ 18 years) must have completely resected stage IB-IIIA (AJCC 7th edition) or stage IIA to IIIB (AJCC 8th edition) NSCLC with a confirmed sensitizing EGFR mutation (exon 19 deletion and/or exon 21 L858R substitution mutation), with or without post-operative adjuvant chemotherapy. 2. Patients should initiate treatment with osimertinib within 10 weeks of complete surgical resection if adjuvant chemotherapy was not administered, or within 26 weeks if adjuvant chemotherapy (platinum-based doublet chemotherapy, maximum of 4 cycles) was administered.

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		3. Patients should have a WHO performance status of 0 or 1 (equivalent to ECOG 0 or 1) and have no significant relevant comorbidities. **Renewal:** 4. Osimertinib should be reimbursed for a total duration of 3 years in patients who continue to receive clinical benefit from treatment and do not have intolerable toxicity. 5. Patients should be regularly monitored for toxicity and disease recurrence. **Discontinuation:** 6. Treatment with osimertinib should be discontinued upon disease recurrence or unacceptable toxicity. **Prescribing:** 7. Osimertinib should only be prescribed and monitored by clinicians trained in oncology and experienced in the treatment of NSCLC. **Pricing:** 8. Reduction in price. **Guidance on sequencing:** Osimertinib is indicated and reimbursed as first-line treatment for patients with locally advanced (unresectable) or metastatic NSCLC whose tumours harbour *EGFR* mutations (exon 19 deletions or exon 21 [L858R] substitutions). pERC agreed that in the absence of evidence, retreatment with osimertinib in the metastatic setting would be reasonable if patients experienced disease relapse off treatment after either discontinuing osimertinib due to toxicity or completing 3 years of adjuvant osimertinib. pERC also agreed with the clinical experts that rechallenge with osimertinib after a 6-month off-treatment interval is reasonable unless the patient experiences a recurrence. Retreatment with osimertinib in the metastatic setting would not be indicated in patients who progress while on osimertinib or within 6 months of their last dose of osimertinib in the adjuvant treatment setting.
Osimertinib (Tagrisso)	January 4, 2019	pERC recommends reimbursement of Osimertinib (Tagrisso) in the first-line treatment of patients with locally advanced (not amenable to curative intent therapy) or metastatic non-small cell lung cancer (NSCLC) whose tumours have epidermal growth factor

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		receptor (EGFR) mutations (exon 19 deletion [exon 19 del] or exon 21 [L858R]) only if both of the following conditions are met: • cost-effectiveness is improved to an acceptable level • feasibility of adoption (budget impact) is addressed. If the aforementioned conditions cannot be met, pERC does not recommend reimbursement of osimertinib. Eligible patients should be previously untreated in the locally advanced or metastatic setting and have a good performance status. Treatment should continue until clinically meaningful disease progression or unacceptable toxicity. pERC made this recommendation because the committee was confident of the net clinical benefit of osimertinib based on a considerable improvement in progression-free survival (PFS) that was statistically significant and clinically meaningful. Osimertinib also had a manageable toxicity profile and, based on the available data, treatment did not result in a decrement in patients' quality of life (QoL). Osimertinib aligned with the patient values of maintaining QoL, being an effective first-line treatment option, and potentially providing an improvement in PFS for patients with central nervous system (CNS) metastases. The committee concluded that, at the submitted price, osimertinib was not cost-effective compared with standard tyrosine kinase inhibitors (TKIs) and would require a substantial price reduction. pERC also highlighted that the potential budget impact of osimertinib was underestimated, and that the actual budget impact would be substantially greater given that the market share was underestimated and only the Ontario perspective was considered. pERC therefore had significant concerns about the capacity for jurisdictions to implement the therapy due to the high cost of Osimertinib. **Guidance on sequencing:** pERC noted that there is no clinical trial evidence to inform the optimal sequencing of osimertinib and other treatments now available for the treatment of patients with locally advanced or metastatic NSCLC whose tumours have epidermal growth factor receptor (EGFR) mutations (exon 19 del or L858R). However, pERC agreed that treatment with

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		osimertinib is likely to be followed by doublet chemotherapy as second-line treatment. Upon implementation of osimertinib reimbursement, pERC recognized that collaboration among provinces to develop a common approach for treatment sequencing would be of value.
Atezolizumab (Tecentriq)	June 20, 2018	pERC recommends reimbursement of atezolizumab (Tecentriq) for patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) and who have disease progression on or after cytotoxic chemotherapy only if the following conditions are met: • cost-effectiveness being improved to an acceptable level and • the drug plan cost of treatment with atezolizumab should not exceed the drug plan cost of treatment with the least costly alternative immunotherapy. Patients with genomic tumour driver aberrations (e.g. epidermal growth factor receptor [EGFR] or anaplastic lymphoma kinase [ALK]) should first be treated with targeted agents followed by cytotoxic chemotherapy prior to receiving atezolizumab. Treatment with atezolizumab should continue until confirmed disease progression or unacceptable toxicity. pERC made this recommendation because it was satisfied that there is a net overall clinical benefit with atezolizumab compared with docetaxel, based on statistically significant and clinically meaningful improvements in overall survival, a meaningful improvement in the toxicity profile, and no detriment in quality of life. The Committee was satisfied that atezolizumab aligned with patient values in that it improved survival, had manageable side effects, it reduced disease related symptoms and would also be an additional treatment option for patients. In the absence of a direct comparison, the committee considered evidence provided through an indirect treatment comparison with nivolumab and pembrolizumab, the most relevant comparators in this setting. pERC concluded that atezolizumab is likely similar in terms of efficacy and safety compared to these agents. pERC concluded that atezolizumab, compared with docetaxel, could not be considered cost-effective in

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		patients with metastatic NSCLC who have disease progression on or after cytotoxic chemotherapy. Given the likelihood of similarity in efficacy and safety among atezolizumab, pembrolizumab, and nivolumab, pERC concluded that the price of atezolizumab should not exceed the public drug plan cost of treatment with the least costly alternative immunotherapy. **Guidance on sequencing:** pERC concluded that the optimal sequencing of atezolizumab and other treatments now available for the treatment of advanced or metastatic NSCLC is currently unknown. pERC was, therefore, unable to make an evidence-informed recommendation on sequencing following treatment with atezolizumab. pERC also noted that there is no direct evidence to inform the comparative efficacy of atezolizumab with other PD-1 inhibitors (nivolumab and pembrolizumab). Thus, with their overlapping indications, there is no evidence to inform the choice of atezolizumab over the other available agents, or vice versa. There is also no evidence to support using PD-L1/PD-1 inhibitors in sequence (e.g., atezolizumab then nivolumab or pembrolizumab, or vice versa).
Osimertinib (Tagrisso)	May 4, 2017	pERC recommends reimbursement of Osimertinib (Tagrisso) in patients with locally advanced or metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC) who have progressed on EGFR tyrosine kinase inhibitor (TKI) therapy conditional on the cost-effectiveness being improved to an acceptable level. pERC made this recommendation because the Committee was confident of the net clinical benefit of osimertinib based on a substantial improvement in progression-free survival (PFS) that was statistically significant and clinically meaningful. Osimertinib also had a manageable toxicity profile and, based on the available data, treatment did not result in a decrement or an improvement in patients' quality of life. Osimertinib also aligned with patient values. The Committee concluded that, at the submitted price, osimertinib was not cost-effective compared with chemotherapy and would require a substantial price reduction.

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		Guidance on sequencing: pERC noted that there is no clinical trial evidence to inform the optimal sequencing of osimertinib and other treatments now available for the treatment of patients with locally advanced or metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive NSCLC. However, pERC agreed that treatment with osimertinib is likely to be followed by doublet chemotherapy as third-line treatment (second line in patients with *de novo* T790M mutation) and subsequently with immune checkpoint inhibitors. Upon implementation of osimertinib reimbursement, pERC recognized that collaboration among provinces to develop a common approach for treatment sequencing would be of value.
Pembrolizumab (Keytruda)	November 3, 2016	pERC recommends reimbursement of pembrolizumab (Keytruda) conditional on the cost-effectiveness being improved to an acceptable level. Funding should be for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumour express PD-L1 (as determined by a validated test) and who have disease progression on or after cytotoxic chemotherapy. Patients with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumour aberrations should have disease progression on authorized therapy for these aberrations and cytotoxic chemotherapy prior to receiving pembrolizumab. Patients could receive up to 12 months of pembrolizumab if they experienced an investigator-determined confirmed radiographic disease progression, according to immune-related response criteria after stopping their initial treatment with pembrolizumab due to achievement of a confirmed complete response or having experienced 35 administrations of pembrolizumab. Funding should be for patients with a Tumour Proportion Score (TPS) of PD-L1 ≥ 1% and who have good performance status. Treatment should continue until confirmed disease progression or unacceptable toxicity, or to a maximum of two years, whichever comes first. pERC made this recommendation because it was satisfied that there is a net overall clinical benefit with pembrolizumab compared with docetaxel, based on the statistically significant and clinically meaningful improvements in overall survival, durable response, a

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		meaningful improvement in the toxicity profile, and no detriment in quality of life. The Committee was satisfied that pembrolizumab aligned with patient values. pERC concluded that pembrolizumab, compared with docetaxel, could not be considered cost-effective in patients with metastatic NSCLC whose tumour express PD-L1 (as determined by a validated test) and who have disease progression on or after cytotoxic chemotherapy. **Guidance on sequencing:** pERC concluded that the optimal sequencing of pembrolizumab and other treatments now available for the treatment of advanced or metastatic NSCLC is currently unknown. pERC was, therefore, unable to make an evidence-informed recommendation on sequencing following pembrolizumab. pERC also noted that there is no direct evidence to inform the comparative efficacy of pembrolizumab with other PD-1 inhibitors. Thus, with their overlapping indications, there is no evidence to inform the choice of pembrolizumab over nivolumab, or vice versa. There is also no evidence to support using PD-1 inhibitors in sequence (e.g., pembrolizumab then nivolumab, or vice versa). However, pERC recognized that provinces will need to address this issue upon implementation of reimbursement of pembrolizumab and noted that collaboration among provinces to develop a common approach would be of value, as would the development and implementation of an evidence-based clinical practice guideline.
Nivolumab (Opdivo)	June 3, 2016	pERC recommends funding nivolumab (Opdivo) conditional on the cost-effectiveness being improved to an acceptable level. Funding should be for the treatment of adult patients with advanced or metastatic non-small cell lung cancer (NSCLC) with disease progression on or after cytotoxic chemotherapy for advanced disease and have a good performance status. Treatment should continue until confirmed disease progression or unacceptable toxicity. pERC made this recommendation because it was satisfied that there is a net overall clinical benefit with nivolumab, based on the statistically significant and clinically meaningful improvements in overall survival and objective response rate, a meaningful improvement in the toxicity profile, and at least stable quality of life

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		compared with docetaxel. The Committee was satisfied that nivolumab also aligned with patient values. pERC concluded that nivolumab compared with docetaxel could not be considered cost-effective in patients with advanced or metastatic NSCLC with disease progression on or after cytotoxic chemotherapy. **Guidance on sequencing:** pERC concluded that the optimal sequencing of nivolumab and other treatments now available for the treatment of advanced or metastatic NSCLC is currently unknown. pERC was, therefore, unable to make an evidence-informed recommendation on sequencing. However, pERC recognized that provinces will need to address this issue upon implementation of nivolumab funding and noted that collaboration among provinces to develop a common approach would be of value, as would the development and implementation of an evidence-based clinical practice guideline.
Afatinib (Giotrif)	May 2, 2014	The pCODR Expert Review Committee (pERC) recommends funding afatinib (Giotrif) if cisplatin-pemetrexed is currently the main treatment option. pERC also recommends funding afatinib as an alternative treatment option to gefitinib, conditional on the cost-effectiveness of afatinib being improved to an acceptable level. Funding should be in the first-line setting for patients with EGFR mutation positive advanced or metastatic adenocarcinoma of the lung and with an ECOG performance status 0 or 1. pERC made this recommendation because it was satisfied that there is a net clinical benefit of afatinib compared with cisplatin-pemetrexed. In addition, although there were substantive deliberations and various opinions expressed, the majority of pERC members considered that there could be similar clinical benefit of afatinib and gefitinib, despite the lack of evidence from head-to-head randomized controlled trials. In addition, providing access to afatinib aligns with patient values of having access to more treatment options. Also, at the submitted price, afatinib is cost-effective compared with cisplatin-pemetrexed but may not be considered cost-effective compared with gefitinib. **Guidance on sequencing:** pERC noted that there is variability across provinces in the availability and

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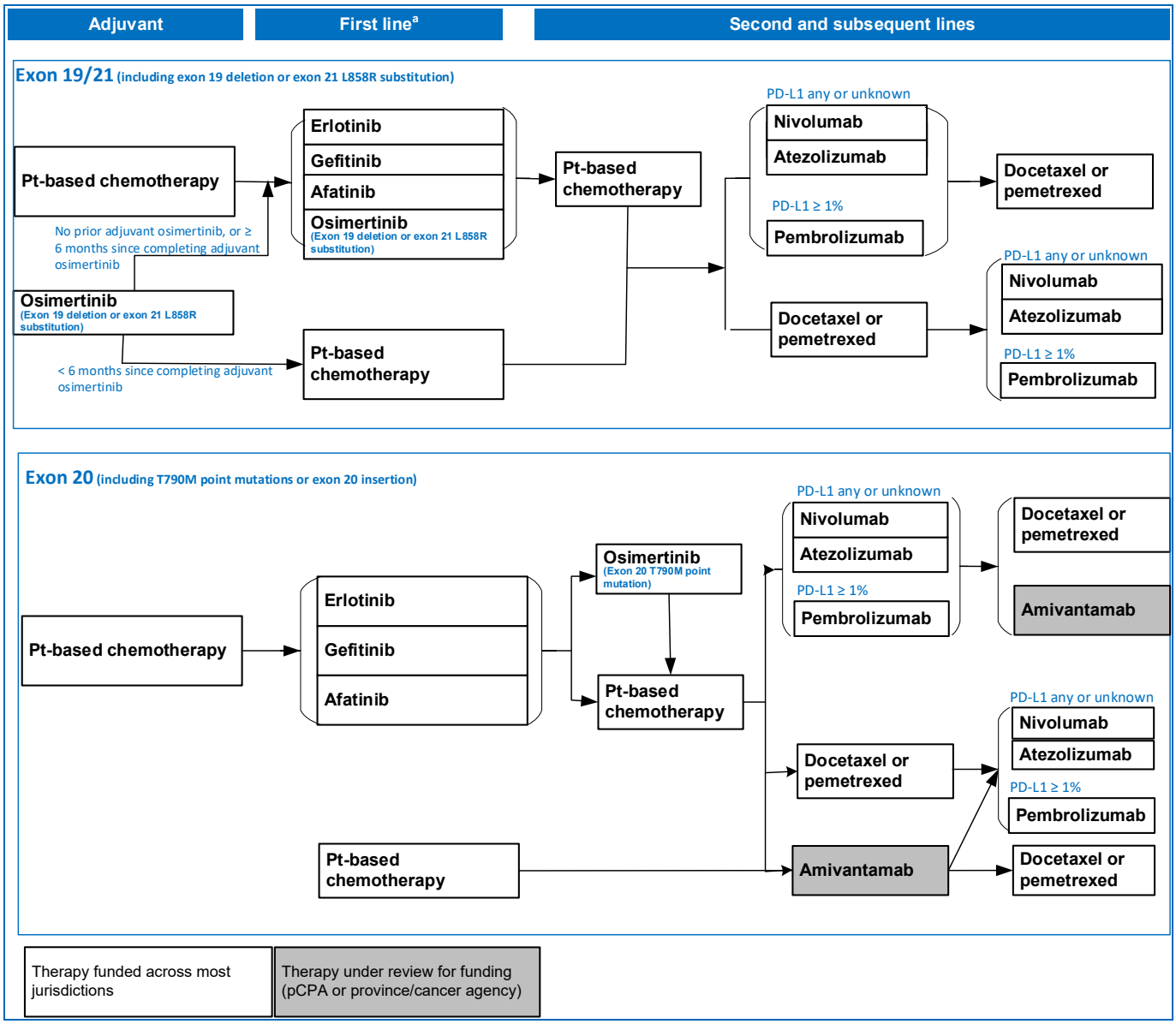
		sequencing of treatments for patients with EGFR mutation positive advanced adenocarcinoma of the lung. pERC discussed that the optimal sequencing of agents in this setting is currently unknown. However, pERC recognized that provinces may need to address this issue upon implementation of afatinib funding and noted that the development and implementation of an evidence-based guideline would be of value.
Pemetrexed (Alimta)	November 19, 2013	pERC recommends funding pemetrexed (Alimta) as a maintenance treatment following first-line treatment with pemetrexed plus cisplatin in patients with advanced or metastatic non-squamous non-small cell lung cancer (NS-NSCLC) conditional on its cost-effectiveness being improved to an acceptable level. Funding should be for patients who achieved stable disease or better with 4 cycles of induction pemetrexed plus cisplatin and with an ECOG performance status of 1 or 1 after induction therapy. The Committee made this recommendation because it was satisfied that there is a net clinical benefit of pemetrexed in this setting based on an improvement in progression-free survival and overall survival. However, at the submitted price, pemetrexed could not be considered cost-effective compared with no maintenance therapy.
Erlotinib (Tarceva)	December 6, 2005	The Canadian Expert Drug Advisory Committee (CEDAC) recommends that erlotinib be listed for patients with NSCLC after failure of at least one prior chemotherapy regimen, and whose EGFR expression status is positive or unknown.
Gefitinib (Iressa)	June 23, 2004	**Indication reviewed:** As monotherapy for the third line treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior platinum-based and docetaxel chemotherapy. The Canadian Expert Drug Advisory Committee (CEDAC) recommends that gefitinib not be listed.

AJCC = American Joint Committee on Cancer; ALK = anaplastic lymphoma kinase; BICR = blinded independent central review; CEDAC = Canadian Expert Drug Advisory Committee; CNS = central nervous system; ECOG = Eastern Cooperative Oncology Group; NGS = next generation sequencing; NSCLC = non–small cell lung cancer; pERC = pCODR Expert Review Committee; PCR = polymerase chain reaction; PD -1 = programmed cell death 1 protein; PD-L1 = programmed cell death 1 ligand 1; PFS = progression-free survival; QoL = quality of life; TKI = tyrosine kinase inhibitors; TPS = Tumour Proportion Score; vs. = versus.

Provisional Funding Algorithm

Figure 1: Provisional Funding Algorithm Diagram for *EGFR*-Positive NSCLC



pCPA = pan-Canadian Pharmaceutical Alliance; PD-L1 = programmed cell death 1 ligand 1; Pt = platinum.

Notes: Chemotherapy composition depends on histology (squamous versus nonsquamous). Pemetrexed maintenance therapy may follow platinum-based chemotherapy for those with a nonsquamous histology.

Erlotinib may be funded as a last line therapy in certain jurisdictions.

[a] Patients with de novo disease should start at that step of the algorithm sequence.

Description of the Provisional Funding Algorithm

Patients With Exon 19 or 21 Mutations

Patients with *EGFR*-positive NSCLC with exon 19 or 21 mutations include those with an exon 19 deletion or exon 21 L858R substitution.

For these patients, the adjuvant treatment options include platinum-based chemotherapy or osimertinib.

Upon progression to advanced or metastatic disease, patients may have the following first-line options if they have no prior adjuvant osimertinib or it has been 6 months or longer since completing adjuvant osimertinib: erlotinib, gefitinib, afatinib, or osimertinib (specifically for exon 19 deletions or exon 21 L858R substitutions). Patients with de novo metastatic disease will have access to these options as well if they also have exon 19 or 21 mutations.

For patients for whom it has been less than 6 months since completing adjuvant osimertinib, the first-line option in the advanced or metastatic setting is platinum-based chemotherapy.

As second-line options, patients who have received the tyrosine kinase inhibitors erlotinib, gefitinib, afatinib, or osimertinib should receive platinum-based chemotherapy.

For patients who have received platinum-based chemotherapy, their subsequent options can be immunotherapy or docetaxel or pemetrexed for patients with nonsquamous histology. Immunotherapy options include nivolumab or atezolizumab for patients with unknown or any programmed cell death 1 ligand 1 (PD-L1) status or pembrolizumab for patients with a PD-L1 of 1% or greater.

The subsequent treatment options for patients who have received immunotherapy include docetaxel or pemetrexed. Likewise, the subsequent treatment options for those who have received docetaxel or pemetrexed are immunotherapy options with nivolumab or atezolizumab for patients with unknown or any PD-L1 status or pembrolizumab for patients with a PD-L1 of 1% or more.

Patients With Exon 20 Mutations

Patients with *EGFR*-positive NSCLC with exon 20 mutations include those with exon 20 T790 point mutations or exon 20 insertions.

For these patients, the adjuvant treatment option is platinum-based chemotherapy.

Upon progression to advanced or metastatic disease, patients may have the following first-line option of tyrosine kinase inhibitors: erlotinib, gefitinib, or afatinib. Patients with de novo metastatic disease will have access to these options if they also have exon 20 mutations. Another option is platinum-based chemotherapy.

Second-line options include osimertinib for individuals with a confirmed exon 20 T790 point mutation or who have received platinum-based chemotherapy.

Subsequent options include immunotherapy, docetaxel or pemetrexed, or amivantamab. Immunotherapy options include nivolumab or atezolizumab for patients with unknown or any PD-L1 status or pembrolizumab for patients with a PD-L1 of 1% or greater. Patients can also receive docetaxel or pemetrexed if they have nonsquamous histology. Amivantamab is the treatment option for patients with an exon 20 insertion whose disease has progressed on, or after platinum-based chemotherapy. Amivantamab is currently under review for funding.

The next line of therapy options for patients who have received immunotherapy include docetaxel or pemetrexed or amivantamab, especially if immunotherapy has been started before amivantamab become an available option. Likewise, the subsequent options for patients who have received docetaxel or pemetrexed can be immunotherapy with nivolumab or atezolizumab for patients with unknown or any PD-L1 status or pembrolizumab for patients with a PD-L1 of 1% or greater. The next line of therapy for patients who have received amivantamab can be immunotherapy with nivolumab or atezolizumab for patients with unknown or any PD-L1 status or pembrolizumab for patients with a PD-L1 of 1% or greater, or docetaxel or pemetrexed if they have nonsquamous histology.