6.01 AMIVANTAMAB, Solution concentrate for I.V. infusion 350 mg in 7 mL, Rybrevant®, Janssen-Cilag Pty Ltd.

1 Purpose of submission

1.1 The Category 2 submission requested Section 100 (Efficient Funding of Chemotherapy Program) Authority Required listing for amivantamab in combination with platinum-based doublet chemotherapy (PDC) for the treatment of patients with epidermal growth factor receptor gene mutated (EGFRm) locally advanced/metastatic non-small cell lung cancer (NSCLC) where the condition has progressed on or after osimertinib.

1.2 Listing was requested on the basis of a cost-effectiveness analysis of amivantamab plus carboplatin and pemetrexed (AmiCP) versus PDC and atezolizumab + bevacizumab + carboplatin + paclitaxel (ABCP). Carboplatin and pemetrexed (CP) was the chemotherapy used in the clinical trial evidence and was used to represent PDC in this submission.

Table 1: Key components of the clinical issue addressed by the submission (as stated in the submission)

Component	Description
Population	Patients with EGFRm locally advanced/metastatic (Stage IIIB-IV) NSCLC where the condition has progressed on or after osimertinib
Intervention	Amivantamab IV infusion in combination with PDC (carboplatin/cisplatin in combination with pemetrexed) for up to 4 cycles followed by amivantamab IV infusion and pemetrexed IV infusion until disease progression
Comparator	PDC: carboplatin/cisplatin in combination with pemetrexed ABCP: atezolizumab + bevacizumab + carboplatin + paclitaxel
Outcomes	PFS (assessed by BICR and INV), OS, ORR, icPFS, HRQoL and safety
Clinical claim	In patients with EGFRm locally advanced/metastatic NSCLC where the condition has progressed on or after osimertinib, amivantamab in combination with PDC provides: • Superior clinical effectiveness and inferior but manageable safety compared with PDC • Superior clinical effectiveness and non-inferior safety compared with ABCP

Source: Table 1.1, p21 of the submission

Abbreviations: ABCP= atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; BICR=blinded independent central review; EGFRm= epidermal growth factor receptor gene mutated; HRQoL=health-related quality of life; icPFS=intracranial PFS; INV=investigator assessment; IV=intravenous; NSCLC=non-small cell lung cancer; OS=overall survival; ORR=objective response rate; PDC=platinum-based doublet chemotherapy; PFS=progression free survival

2 Background

Registration status

2.1 Amivantamab was TGA registered on 3 February 2025 for the following indications:

- in combination with carboplatin and pemetrexed for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, whose disease has progressed on or

after treatment with an EGFR tyrosine kinase inhibitor (TKI). This indication is relevant to this submission and is informed by the MARIPOSA-2 trial.

- in combination with lazertinib for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations.
- in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with activating EGFR exon 20 insertion mutations.
- as monotherapy 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.

Previous PBAC consideration

2.2 The PBAC has not previously considered AmiCP for this indication.

2.3 Amivantamab was recommended at the November 2024 PBAC meeting for the treatment of patients with EGFR exon 20 insertion mutation positive locally advanced or metastatic NSCLC in the first- and second-line setting.

2.4 Amivantamab in combination with lazertinib for the first-line treatment of patients with locally advanced or metastatic NSCLC with evidence in tumour material of an activating EGFRm known to confer sensitivity to EGFR TKIs was not recommended at the March 2025 PBAC meeting. The primary reason for this outcome was due to the economic analysis provided in the submission. The PBAC also noted that the clinical place in therapy of this combination in EGFRm NSCLC relative to osimertinib monotherapy and osimertinib in combination with chemotherapy required further consideration due to concerns regarding comparative effectiveness and safety (paragraph 72, amivantamab and lazertinib public summary document [PSD], March 2025 PBAC meeting).

2.5 Osimertinib (as monotherapy) is currently listed on the PBS as adjuvant therapy in EGFR pathogenic variant positive patients with resected Stage IB to IIIA NSCLC (recommended at the November 2023 PBAC meeting) and for the first- and second-line treatment of advanced stage (IIIB to IV) EGFR pathogenic variant positive NSCLC (recommended at the July 2020 and November 2018 PBAC meetings, respectively).

2.6 At the July 2025 meeting, the PBAC recommended osimertinib (as monotherapy) for the treatment of patients with unresectable locally advanced (Stage III) EGFR pathogenic variant positive NSCLC whose disease has not progressed during or following platinum-based chemoradiation therapy (CRT).

2.7 At the September 2025 meeting, the PBAC recommended the listing of osimertinib, in combination with chemotherapy, for the first-line treatment of patients with locally advanced or metastatic NSCLC with evidence of an activating epidermal growth factor receptor mutation (EGFRm) in tumour material. The PBAC considered a single osimertinib restriction covering all patient populations with EGFRm NSCLC was appropriate.

3 Requested listing

3.1 The requested restriction is presented below. Secretariat suggested additions are in italics and deletions in strikethrough.

MEDICINAL PRODUCT Form	Dispensed Price Max Amt	Max. Amount	№.of Rpts
AMIVANTAMAB	**Public prices** $8,995.23 published $[redacted] effective **Private prices** $9,165.56 published $[redacted] effective	2,100 mg	5 (initial) 7 (continuing)
Available brands			
Rybrevant Amivantamab, 350 mg solution for infusion, 1 vial			

Category / Program: Section 100/Section 100 – Efficient Funding of Chemotherapy
Prescriber type: ☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐
Restriction type: ☒Authority Required (telephone/online PBS Authorities system)
Indication: Stage IIIB/ IIIC (locally advanced) or Stage IV (metastatic) non-small cell lung cancer (NSCLC)
Treatment Phase: Initial *treatment – For patients whose condition progressed on or after osimertinib therapy*
Clinical criteria:
Patient must have/have had a WHO performance status of no greater than 2 at treatment initiation with this drug for this condition
AND
Clinical criteria:
Patient must not have previously received this drug for this condition; OR
Patient must be each of: (i) currently receiving non-PBS-subsidised supply for this drug for this PBS indication, (ii) free of disease progression since commencing non-PBS-subsidised supply.
~~**Treatment**~~ ***Clinical*** **criteria:**
The treatment must be/have been initiated in combination with platinum-based chemotherapy (PDC)
~~**Population**~~ ***Clinical*** **criteria:**
Patient must have ~~progressive~~ disease *progression* on or after osimertinib
Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333. No increase in the maximum amount or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply. A patient may only qualify for PBS-subsidised treatment under this restriction once. Following completion of the initial PBS-subsidised course, further applications for treatment will be assessed under the continuing treatment restriction.

Source: Table 1.13, p70-71 of the submission

Category / Program: Section 100/Section 100 – Efficient Funding of Chemotherapy
Prescriber type: ☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐
Restriction type: ☒Authority Required (telephone/online PBS Authorities system)
Indication: Stage IIIB/ IIIC (locally advanced) or Stage IV (metastatic) non-small cell lung cancer (NSCLC)
Treatment Phase: Continuing *treatment – For patients whose condition progressed on or after osimertinib therapy*
Clinical criteria:
Patient must have previously received PBS-subsidised treatment with this drug for this condition;
AND
Clinical criteria:
Patient must not have developed disease progression while receiving treatment with this drug for this condition.
Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333. No increase in the maximum amount or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.

Source: Table 1.13, p70-71 of the submission

3.2 The submission proposed a special pricing arrangement, whereby the effective approved ex-manufacturer price (AEMP) per 350 mg vial of amivantamab is $[redacted].

3.3 The submission's proposed population criterion states that the 'Patient must have progressive disease on or after osimertinib', thus allowing patients to have access to AmiCP on or after progression with osimertinib, irrespective of the disease stage/setting where osimertinib was given or the type of osimertinib regimen (i.e., monotherapy or in combination with chemotherapy) that was used. The eligibility criteria of the MARIPOSA-2 trial required documented progression on osimertinib monotherapy as the most recent line of therapy. The proposed PBS listing is broader than the patients included in the MARIPOSA-2 trial which did not include patients who progressed on osimertinib in the adjuvant setting or early cancer stage disease or progressed on osimertinib in combination with PDC. The ESC considered it was appropriate for AmiCP to be limited to patients that have progressed on osimertinib monotherapy in the advanced/ metastatic setting. The pre-PBAC response noted that the MARIPOSA-2 trial included patients with locally advanced/metastatic disease who had progressed on osimertinib monotherapy, however considered that restricting the PBS listing to this population would result in exclusion of other osimertinib-progressed patients with equally high need and no effective alternatives.

3.4 The requested restriction differs from the MARIPOSA-2 trial in that it allows a WHO performance status of 2 or less prior to starting amivantamab, whereas the MARIPOSA-2 trial included patients with WHO score of 0 or 1.

3.5 The submission proposed wording in the initial treatment criteria to accommodate access for patients that will receive amivantamab through a compassionate access program (eligibility aligned with proposed PBS restriction i.e. progressed on or after treatment with osimertinib).

3.6 Additionally, the submission requested that patients treated under the self-funded access program (who progressed on prior EGFR TKIs, consistent with the TGA approved indication, which does not specify osimertinib) be eligible for grandfathering. However, the submission did not propose a grandfather restriction to accommodate access for this patient population.

3.7 The proposed criteria did not specify the type of EGFR mutation as part of the eligibility criteria, despite the TGA indication referring to patients with exon19del or exon 21 L858R mutations.

3.8 The proposed criteria required initiation of amivantamab treatment to be in combination with PDC. The submission stated that the wording 'initiated' was included as patients might discontinue chemotherapy (due to intolerability) and continue amivantamab monotherapy which was also supported in the MARIPOSA-2 trial.

For more detail on PBAC's view, see section 7 PBAC outcome.

4 Population and disease

4.1 Lung cancer is the fourth most commonly diagnosed cancer for Australian men and women, with an estimated 15,100 people diagnosed in 2025.[1] Lung cancer is the leading cause of cancer mortality, with an estimated 9,000 people expected to die from the disease in 2025. Of the five most common cancers in Australia, survival rates for lung cancer have been the lowest with a 5-year survival of 27% in 2017-2021.

4.2 For patients with locally advanced or metastatic (Stage IIIB-IV) NSCLC who are not amenable to curative surgery or radiotherapy, and whose tumours harbour EGFRm, the first-line standard of care consists of treatment with EGFR TKIs. Osimertinib, a third-generation EGFR TKI, is currently the most commonly utilised option, replacing earlier generation TKIs (gefitinib, erlotinib, afatinib).

4.3 The proposed listing is for patients with EGFRm locally advanced/metastatic (Stage IIIB-IV) NSCLC who have progressed on or after osimertinib. For these patients, subsequent treatment options do not demonstrate clinically meaningful improvements in delaying disease progression or death. Australian registry data as well as international studies report a median overall survival (OS) of between 10 and 14.1 months for these patients.[2,3]

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[1] Australian Institute of Health and Welfare (AIHW), 2025. Overview of cancer in Australia. https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/overview#lung

[2] Attili et al. "Post-progression analysis of EGFR-mutant NSCLC following osimertinib therapy in real-world settings." Cancers 16.14 (2024): 2589.

[3] Rotow et al. "Real-world genomic profile of EGFR second-site mutations and other osimertinib resistance mechanisms and clinical landscape of NSCLC post-osimertinib." Journal of Thoracic Oncology 19.2 (2024): 227-239.

4.4 The European Society for Medical Oncologists (ESMO)[4] and National Comprehensive Cancer Network (NCCN) NSCLC[5] clinical guidelines suggest AmiCP, PDC or ABCP following progression with osimertinib. The NCCN guidelines recommend AmiCP (preferred treatment option), amivantamab plus lazertinib, or systemic therapy (including PDC, ABCP) following widespread systemic progression with osimertinib.

4.5 The submission proposed that AmiCP could be used after osimertinib progression irrespective of the first administration setting (i.e. applicable to all current osimertinib PBS listings). The concerns relating to the proposed request are discussed in paragraph 3.3.

4.6 Amivantamab is a fully human, immunoglobulin G1 (IgG1) bispecific antibody with high affinity for both EGFR and mesenchymal-epidermal transition (MET) receptors. Unlike EGFR TKIs, amivantamab binds extracellularly and is therefore not affected by co-mutations in the EGFR TKI binding pocket.[6] MET mutations, particularly MET amplifications, are common resistance mechanisms. The high affinity of amivantamab for MET receptors therefore offers a potential treatment advantage over other EGFR therapies in those with co-mutations.

For more detail on PBAC's view, see section 7 PBAC outcome.

5 Comparator

5.1 The submission nominated PDC and ABCP therapies as the main comparators. The main arguments provided in support of this nomination were that PDC and ABCP were among the most commonly used regimens in patients that have progressed on or after osimertinib based on PBS data provided by the DUSC Secretariat and the AUstralian Registry and biObank of thoracic cAncers (AURORA) study. AURORA is a multi-site longitudinal cohort study enrolling patients with thoracic malignancies from eight Australian hospitals across three states (Victoria, New South Wales, Western Australia).[7,8]

5.2 The 100% PBS data analysis included in the submission suggest that a large proportion (59.2%) of patients were re-treated with osimertinib post-osimertinib initiation,

[4] ESMO Oncogene-Addicted Non-Small Cell Lung Cancer Living Guideline v1.3,February 2026. Retrieved from: https://www.esmo.org/guidelines/living-guidelines/esmo-living-guideline-oncogene-addicted-metastatic-non-small-cell-lung-cancer/management-of-advanced-and-metastatic-disease/egfr-mutation/stage-iv-mnsclc-with-egfr-activating-mutation-after-systemic-progression/egfr-activating-mutation-after-systemic-progression-if-prior-third-generation-tki

[5] NCCN Clinical Practice Guidelines in Oncology. Non-small cell lung cancer, version 1.2026- November 6, 2025

[6] Moores et al, (2016) 'A novel bispecific antibody targeting EGFR and cMet is effective against EGFR inhibitor–resistant lung tumors.' Cancer research 76.13: 3942-3953.

[7] Chazan et al. 'Treatment patterns, prognostic factors and survival for ALK+ advanced NSCLC in Australia; results from the AUstralasian thoRacic cancers lOngitudinal cohoRt study and biobAnk (AURORA).' JTO Clinical and Research Reports (2025): 100924.

[8] Brown et al. "First-line chemoimmunotherapy and immunotherapy in patients with non-small cell lung cancer and brain metastases: a registry study." Frontiers in Oncology 14 (2024): 1305720.

despite not being permitted on the PBS. The next most commonly used options were PDC and ABCP accounting for 16.1% and 11.5% of subsequent treatment utilisation respectively. Data from the AURORA study indicates that most patients were treated with ABCP (28.3%) as the second-line treatment option post-osimertinib progression followed by chemotherapy (19.8%).

5.3 The submission proposed a comparator split of 83.08% for ABCP and 16.92% for PDC based on its analysis of the 100% PBS data from DUSC, derived as shown in **Error! Reference source not found.**.

Table 2: Derivation of proposed comparator split using PBS data

	Patient Initiations	%	Patient Initiations	Re-distributed %	Proposed comparator split
Osimertinib retreatment	906	59.18%	906	62.31%	-
Platinum based chemotherapy doublet	246	16.07%	246	16.92%	16.92%
ABCP	176	11.50%	176	12.10%	83.03% [c]
1/2 Gen TKIs	70	4.57%	70	4.81%	-
Single chemotherapy agent	48	3.14%	Removed [a]	-	-
IO Regimens	36	2.35%	36	2.48%	-
Other	29	1.89%	Removed [b]	-	-
Bev regimens	20	1.31%	20	1.38%	-
TOTAL	**1531**	**100.0%**	**1454**	**100.0%**	**100.0%**

Source: Table 1.9, p55 of the submission

Abbreviations: ABCP = atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; IO=immune-oncology; PBS= pharmaceutical benefit scheme; TKIs= tyrosine kinase inhibitors

[a] Removed by the submission as assumed these patients would not fit enough to receive PDC regimens, thus would not be treated with AmiCP

[b] Removed by the submission as were not considered treatments for NSCLC (e.g., tamoxifen and lipefilgrastim)

[c] ACBP proportion combines proportions from osimertinib retreatment, ABCP, 1/2 Gen TKIs, IO regiments and Bev regimens.

Note: Comparator split derived during the evaluation based on ABCP and PDC counts alone was based on 246 PDC patients + 176 ABCP patients (total = 422) as the substituted population, with PDC representing 58.3% and ABCP 41.7%.

5.4 There are several concerns with the submission's approach to the proposed comparator split:

- The submission assumed that all patients who received osimertinib re-treatment, first-/second-generation TKIs, immunotherapy and bevacizumab regimens would be included as part of the ABCP category as these were considered higher cost medicines compared to PDC.
- The 100% PBS data indicated that a proportion of patients may be retreated with osimertinib despite it not being permitted on the PBS for this indication (see paragraph 5.2). The evaluation considered the data may not fully represent retreatment but may include some miscoding.
- In the Pre-Sub-Committee Response (PSCR), the sponsor cited the highly fragmented treatment utilisation in the post-osimertinib setting and considered the split of 83.08% for ABCP and 16.92% for PDC to be a pragmatic approach.

5.5 The ESC noted the use of osimertinib in the retreatment setting was not permitted on the PBS and considered the high proportion of use in the analysis of PBS data was

likely due to miscoding. Additionally, the ESC noted the cost-effectiveness of retreatment has not been assessed.

5.6 The ESC considered that, in clinical practice, AmiCP was most likely to replace chemotherapy with or without atezolizumab and bevacizumab. On balance, the ESC considered 30% of patients would receive atezolizumab and bevacizumab and noted this was consistent with the AURORA study (see paragraph 5.2) and PBAC's previous consideration of osimertinib (paragraph 7.8, osimertinib PSD, July 2025 PBAC meeting). In the pre-PBAC response, the sponsor noted that the submitted comparator split was intended to capture real-world utilisation of all systemic therapies used post-osimertinib. The sponsor considered that the previous consideration of the proposed 30% / 70% split was to inform subsequent therapies in the economic model evaluation for the PBS listing of osimertinib in stage 3 unresectable NSCLC (paragraph 7.8, osimertinib PSD, July 2025), and the basis of the estimate was unclear. The sponsor also noted that in a previous PBAC consideration (paragraph 6.3, osimertinib PSD, November 2023), ESC suggested that ABCP utilisation could be as high as 60%.

5.7 The PBAC noted the clinical evidence for ABCP (and immunotherapy more broadly) in patients with EGFRm NSCLC was limited; however, acknowledged it was used in select, fit patients with a high disease burden.

For more detail on PBAC's view, see section 7 PBAC outcome.

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer inputs

6.2 The PBAC welcomed the input from individuals (18), health care professionals (3) and organisations (2) via the Office of Health Technology Assessment Consultation Hub. The inputs described a range of harms of treatment with the current standard of care such as lethargy, pain, breathing difficulties, reduced mobility and significant emotional strain associated with progressive lung disease, and the limited treatment options currently available. The comments from individuals expressed hope that amivantamab could improve quality of life and prolong survival, and highlighted access to amivantamab is prohibitive due to the significant cost. Health care professionals described amivantamab as offering valuable improvements in progression-free and overall survival for patients with EGFR-mutated NSCLC, noting that the current second line option (primarily PDC) provided "minimal and very short term responses," while describing its toxicities as manageable and acceptable with regard to the survival benefits. The inputs emphasised amivantamab plus chemotherapy is considered standard of care internationally for second-line EGFR-

mutated lung cancer and considered timely access for Australians a critical equity issue.

6.3 The PBAC noted input from Lung Foundation Australia, which highlighted limited treatment options and a high unmet need for this population of patients.

6.4 The PBAC noted the advice received from The Thoracic Group of Australasia (TOGA) clarifying the likely use of amivantamab in clinical practice.

Clinical trials

6.5 The submission was based on one head-to-head randomised trial comparing amivantamab in combination with carboplatin and pemetrexed (AmiCP) to carboplatin and pemetrexed (N=394): MARIPOSA-2 trial. Evidence presented in the submission was based on data from the primary analysis at the clinical cut-off (CCO) of July 2023, after a median follow-up of 8.7 months. The first interim analysis of OS occurred at the primary analysis, and a second pre-specified interim analysis (IA2) was performed at the CCO of April 2024 after a median follow-up of 18.1 months.

6.6 No head-to-head trials were available for the comparison of AmiCP with ABCP therefore, a literature search was conducted to identify clinical trials with a common comparator arm. The results from subgroup analyses relevant to the proposed patient population from the ATTLAS trial were used to support the clinical claim. The ATTLAS trial (N=228) is an open-label, multicentre, Phase III RCT conducted in Korea which compared ABCP and PDC in patients with EGFRm or ALK-rearranged or translocated NSCLC upon progression on (any) TKI therapy. 40.4% of the intention-to-treat (ITT) population had prior osimertinib treatment, thus formed the subgroup relevant to this submission.

6.7 Details of the trials presented in the submission are provided below in **Error! Reference source not found.**.

Table 3: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
AmiCP vs CP		
MARIPOSA-2 (NCT04988295)	Califano R, Passaro A, Tan JL, et al. Amivantamab plus chemotherapy vs chemotherapy in EGFR-mutant advanced NSCLC after disease progression on osimertinib: outcomes by osimertinib resistance mechanisms in MARIPOSA-2.	*J Clin Oncol* 2025; 43(16_suppl): 8639.
	Passaro A, Wang J, Wang Y, et al. Amivantamab plus chemotherapy with and without lazertinib in EGFR-mutant advanced NSCLC after disease progression on osimertinib: primary results from the phase III MARIPOSA-2 study.	*Ann Oncol* 2024; 35(1): 77–90.
	Tomasini P, Cordellat AB, Dooms C, et al. 8P Amivantamab plus chemotherapy vs chemotherapy in EGFR-mutant advanced NSCLC after progression on osimertinib: secondary analyses of patient-relevant endpoints from MARIPOSA-2.	*ESMO Open* 2024; 9.
	Popat S, Reckamp KL, Califano R, et al. LBA54 Amivantamab plus chemotherapy vs chemotherapy in EGFR-mutated, advanced non-small cell lung cancer after disease progression on osimertinib: second interim overall survival from MARIPOSA-2.	*Ann Oncol* 2024; 35: S1244–S1245
	Gentzler RD, Spira A, Melosky B, et al. 3MO Amivantamab plus chemotherapy vs chemotherapy in EGFR-mutant advanced NSCLC after progression on osimertinib: a post-progression analysis of MARIPOSA-2. ESMO Open 2024; 9.	*ESMO Open* 2024; 9.
	Passaro A, Cho BC, Wang Y, et al. LBA15 Amivantamab plus chemotherapy (with or without lazertinib) vs chemotherapy in EGFR-mutated advanced NSCLC after progression on osimertinib: MARIPOSA-2, a phase III, global, randomized, controlled trial.	*Ann Oncol* 2023; 34: S1307
	Shih JY, Wang J, Wang Y, et al. LBA11 Amivantamab plus chemotherapy vs chemotherapy among Asian patients with EGFR-mutant advanced NSCLC after progression on osimertinib: a MARIPOSA-2 subgroup analysis. Ann Oncol 2023; 34: S1661–S1662.	*Ann Oncol* 2023; 34: S1661–S1662
ABCP vs CP		
ATTLAS (NCT03991403)	Park S, Kim TM, Han JY, et al. Phase III, randomized study of atezolizumab plus bevacizumab and chemotherapy in patients with EGFR- or ALK-rearranged or translocated non–small-cell lung cancer (ATTLAS, KCSG-lu19-04).	*J Clin Oncol* 2024; 42(11): 1241–1251
	Kim H, Park S, Kim TM, et al. 631P Exploratory biomarker analysis in EGFR-mutated NSCLC patients who were treated with atezolizumab plus bevacizumab and chemotherapy from phase III ATTLAS trial.	*Ann Oncol* 2024; 35: S1636
	Ahn MJ, Park S, Kim TM, et al. LBA67 A phase III, randomized study of atezolizumab plus bevacizumab and chemotherapy in patients with EGFR- or ALK-mutated non-small cell lung cancer (ATTLAS, KCSG-LU19-04).	*Ann Oncol* 2023; 34: S1311
	Park S, Lee YG, Park JH, et al. A phase III, open-label, randomized study of atezolizumab in combination with carboplatin + paclitaxel + bevacizumab compared with pemetrexed + cisplatin or carboplatin in stage IV non-squamous non-small cell lung cancer (NSCLC) with activating EGFR mutation or ALK translocation (ATLAS Trial).	*J Clin Oncol* 2020; 38(15_suppl): TPS9636.

Source: Table 2.7, p86 of the submission.

Abbreviations: ABCP= atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; ALK= Anaplastic Lymphoma Kinase; AmiCP= amivantamab in combination with carboplatin and pemetrexed; CP= carboplatin plus pemetrexed; EGFR= epidermal growth factor receptor; NSCLC= non-small cell lung cancer

6.8 The key features of the included evidence are summarised in **Error! Reference source not found.**.

Table 4: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
AmiCP vs. CP						
MARIPOSA-2	395 [a]	R, OL, MC 8.7 mths (primary) 18.1 mths (IA2)	Some concerns	Stage IIIb-IV EGFRm patients who had progressed on or after osimertinib	PFS, OS, ORR, icPFS, HRQoL and safety	PFS, OS, TTTD, HRQoL
ABCP vs. CP						
ATTLAS	310 [b]	R, OL 26.1 mths	Some concerns	Stage III-IV EGFRm and ALK positive patients who had progressed on or after any EGFR TKI	PFS, OS	Not used

Source: Compiled during the evaluation using information presented in the submission

Abbreviations: ABCP = atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; AmiCP = amivantamab in combination with carboplatin and pemetrexed; CP= carboplatin plus pemetrexed; DB = double blind; IA2= interim analysis 2; MC = multi-centre; mths= months; OL = open label; OS = overall survival; PFS = progression-free survival; R= randomised, TTTD= time to treatment discontinuation.

[a] The MARIPOSA-2 trial was designed as a three-armed study (including a lazertinib, amivantamab, carboplatin, and pemetrexed arm). This was not included as it is not relevant to this submission. The trial was designed to have a dual primary hypothesis to independently evaluate the efficacy of treatment comparisons.

[b] This reflects the whole trial population.

6.9 The submission considered that there was an overall low risk of bias associated with the MARIPOSA-2 and ATTLAS trials. Due to the open-label nature of both trials, unblinded treatment allocation may have introduced performance and detection biases. Awareness of the treatment allocation may also have impacted on how patients report adverse events, quality of life outcomes and treating clinician management decisions. Further, the lack of blinding may cause bias if it leads to deviations from the intended intervention and knowledge of this may also have introduced bias. It is noted that most outcomes were assessed by blinded independent central review (BICR) in the MARIPOSA-2 trial while for ATTLAS, all outcomes were investigator-assessed. Based on the potential sources of bias described, there are some concerns with the overall risk of bias.

6.10 The ESC considered the MARIPOSA-2 trial population was representative of the Australian population. However, the PBAC noted MARIPOSA-2 was limited to patients previously treated with osimertinib as monotherapy in the advanced/ metastatic setting (paragraph 3.3) which may not reflect the broader post-osimertinib patient population.

Comparative effectiveness

Direct comparison: AmiCP vs. CP

6.11 A summary of the efficacy results for progression free survival (PFS), overall survival (OS), objective response rate (ORR) and intracranial progression free survival (icPFS) from the full analysis set (FAS) population in the MARIPOSA-2 trial is presented in **Error! Reference source not found.**.

Table 5: Summary of PFS, OS and ORR outcomes in MARIPOSA-2 trial (FAS)

	AmiCP (n=131)	CP (n=263)
Progression free survival (PFS) by BICR – primary analysis		
Number of events (%)	74 (56.5)	171 (65.0)
Censored (%)	57 (43.5)	92 (35.0)
Time to event (months)		
25th percentile (95% CI)	4.37 (4.17, 5.39)	2.50 (1.51, 2.83)
Median, months (95% CI)	6.28 (5.55, 8.41)	4.17 (4.04, 4.44)
75th percentile (95% CI)	11.76 (9.72, NE)	6.93 (5.78, 8.31)
Range	(0.0+, 14.9)	(0.0+, 14.0+)
6-month event-free rate (95% CI)	0.51 (0.41, 0.60)	0.30 (0.23, 0.36)
9-month event-free rate (95% CI)	0.38 (0.28, 0.48)	0.16 (0.11, 0.23)
12-month event-free rate (95% CI)	0.22 (0.12, 0.34)	0.13 (0.08, 0.20)
HR (95% CI); p-value [a]	**0.48 (0.36, 0.64); p<0.0001**	
Overall survival (OS) – interim analysis 2		
Number of events (%)	65 (49.6)	143 (54.4)
Censored (%)	66 (50.4)	120 (45.6)
Time to event (months)		
25th percentile (95% CI)	10.78 (8.41, 13.83)	8.51 (7.29, 9.86)
Median, months (95% CI)	17.74 (15.97, 22.37)	15.34 (13.73, 16.76)
75th percentile (95% CI)	NE (22.37, NE)	NE (20.53, NE)
Range	(0.5, 24.6+)	(0.0+, 25.3+)
6-month event-free rate (95% CI)	0.91 (0.84, 0.95)	0.87 (0.82, 0.90)
9-month event-free rate (95% CI)	0.80 (0.72, 0.86)	0.73 (0.67, 0.78)
12-month event-free rate (95% CI)	0.70 (0.61, 0.77)	0.63 (0.57, 0.69)
18-month event-free rate (95% CI)	0.50 (0.40, 0.59)	0.40 (0.33, 0.46)
HR (95% CI); p-value[a]	**0.73 (0.54, 0.99), p=0.0386**	
Objective response rate (ORR) – primary analysis		
Number of patients with measurable disease at baseline	130	260
Objective response rate (CR + PR)	83 (63.8%)	94 (36.2%)
95% CI	(55.0%, 72.1%)	(30.3%, 42.3%)
Odds ratio (95% CI), p-value[a,b]	**3.10 (2.00, 4.80); p<0.0001**	
Best Overall Response		
Complete Response (CR)	2 (1.5%)	1 (0.4%)
Partial Response (PR)	81 (62.3%)	93 (35.8%)
Stable Disease (SD)	30 (23.1%)	82 (31.5%)
Progressive Disease (PD)	10 (7.7%)	52 (20.0%)
Not Evaluable (NE)	7 (5.4%)	32 (12.3%)
Intracranial PFS– interim analysis 2		
Number of events (%)	86 (65.6%)	174 (66.2%)
Censored	45 (34.4%)	89 (33.8%)
Time to event (months)		
25th percentile (95% CI)	7.95 (5.78, 8.48)	4.93 (3.48, 5.75)
Median, months (95% CI)	12.45 (10.58, 14.36)	8.90 (8.15, 11.07)
75th percentile (95% CI)	19.29 (16.72, 22.37)	15.57 (13.90, 17.08)
HR (95% CI); p-value[a]	**0.65 (0.49, 0.84); p=0.0012**	

Source: Tables 2.27, 2.29, 2.30, 2.32, p135, 141, 142, 143 of the submission

Abbreviations: AmiCP = amivantamab in combination with carboplatin and pemetrexed; BICR=blinded independent central review; CP= carboplatin plus pemetrexed; +=censored observation; CI= confidence interval; FAS=full analysis set; PFS= progression free survival; NE=not estimable.

[a] Hazard ratio is from stratified proportional hazards model. Hazard ratio <1 favours experimental treatment. p-value is from a log-rank test stratified by osimertinib line of therapy (first-line vs second-line), history of brain metastases (yes or no), and Asian race (yes vs no).

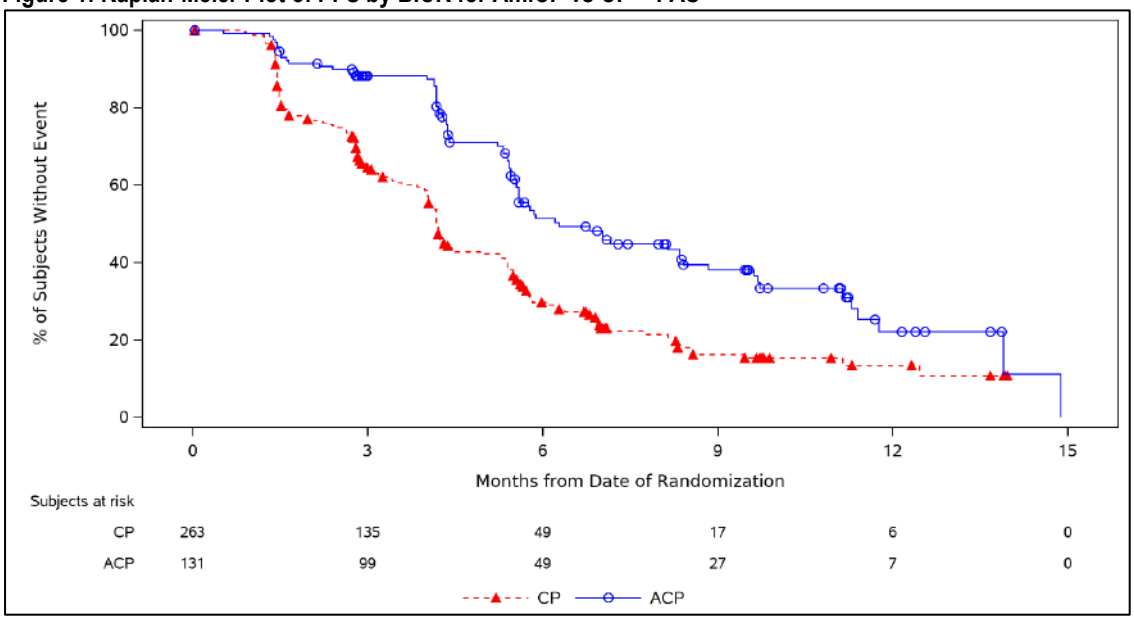
Bold text indicates statistically significant results.

Note: Median follow up for primary analysis (clinical cutoff of July 2023) = 8.7 months and for IA2 (clinical cutoff of April 2024 = 18.1 months

6.12 After a median follow-up period of 8.7 months, the median PFS for the AmiCP and CP arms were 6.28 months and 4.17 months, respectively. This was a statistically significant difference (hazard ratio (HR) 0.48 (95% confidence interval [CI] 0.36, 0.64). Median PFS was prolonged by 2.1 months in patients treated with AmiCP compared to patients treated with CP alone.

6.13 The Kaplan Meier (KM) curves for PFS in the MARIPOSA-2 trial are presented in Figure 1.

Figure 1: Kaplan-Meier Plot of PFS by BICR for AmiCP vs CP – FAS

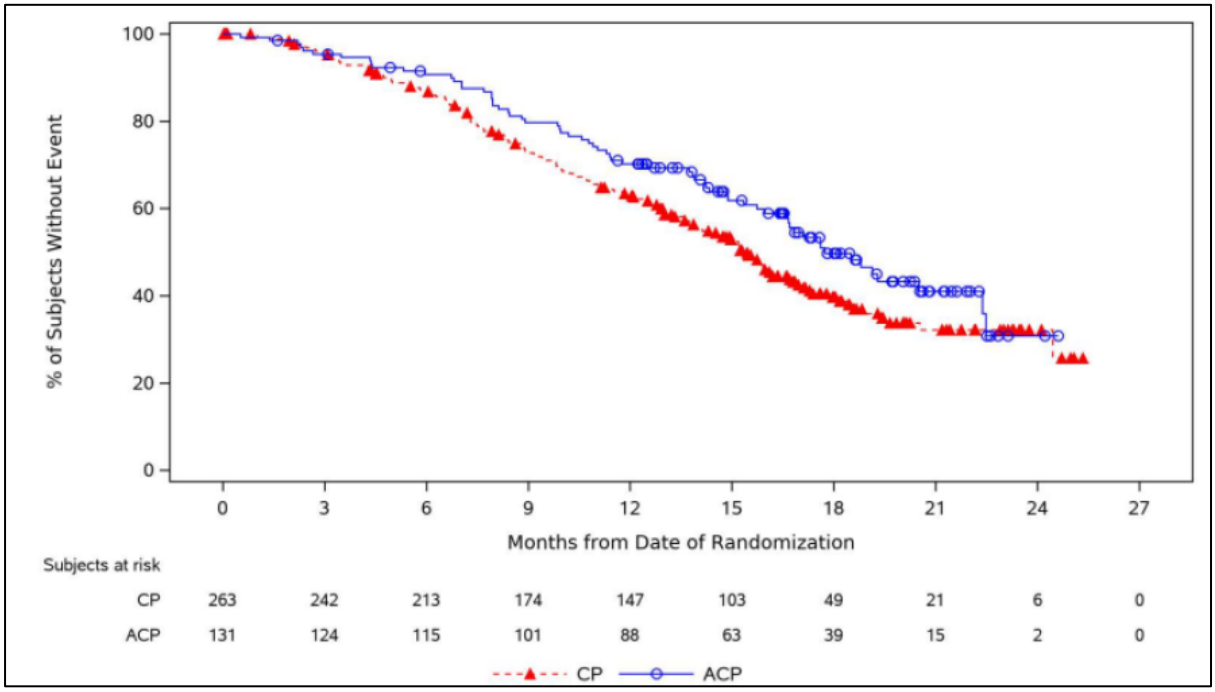


Source: Figure 2.8, p135 of the submission
Abbreviations: AmiCP = amivantamab in combination with carboplatin and pemetrexed; BICR=blinded independent central review; CP=carboplatin plus pemetrexed; PFS= progression free survival; FAS=full analysis set

6.14 Secondary outcomes used to support the clinical claim included OS, ORR and icPFS. For the OS outcome, results from the interim analysis 2 (IA2) clinical cutoff of April 2024 showed a statistically significant reduction in the risk of death for AmiCP vs CP (HR=0.73; 95% CI: 0.54, 0.99; p=0.0386). The 95% CI of the event free rates were overlapping across all nominated time points (**Error! Reference source not found.**).

6.15 The KM curves for OS in the MARIPOSA-2 trial are presented in Figure 2. The OS curves appear to converge between 22 and 23 months likely due to low numbers of patients remaining at risk.

Figure 2: Kaplan-Meier Plot of OS for AmiCP and CP – FAS



Source: Figure 2.14, p141 of the submission
Abbreviations: Ami=amivantamab; CP= carboplatin plus pemetrexed; FAS=full analysis set; IA=interim analysis; OS= overall survival.

6.16 AmiCP prolonged median overall survival by 2.4 months compared to CP (median OS 17.7 months vs. 15.3 months).

6.17 After a median follow-up of 8.7 months, the objective response rate was higher in the AmiCP arm (63.8%) compared to the CP arm (36.2%), resulting in an odds ratio of 3.1 (95% CI: 2.00, 4.80; p<0.0001).

6.18 Results for icPFS from the IA2 analysis showed a statistically significant difference in risk of intracranial disease progression for AmiCP versus CP (HR=0.65 [95% CI: 0.49, 0.84], nominal p=0.0012).

6.19 The patient-reported outcome measures included in the MARIPOSA-2 trial included the EQ-5D-5L and were analysed as an exploratory endpoint. EQ-5D-5L utility scores (based on the UK value set) were maintained across all treatment cycles and differences between treatment arms were not statistically significant (p>0.05).

Evidence for AmiCP vs. ABCP

6.20 The submission did not present comparative evidence to support the claim that AmiCP was superior compared with ABCP. Based on the subgroup results from ATTLAS, the submission argued that the efficacy of CP in MARIPOSA-2 study is representative of the efficacy of ABCP. This was based on the lack of demonstrated difference between ABCP and CP in the ATTLAS trial. This in turn was the basis for the claim that AmiCP is superior to ABCP based on PFS and OS outcomes. The submission further noted that at the March 2019 PBAC meeting, the claim of superior clinical effectiveness for ABCP

compared to PDC in the EGFR/ALK mutation positive population was considered reasonable but noted that this was based on an ITC of a small subgroup and so the magnitude of the benefit remained highly uncertain (paragraph 6.34, atezolizumab PSD, March 2019 PBAC meeting).

6.21 **Error! Reference source not found.** presents the results of the Bucher ITC conducted during the evaluation. The subgroup analyses from ATTLAS are exploratory, with small sample size, and lack of clarity of the patient characteristics and their comparability across arms.

Table 6: Results of the indirect comparison for PFS

Trial	Outcome	AmiCP n/N (%)	CP n/N (%)	Absolute difference	HR (95% CI)
Prior osimertinib in 1L					
MARIPOSA-2	Progressed	54/97 (56%)	117/181 (65%)		-
	Median months PFS	6.28	4.07	2.21	0.47 (0.34, 0.66)
Comparators		**ABCP n/N (%)**	**CP n/N (%)**	**Absolute difference**	**HR (95% CI)**
ATTLAS	Progressed	9/12 (75%)	9/9 (100%)		-
	Median months PFS	6.47	4.14	2.33	0.52 (0.19, 1.41)
Indirect comparison AmiCP vs. ABCP					0.9 (0.31, 2.6) p=0.85
Prior osimertinib in 2L					
MARIPOSA-2	Progressed	20/34 (59%)	54/82 (66%)		-
	Median months PFS	6.21	5.26	0.95	0.55 (0.32, 0.93)
Comparators		**ABCP n/N (%)**	**CP n/N (%)**	**Absolute difference**	**HR (95% CI)**
ATTLAS	Progressed	**44/50 (88%)**	17/20 (85%)		-
	Median months PFS	8.31	6.93	1.38	1.07 (0.59, 1.94)
Indirect comparison AmiCP vs. ABCP					0.51 (0.23, 1.14) p=0.10

Source: Calculated during the evaluation using subgroup analysis data from MARIPOSA-2 and ATTLAS
Abbreviations: 1L = first line treatment; 2L= second line treatment; AmiCP = amivantamab in combination with carboplatin and pemetrexed; ABCP = atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; CP = carboplatin plus pemetrexed; HR = hazard ratio; n= number of patients with event; N= total number of patients; NA = not available.

6.22 The HRs from the ITC results appear to favour AmiCP arm but were not statistically significant. There is uncertainty in these results given the limitations with the small sample sizes and issues with transitivity including differences in race and ECOG status, where ATTLAS recruited majority Asian patients (based in Korea) and a large proportion with ECOG performance status of 1 (up to 90.3%) and duration of follow up (e.g. 8.7 months in the MARIPOSA-2 trial for PFS outcome vs. 26.1 months in ATTLAS).

6.23 The PBAC noted the progression free survival from ATTLAS in the broader population of patients with EGFRm NSCLC (n=215) was 8.71 months for ABCP patients and 5.62 months for CP patients (HR 0.60, 95%CI: 0.43, 0.84)[9].

Comparative harms

Direct comparison: AmiCP vs. CP

6.24 A summary of the comparative harms for AmiCP vs. CP from the MARIPOSA-2 trial after a median of 8.7 months follow up is presented in **Error! Reference source not found.**. Patients in the AmiCP arm had a greater risk of experiencing Grade ≥3 treatment emergent adverse events (TEAEs) related to the study treatment compared to the CP arm (72.3% vs. 48.1%), a greater risk of serious adverse events (AEs) (32.3% vs. 20.2%), a greater risk of AEs leading to treatment discontinuation (18.5% vs. 3.7%), dose reduction (40.8% vs. 15.2%) and drug interruption (64.6% vs. 33.3%).

Table 7: Overall summary of TEAE incidence – Primary analysis CCO (SAS population)

	AmiCP (n=130)	CP (n=243)	Risk difference (95% CI)	Relative risk (95% CI)
Grade ≥3 AEs	94 (72.3%)	117 (48.1%)	24.16% (14.23, 34.09)	1.50 (1.27, 1.78)
Grade ≥3 AEs related to study treatment [a]	87 (66.9%)	86 (35.4%)	31.53% (21.45, 41.61)	1.89 (1.54,2.33)
Related to amivantamab	54 (41.5%)	0	41.5% (NC)	NC
Serious AEs	42 (32.3%)	49 (20.2%)	12.14% (2.65, 21.63)	1.60 (1.13, 2.28)
SAEs related to study treatment [a]	30 (23.1%)	21 (8.6%)	14.43% (6.38, 22.49)	2.67 (1.60, 4.47)
Related to amivantamab	15 (11.5%)	0	11.5% (NC)	NC
AEs leading to discontinuation of any study treatment	24 (18.5%)	9 (3.7%)	14.8% (7.68, 21.84)	4.98 (2.39,10.41)
AEs leading to dose reduction of any study agent	53 (40.8%)	37 (15.2%)	25.54% (15.96, 35.12)	2.68 (1.87, 3.85)
AEs leading to drug interruption of any study agent	84 (64.6%)	81 (33.3%)	31.28% (21.15, 41.42)	1.94 (1.56, 2.41)
AEs leading to death [b]	3 (2.3%)	3 (1.2%)	1.07% (-1.86,4.00)	1.87 (0.38, 9.13)
Related to study treatment [a]	2 (1.5%)	1 (0.4%)	1.13 (-1.14, 3.39)	3.74 (0.34, 40.84)
Most commonly reported toxicity Grade ≥ 3 TEAEs				
Neutropenia	59 (45.4%)	52 (21.4%)	23.99% (13.99, 33.98)	2.12 (1.56, 2.88)
Leukopenia	26 (20.0%)	23 (9.5%)	10.53% (2.74, 18.33)	2.11 (1.26, 3.55)
Anaemia	15 (11.5%)	23 (9.5%)	2.07% (-4.54, 8.68)	1.22 (0.66, 2.25)
Thrombocytopenia	19 (14.6%)	22 (9.1%)	5.56% (-1.50, 12.63)	1.61 (0.91, 2.87)

Source: Table 2.46, p164 of the submission and RR and RDs added during the evaluation
Abbreviations: AmiCP=amivantamab plus carboplatin and pemetrexed; AE=adverse event; CCO= clinical cut off; CI= confidence interval; CP= carboplatin plus pemetrexed; SAE=serious adverse event; NC= not calculatable; TEAE=treatment-emergent adverse event
[a] AE assessed by the investigator as related to study agent
[b] AEs leading to death are based on AE outcome of Fatal

[9] Park S, Kim TM, Han JY, et al. Phase III, randomized study of atezolizumab plus bevacizumab and chemotherapy in patients with EGFR- or ALK-rearranged or translocated non–small-cell lung cancer. *J Clin Oncol* 2024; 42(11): 1241–1251

6.25 There were substantially more patients in the AmiCP arm experiencing Grade ≥3 TEAEs compared to CP arm (72.3% vs. 48.1% respectively). The most common Grade ≥3 TEAEs were blood and lymphatic system disorders such as neutropenia (45.4% vs. 21.4%), leukopenia (20.0% vs. 9.5%) and anaemia (11.5% vs. 9.5%).

6.26 TEAEs leading to death were reported in three patients (2.3%) in the AmiCP arm and three (1.2%) in the CP arm. Two of the deaths in the AmiCP arm were assessed as being related to study treatment, one death due to sepsis (assessed as related to carboplatin and pemetrexed) and another due to Grade 3 infectious pleural effusion and ventricular fibrillation (assessed as related to amivantamab and pemetrexed).

6.27 Rash, IRRs and pneumonitis / interstitial lung disease (ILD) were pre-identified AEs of special interest (AESIs). AESIs were reported more often in the AmiCP arm (88.5%) compared to the CP arm (15.6%), primarily driven by higher incidences of rash and IRRs. Most were reported to be Grade 1 or 2 AEs and managed through dose reductions or interruptions or in the case of IRRs, pre-specified pre-infusion medications. The PBAC noted Grade 3 - 4 rash occurred in 11% of AmiCP patients[10].

Indirect comparison: AmiCP vs. ABCP

6.28 The submission presented a side-by-side comparison of the safety data from MARIPOSA-2 and ATTLAS trials (**Error! Reference source not found.**). Data for the whole trial population from both trials were used as safety data specific to the subgroup of patients who had prior osimertinib treatment from the ATTLAS trial was not reported.

Table 8: Comparison of safety data from MARIPOSA-2 and ATTLAS

	MARIPOSA-2		ATTLAS	
	AmiCP (n=130)	**CP (n=243)**	**ABCP (n=151)**	**CP (n=74)**
Median f/up, mths	8.7		26.1	
Median DoT, mths	6.3	3.7	NR	NR
Reported AEs				
1 or more	130 (100%)	227 (93.4%)	149 (98.7%)	62 (83.8%)
Related to study treatment	129 (99.2%)	210 (86.4%)	146 (96.7%)	56 (75.7%)
Grade ≥3	94 (72.3%)	117 (48.1%)	61 (40.4%)	16 (21.6%)
Related to study treatment	87 (66.9%)	86 (35.4%)	53 (35.1%)	11 (14.9%)
Serious AEs	42 (32.3%)	49 (20.2%)	33 (21.9%)	1 (1.4%)
Led to death[b]	2 (1.5%)	1 (0.4%)	3 (2.0%)	0

Source: Table 2.62, p192 of the submission

Abbreviations: AEs= adverse events; AmiCP= amivantamab in combination with carboplatin and pemetrexed; ABCP= atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; CP= carboplatin plus pemetrexed; f/up= follow up; DoT= duration of treatment; mths= months; n= number of patients; RD=risk difference; RR=risk ratio

[a] MARIPOSA-2 reported AEs related to drug discontinuation/interruption/reduction by individual study agent

Bold text indicates significant results.

6.29 The submission noted that compared to CP, ABCP (relative difference [RD]=0.15, relative risk [RR]=1.18) reported higher relative rates for AEs of any grade compared to AmiCP (RD=0.07, RR=1.07). Conversely, AmiCP had a higher RD but lower RR for Grade ≥3 AEs than ABCP (AmiCP: RD=0.24, RR=1.50; ABCP: RD=0.19, RR=1.87).

[10] Table 9, amivantamab TGA Product Information.

6.30 In general, it is observed that the reported rates for AEs in the AmiCP arm were higher than those in the CP arm in the MARIPOSA-2 trial and similarly, rates in the ABCP arm were higher than the CP arm in the ATTLAS trial. However, comparisons between trials may be limited for reasons described in paragraph 6.22.

6.31 The submission noted that the rates of reported AEs were higher in the CP arm in the MARIPOSA-2 trial compared to those in the ATTLAS trial and suggested that this may be due to the underlying differences in patient profiles and this may bias against AmiCP. As described in paragraph 6.22, more patients in the ATTLAS trial had a higher ECOG performance score and were likely exposed to longer durations of treatments compared to patients in the MARIPOSA-2 trial, therefore it is not reasonable to assume that this would bias against AmiCP.

Benefits/harms

6.32 A summary of the comparative benefits and harms for AmiCP versus CP is presented in **Error! Reference source not found.**.

Table 9: Summary of comparative benefits and harms for AmiCP and CP

Benefits				
Progression free survival (median duration of follow up 8.74 months)				
Event	**AmiCP**	**CP**	**Absolute Difference**	**HR (95% CI)**
Progressed, n (%)	74/131 (56.5%)	171/263 (65.0%)	-	**0.48 (0.36, 0.64); p<0.0001**
Median PFS, months (95% CI)	6.28 (5.55, 8.41)	4.17 (4.04, 4.44)	2.11	
% not progressed at 6 months (95% CI)	51 (41, 60)	30 (23, 36)	21	
% not progressed at 9 months (95% CI)	38 (28, 48)	16 (11, 23)	22	
% not progressed at 12 months (95% CI)	22 (12, 34)	13 (8.0, 20)	9	
Overall survival (median duration of follow up 18.1 months)				
Deaths, n/N (%)	65/131 (49.6%)	143/263 (54.4%)	-	**0.73 (0.54, 0.99), p=0.0386**
Median OS, months (95% CI)	17.74 (15.97, 22.37)	15.34 (13.73, 16.76)	2.4	
% Alive at 6 months (95% CI)	91 (84, 95)	87 (82, 90)	4	
% Alive at 9 months (95% CI)	80 (72, 86)	73 (67, 78)	7	
% Alive at 12 months (95% CI)	70 (61, 77)	63 (57, 69)	7	
% Alive at 18 months (95% CI)	50 (40, 59)	40 (33, 46)	10	

Harms						
	AmiCP n/N	**CP n/N**	**RR (95% CI)**	**Event rate/100 patients***		**RD as % (95% CI)**
				AmiCP	**CP**	
Rash	56/130	12/243	8.72 (4.86, 15.67)	43	5	38.14 (29.20, 47.08)
Infusion Related Reaction	76/130	1/243	142.06 (19.98,1009.88)	59	0.4	58.05 (49.54, 66.56)
Grade ≥ 3 neutropenia	59/130	52/243	2.12 (1.56, 2.88)	45	21	23.99 (13.99, 33.98)
Grade ≥ 3 leukopenia	26/130	23/243	2.11 (1.26, 3.55)	20	10	10.53 (2.74, 18.33)

Source: Table 2.47 p165, Table 2.48 p167 of the submission; Table 2.27, p135 of the submission, Table 2.29, p141 of the submission.
Abbreviations: AmiCP = amivantamab in combination with carboplatin and pemetrexed; CI= confidence interval; CP= carboplatin plus pemetrexed; HR = hazard ratio; n=number of patients experiencing event; N= total number of patients; PBO = placebo; RD = risk difference; RR = risk ratio
Bold text indicates statistically significant results

6.33 On the basis of direct evidence presented by the submission, for every 100 patients treated with AmiCP in comparison with CP:

- Approximately 21 additional patients will remain progression-free after 6 months.
- Approximately 4 additional patients will remain alive after 6 months.

6.34 On the basis of direct evidence presented by the submission, for every 100 patients treated with AmiCP in comparison with CP over a median of 8.71 months duration of follow-up:

- Approximately 38 additional patients had a rash.
- Approximately 58 additional patients had an infusion related reaction.
- Approximately 24 additional patients had a Grade ≥ 3 neutropenia.

- Approximately 11 additional patients would be diagnosed with Grade 3 or 4 leukopenia (a decrease in the white blood cell count).

6.35 The 'side by side' comparison between AmiCP and ABCP presented in the submission did not allow for a quantitative comparison of the benefits and harms of AmiCP and ABCP. Accordingly, a benefits/harms table has not been presented for this indirect comparison.

Clinical claim

6.36 The submission claimed AmiCP is superior in terms of effectiveness compared with CP. The ESC considered this claim is adequately supported based on the statistically significant difference in PFS (HR=0.48; 95% CI: 0.36, 0.64; p<0.0001), OS (HR=0.73; 95% CI: 0.54, 0.99; p=0.0386), ORR (OR=3.1; 95% CI: 2.00, 4.80; p<0.0001) and icPFS (HR=0.65; 95% CI: 0.49, 0.84; nominal p=0.0012) for AmiCP compared to CP presented in the MARIPOSA-2 trial. The respective differences between the two treatment arms for PFS and OS were 2.1 months and 2.4 months.

6.37 The submission claimed AmiCP is inferior but manageable in terms of safety compared to CP. The ESC considered the claim of inferior safety was adequately supported. Although there were substantially more patients in the AmiCP arm experiencing Grade ≥3 TEAEs compared to CP arm (72.3% vs. 48.1%) and SAEs (32.3% vs. 20.2%), the evaluation noted most were related to blood and lymphatic system disorders (neutropenia, leukopenia and anaemia) and infusion related reactions which could be managed through dose interruptions or reductions and/or pre-infusions medications.

6.38 The ESC considered the submission's conclusion that AmiCP is superior to ABCP is not well supported based on the approach taken and the evidence presented. The submission claimed that AmiCP is superior in terms of effectiveness compared with ABCP and non-inferior in terms of safety compared to ABCP, however:

- The clinical claim was 'inferred' based on ABCP not having demonstrated superiority to CP in the proposed patient population using exploratory subgroup analysis results from the ATTLAS trial and that AmiCP has demonstrated superiority to CP based on the results from the MARIPOSA-2 trial.
- The results from the Bucher ITC analysis conducted during the evaluation indicated that there was no statistically significant differences between AmiCP and ABCP for either of the prior osimertinib in first- or second-line treatment subgroups, although noting the limitations of small sample sizes and transitivity concerns in terms of differences in trial design, setting, duration of study follow-up and baseline characteristics such as race and ECOG performance status.

6.39 The PBAC considered that the claim of superior comparative effectiveness and inferior comparator safety compared to CP was reasonable.

6.40 The PBAC considered that the claim of superior comparative effectiveness and non-inferior safety compared to ABCP was not supported by the data.

Economic analysis

6.41 The submission presented a modelled cost utility analysis (CUA) using a three-state partitioned survival model over a seven-year time horizon, comparing AmiCP with CP. Additionally, the same model was used to generate an ICER for AmiCP vs ABCP. The base case ICER in the submission was calculated as a weighted ICER applying a comparator split of 83.1% ABCP, 16.9% CP.

6.42 The submission applied the published price of atezolizumab as the base case. Atezolizumab has a SPA in place; therefore, base case ICERs are presented herein using 50% of the published price of atezolizumab.

6.43 A summary of the key components of the economic evaluation is presented in **Error! Reference source not found.** below.

Table 10: Summary of model structure, key inputs and rationale

Component	Summary
Treatments	AmiCP vs CP; AmiCP vs ABCP; and AmiCP vs a weighted comparator mix (83.1% ABCP, 16.9% CP). The model explicitly compared AmiCP with CP using MARIPOSA-2 data and ABCP is represented by applying CP's PFS, OS and TTTD functions from MARIPOSA-2, with ABCP-specific costs and dose intensity.
Time horizon	Seven years in the model base case, described as a lifetime horizon, versus median follow up in MARIPOSA-2 of 8.7 months for PFS and 18.1 months for OS.
Outcomes	Life years (LYs) and quality-adjusted life years (QALYs)
Methods used to generate results	Cohort cost-utility analysis using a three-state partitioned survival model for PFS, post-progression survival and death. Kaplan-Meier (KM) data from MARIPOSA-2 were used.. Subsequent therapy effects were assumed to be fully captured in OS, with only costs of post-progression therapy modelled explicitly. A stepped structure provided trial-based, extrapolated life-year and utility-weighted analyses. The model was implemented in Excel.
Health states	Three mutually exclusive health states: PFS, post-progression (progressed disease) and death.
Cycle length	One week cycle
Allocation to health states	Health state occupancy over time was determined by PFS and OS curves from MARIPOSA-2: the proportion progression-free was taken from PFS, the proportion alive from OS, and the proportion progressed inferred as OS minus PFS at each time point. Background mortality was taken from Australian life tables (2021-23) and applied as a lower bound to OS hazards. For ABCP, CP's PFS, OS and TTTD curves were applied.
Extrapolation method	KM estimates from MARIPOSA-2 informed transitions for PFS, OS and TTTD until fewer than 20% of patients remained at risk (approximately 9.5 vs 5.8 months for PFS and 19.3 vs 17.8 months for OS in the AmiCP vs CP arms) for each endpoint and arm; beyond this, independent parametric survival models were fitted by arm. Base-case selections were loglogistic for AmiCP PFS and generalised gamma for CP/ABCP PFS (both best-fitting by AIC+BIC), and gamma for OS in all arms; for OS, gamma was best-fitting for CP/ABCP but ranked fourth for AmiCP. TTTD used generalised gamma for the amivantamab component, Gompertz for the chemotherapy component in AmiCP and loglogistic for CP/ABCP, all best fitting by AIC/BIC. No explicit convergence of treatment arms was imposed within the seven-year horizon.
Health related quality of life	Utilities were derived from EQ-5D-5L data collected in MARIPOSA-2 and valued using Australian tariffs (Norman et al., 2023). Treatment-specific utilities were applied in the pre-progression state (AmiCP 0.875; CP 0.893), with the AmiCP pre-progression utility also applied to ABCP; a pooled post-progression utility of 0.840 was used for all arms. QALY gains with AmiCP were driven mainly by additional time spent progression free rather than utility differences between arms.
Other key components	Subsequent systemic therapy was simplified to docetaxel monotherapy (four 3-weekly cycles) applied as a one-off cost at progression to 58.3% of AmiCP patients and 70.2% of CP/ABCP patients, without modelling differential survival effects. A one-off end-of-life hospital and health-care cost of $62,814.37 per cancer death was applied.

Source: Table 3.1 (p206), Table 3.4 (p214) and Sections 3.2-3.6 of the submission.
Abbreviations: AmiCP=amivantamab plus carboplatin plus pemetrexed; CP=carboplatin plus pemetrexed; ABCP=atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; PFS=progression free survival; OS=overall survival; TTTD=time to treatment discontinuation; LY=life year; QALY=quality-adjusted life year; KM=Kaplan-Meier; AIC=Akaike information criterion; BIC=Bayesian information criterion; EQ-5D-5L=EuroQol 5-dimension 5-level; PBS=Pharmaceutical Benefits Scheme; SPA=special pricing arrangement.

6.44 A time horizon of 7 years was applied as the base case in the model. This is long relative to the 8.7-month PFS and 18.1-month OS median follow-up in MARIPOSA-2.

6.45 The ESC noted a time horizon of 7.5 years was applied to the economic model for first line use of osimertinib in combination with chemotherapy (paragraph 6.50, 7.13,

osimertinib PSD, May 2025 PBAC meeting). Given that the proposed treatment with AmiCP is positioned as second-line and beyond, a shorter time horizon of 5 years may be more appropriate given the poor prognosis of these patients.

6.46 The submission applied the PFS, OS and TTTD of the CP arm from MARIPOSA2 to ABCP, based on the justification that (1) results from the ATTLAS trials did not show that ABCP improved PFS or OS relative to CP in the prior osimertinib setting, and that (2) there is no head-to-head data comparing AmiCP with ABCP. Consequently, the ABCP arm differed from CP in the economic model primarily through cost inputs and a small pre-progression utility difference. Under the assumed comparator mix (83.1% ABCP; 16.9% CP), this approach effectively assumes that most patients receive a higher-cost regimen that is modelled as providing no additional survival benefit over CP, which materially increases comparator costs and improves the weighted ICER for AmiCP. The ESC noted this effectively resulted in a comparison with treatment that is not cost effective (i.e., additional cost of ABCP with no additional benefit).

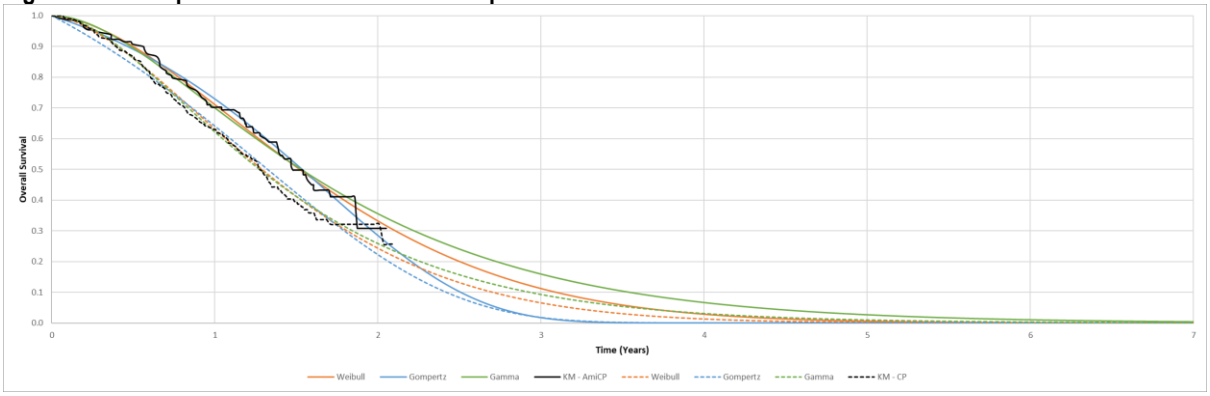
Extrapolations

6.47 The submission justified the use of independent parametric extrapolations for PFS and OS by asserting violation of the proportional hazards assumption based on empirical hazard and log-log plots, without presenting formal statistical tests. The PSCR argued that, although the Schoenfeld test did not demonstrate a statistically significant proportional hazard violation, the cumulative hazard, log–log, and Schoenfeld residual plots suggested time-varying hazards. Therefore, independent fitting might be more appropriate. The ESC noted this was reasonable.

6.48 To extrapolate OS, the submission chose the gamma distribution for AmiCP (fourth-ranking by AIC+BIC) and gamma for CP/ABCP (best fitting by AIC+BIC). The choice of OS distributions for both AmiCP and CP/ABCP remains highly uncertain due to limited observed OS data, uncertainty around durability of the IA2 treatment effect, and the extent of extrapolation beyond the MARIPOSA-2 data.

6.49 Figure 3 overlays the MARIPOSA-2 Kaplan-Meier OS curves for AmiCP and CP with the selected parametric extrapolations.

Figure 3:Trial Kaplan Meier and modelled extrapolated OS curves for AmiCP and CP



Source: Figure 3.15, p230 of the submission.
Abbreviations: AmiCP = amivantamab plus carboplatin plus pemetrexed; CP = carboplatin plus pemetrexed; KM = Kaplan–Meier; OS = overall survival.
Note: Other distributions were presented in the submission but omitted from the figure due to poor statistical fit or not clinically plausible.

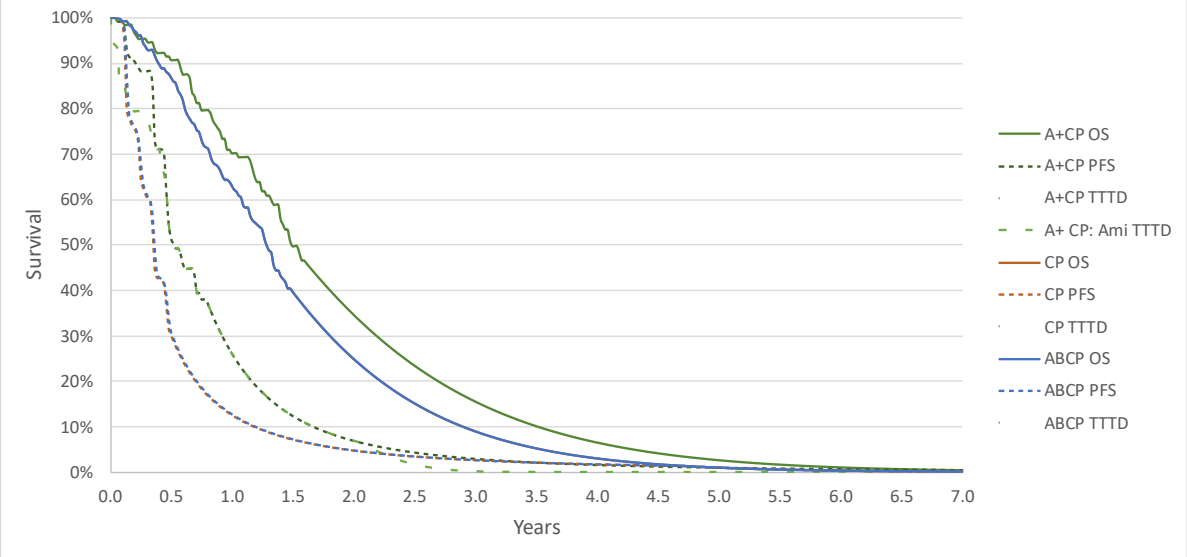
6.50 When the comparator curves are considered alongside the AmiCP curve, the base-case using gamma distribution for both AmiCP and CP/ABCP implies 3-year OS of 16.0% versus 9.4% (an absolute difference of 7 percentage points), whereas using Weibull for AmiCP with gamma for CP/ABCP narrows this gap to about 11.3% versus 9.4% (2 percentage points). The proportions of patients remaining event free at 18 months in the MARIPOSA-2 trial were 50% (95% CI, 40, 59) for the AmiCP arm and 40% (95% CI, 33, 46) for the CP arm. The 95% CI were overlapping therefore, the assumption that the treatment benefit observed from the trial is maintained over the time horizon is highly uncertain. Applying the Weibull and gamma distributions for AmiCP and CP/ABCP respectively provides a more conservative extrapolation and would increase the ICER from $$55,000 to < $75,000/QALY gained to $$115,000 to < $135,000/QALY gained (+[redacted]%). The PSCR noted that applying a Weibull distribution resulted in the hazard for death increasing rapidly in the extrapolated period to the point where they are higher than observed in the trial. The PSCR stated the hazards of death using Weibull are inconsistent with the observed OS KM data and therefore lacked clinical plausibility.

6.51 The submission fitted separate distributions for TTTD for amivantamab (generalised gamma) and CP (Gompertz) for the AmiCP arm, and for the CP/ABCP (log-logistic) arm. These distributions were selected based on best statistical fit (AIC/BIC).

6.52 Although the TTTD Kaplan-Meier data were relatively mature (with 80.2% discontinuation events in both arms), the model used observed KM data until the <20% at-risk cut-off and extrapolated thereafter. Time on treatment was calculated as the minimum of the TTTD and PFS curves (treatment until progression), so the parametric form chosen for amivantamab TTTD only affects costs in periods where modelled TTTD is below modelled PFS (for longer-term progression-free survivors). In sensitivity analyses (Table 14) varying amivantamab TTTD function increased the ICER by up to [redacted]%.

6.53 Figure 4 below shows the three state partitioned survival traces over seven years for AmiCP, CP and ABCP.

Figure 4: Modelled health state traces over seven years (base case economic model)



Source: Figure 3.21, p254 of the submission.
Abbreviations: A+CP = amivantamab plus carboplatin plus pemetrexed; ABCP = atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; Ami = amivantamab; CP = carboplatin plus pemetrexed; OS = overall survival; PFS = progression free survival; TTTD = time to treatment discontinuation

Health state utilities

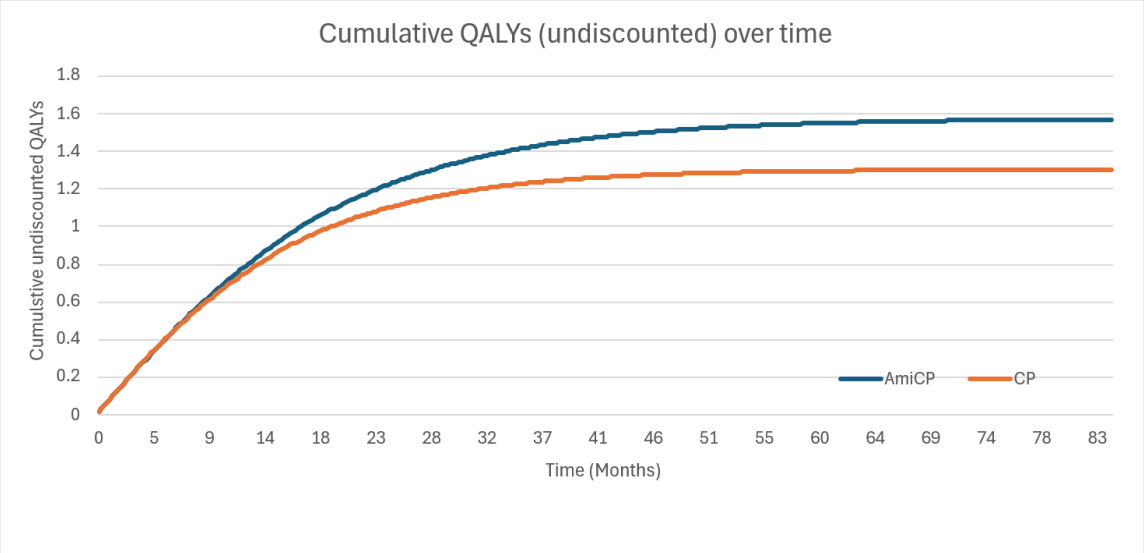
6.54 Quality of life data using the EQ-5D-5L from the MARIPOSA-2 trial were used to inform the utility values for the pre-progression and post-progression health states in the base case analysis. The submission applied treatment-specific pre-progression utilities of 0.875 for AmiCP (also extended to ABCP) and 0.893 for CP to reflect adverse event differences. The submission justified extending AmiCP's utility value to ABCP based on ABCP's inferior adverse event profile relative to CP (due to the additional components in ABCP) and AmiCP's proposed non-inferiority to ABCP in terms of safety.

6.55 For the post-progression health state, the submission applied pooled utility values (0.840) across arms as subsequent therapies were assumed to be similar irrespective of initial treatment.

6.56 The utility values applied were higher than those applied in similar populations considered by the PBAC in previous considerations. For example, in previously untreated EGFR-mutant advanced NSCLC, PBAC suggested progression-free and post-progression utilities of approximately 0.79 and 0.64, respectively (paragraph 6.26, osimertinib PSD, November 2023 PBAC meeting).

6.57 The PSCR noted that the calculation of QALYs was based on 76.1% of the total QALYs accrued during the observed trial period. As such, the PSCR stated the model was based predominantly on observed data rather than long-term extrapolation assumptions. However, the ESC noted the incremental QALYs gained in the trial period was 33%, which indicated that 67% of incremental QALY gain was accrued later in the cycle, within the horizon which is more influenced by extrapolated survival assumptions (see Figure 5).

Figure 5: Cumulative incremental QALYs over time, by treatment arm



Source: Economic model provided with submission
Abbreviations: AmiCP = amivantamab plus carboplatin plus pemetrexed; CP = carboplatin plus pemetrexed; OALYs = Quality adjusted life-years.

Costs

6.58 To calculate the per cycle cost of amivantamab, CP and ABCP, the submission factored in the proportion of skipped/reduced doses, the proportion of patients over (14%)/under 80 kg (86%), and the dose intensity for initial/maintenance treatment based on the MARIPOSA-2 and ATTLAS trials.

6.59 A one-off AE costs of $[redacted] per patient for the AmiCP arm, $[redacted] for CP arm and $[redacted] for the ABCP arm were applied in cycle 1 estimated based on incidence rates of Grade ≥3 and AESI events from MARIPOSA 2 (AmiCP/CP) and ATTLAS (ABCP).

6.60 The submission stated that subsequent therapy costs were applied as a one off when patients progressed, using docetaxel (4 cycles) as the representative regimen; proportions progressing to subsequent therapy were 58.3% (AmiCP) and 70.2% (CP/ABCP). This simplification appears pragmatic but favours AmiCP on costs via lower uptake of subsequent therapy.

6.61 The submission applied an end of life costs of $62,814.37 (2024 AUD) per cancer death derived Langton et al. 2016 which reported health care service use costs in the last six-months of life among patients dying of cancer. The end-of-life cost applied in the model appears high and likely driven by the high inflation rates used.

6.62 **Error! Reference source not found.** summarises the key drivers of the economic model.

Table 11: Key drivers of the model

Description	Method/Value	Impact Base case: $[redacted][1]/QALY [a]
Extrapolation of overall survival (AmiCP and CP/ABCP)	Gamma distributions were used for OS in both AmiCP and CP/ABCP (best fitting for CP/ABCP but ranked fourth for AmiCP)	High, favour AmiCP. The choice of distributions to extrapolate OS for both AmiCP and CP /ABCP is highly uncertain as discussed in paragraph 6.48. For example, applying the Weibull and gamma distributions for AmiCP and CP/ABCP respectively would result in a more conservative extrapolation and would increase the ICER from $[redacted][1]/QALY gained to $[redacted][2]/QALY gained (+[redacted]%).
ABCP/CP comparator split	83.1% ABCP and 16.9% CP. Issues relating to the proposed comparator split are discussed in paragraph 5.4. The comparator split is skewed towards ABCP and favours AmiCP.	High, favours AmiCP. Applying ABCP 30% / 70% CP increased the ICER to $[redacted][3] (+[redacted]%)

Source: Tables 3.39-3.43 of the submission.
Abbreviations: ABCP = atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; AmiCP = amivantamab plus carboplatin plus pemetrexed; CP = carboplatin plus pemetrexed; DUSC = Drug Utilisation Sub-Committee; EQ-5D-5L = EuroQol 5-dimension 5-level questionnaire; ICER = incremental cost-effectiveness ratio; KM = Kaplan–Meier; OS = overall survival; PBAC = Pharmaceutical Benefits Advisory Committee; PBS = Pharmaceutical Benefits Scheme; PFS = progression free survival; QALY = quality-adjusted life year; TTTD = time to treatment discontinuation
[a] ICER based on 50% published price of atezolizumab and comparator split of ABCP/PDC 83.1%/16.9%
[b] Informed by previous PBAC decisions (paragraph 6.26, osimertinib, Public Summary Document, November 2023 PBAC meeting).
Note: As described in paragraphs 6.46 and 6.46, the submission's approach of treating ABCP as equivalent to CP is likely to have important implications on the ICER and this could not be tested during the evaluation due to structure of the model.
The redacted values correspond to the following ranges:
[1] *$55,000 to < $75,000*
[2] *$115,000 to < $135,000*
[3] *$155,000 to < $255,000*

6.63 The results of the stepped economic evaluation are presented in **Error! Reference source not found.** below.

Table 12: Results of the stepped economic evaluation

Step and component	AmiCP	CP	ABCP	Increment vs CP	Increment vs ABCP
Step 1: trial-based analysis (18.1 months, no discounting; drug, administration and adverse event costs only)					
Costs	$[redacted]	$3,320	$37,182	$[redacted]	$[redacted]
LYs	1.212	1.116	1.116	0.096	0.096
Incremental cost per LY gained				$[redacted][1]	$[redacted][2]
Weighted ICER [a]				**$[redacted][3] per LY**	
Step 2: lifetime analysis (7-year horizon) 5% discounting, inclusion of third line and end of life costs					
Costs	$[redacted]	$64,017	$102,410	$[redacted]	$[redacted]
LYs	1.759	1.466	1.466	0.293	0.293
Incremental cost per LY gained				$[redacted][3]	$[redacted][4]
Weighted ICER [a]				**$[redacted][5] per LY**	
Step 3: Same as Step 2 plus utility weights applied					
Costs	$[redacted]	$64,017	$102,410	$[redacted]	$[redacted]
QALYs	1.507	1.263	1.252	0.244	0.255
Incremental cost per QALY gained (base case)				$[redacted][3]	$[redacted][5]
Weighted ICER [a]				**$[redacted][6] per QALY**	

Source: Table 3.39, P256 of the submission.

Abbreviations: ABCP = atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; AmiCP = Amivantamab plus carboplatin plus pemetrexed; CP = carboplatin plus pemetrexed; LYs = life years; QALYs = quality-adjusted life years

[a] Based on comparator split of ABCP/PDC: 83.1%/16.9%.

Notes: All ABCP costs and ICERs are calculated during the evaluation assuming atezolizumab at 50% of its published price. Results applying the effective price of atezolizumab under the SPA are presented in the CIC section. *Analyses in italics were conducted during evaluation.*

The redacted values correspond to the following ranges:

[1] *$455,000 to < $555,000*

[2] *$135,000 to < $155,000*

[3] *$155,000 to < $255,000*

[4] *$35,000 to < $45,000*

[5] *$45,000 to < $55,000*[6] *$55,000 to < $75,000*

6.64 The results of key sensitivity analyses presented by the submission are summarised in Table 13.

Table 13: Results of sensitivity analyses

Analyses	Incremental cost	Incremental QALY	ICER	% Change from Base Case
Base case [a]	**$[redacted]**	**0.253**	**$[redacted][1]**	**-**
Discount rate (base case: 5%)				
0%	$[redacted]	0.277	$[redacted][1]	-[redacted]%
3.50%	$[redacted]	0.260	$[redacted][1]	-[redacted]%
Time horizon (base case: 7 years)				
5 years	$[redacted]	0.242	$[redacted][2]	[redacted]%
Parametric function used for AmiCP OS (base case: Gamma)				
Weibull	$[redacted]	0.160	$[redacted][3]	[redacted]%
Parametric function used for AmiCP: amivantamab TTTD (base case: Generalised Gamma)				
Exponential	$[redacted]	0.253	$[redacted][2]	[redacted]%
Weibull	$[redacted]	0.253	$[redacted][2]	[redacted]%
Gompertz	$[redacted]	0.253	$[redacted][2]	[redacted]%
Gamma	$[redacted]	0.253	$[redacted][2]	[redacted]%
Parametric function used for CP/ ABCP TTTD (base case: Loglogistic)				
Weibull	$[redacted]	0.253	$[redacted][2]	[redacted]%
Gamma	$[redacted]	0.253	$[redacted][2]	[redacted]%
Generalised Gamma	$[redacted]	0.253	$[redacted][2]	[redacted]%

Source: Table 3.41 of the submission and developed during the evaluation using the submitted economic model workbook.
Abbreviations: AmiCP=amivantamab plus carboplatin plus pemetrexed; CP=carboplatin plus pemetrexed; ABCP=atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; ICER=incremental cost-effectiveness ratio; QALY=quality-adjusted life year; SPA=special pricing arrangement; OS=overall survival.
[a] Based on 50% published price of atezolizumab and comparator split of 83.1% ABCP / 16.9% CP
The redacted values correspond to the following ranges:
[1] *$55,000 to < $75,000*
[2] *$75,000 to < $95,000*
[3] *$115,000 to < $135,000*

6.65 Additional sensitivity analyses conducted during the evaluation are presented in Table 14.

Table 14: Results of sensitivity analyses conducted during the evaluation

Analyses	Incremental cost	Incremental QALY	ICER	% Change from Base Case
Base case [a]	**$**	**0.253**	**$** [1]	**-**
Alternative comparative splits (base case: 83.1% ABCP / 16.9% CP)				
ABCP/CP (30% ABCP / 70% CP); consistent with Osimertinib PSD (paragraph 7.11, Osimertinib PSD, July 2025 PBAC meeting)	$	0.248	$ [2]	%
End of life cost (base case: $62,814.37)				
End-of-life cost set to zero for incident deaths)	$	0.253	$ [3]	%
Utility values (base case: pre-progression (AmiCP 0.875/ CP 0.893); post progression pooled (0.840))				
Pooled utilities scenario: pre-progression utility 0.79 (FLAURA trial) and post-progression utility 0.64 (Labbe et al 2017) applied to AmiCP, CP and ABCP (replacing trial-based utilities)	$	0.226	$ [3]	%
KM-to-parametric switch point (base case: switch at the 20% at-risk cut-off)				
Switch at the 10% at-risk cut-off	$	0.259	$ [3]	%
Multivariate analyses				
#1: comparator split (30% ABCP / 70% CP) + AmiCP OS extrapolated using Weibull	$	0.154	$ [4]	%
#2: #1 + 5-year time horizon	$	0.157	$ [4]	%
#3: #2 + End-of-life cost set to zero	$	0.157	$ [4]	%

Source: Table 3.41 of the submission and developed during the evaluation using the submitted economic model workbook.
Abbreviations: AmiCP=amivantamab plus carboplatin plus pemetrexed; CP=carboplatin plus pemetrexed; ABCP=atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; ICER=incremental cost-effectiveness ratio; QALY=quality-adjusted life year; SPA=special pricing arrangement; OS=overall survival.
[a] Based on 50% published price of atezolizumab.
[b] Using data from the proportion of patients with first-post osimertinib treatment (2L)
[c] Using the combined data from the proportion of patients with first- and second-post osimertinib treatment (2L and 3L)
The redacted values correspond to the following ranges:
[1] *$55,000 to < $75,000*
[2] *$155,000 to < $255,000*
[3] *$75,000 to < $95,000*
[4] *$255,000 to < $355,000*

6.66 The ESC noted the base case ICER using the economic model comparing AmiCP vs CP (the most robust model, see paragraph 6.41) was $155,000 to < $255,000 per QALY gained (see **Error! Reference source not found.**) and the weighted ICER assuming 30% ABCP use was $155,000 to < $255,000 per QALY (see Table 14). In the pre-PBAC response, the sponsor considered the 30% ABCP use undervalued the clinical benefit of AmiCP in EGFRm NSCLC post-osimertinib.

6.67 The PBAC noted that economic and financial models calculated a weighted average of 75.1 vials of amivantamab administered over an average of 13.25 three weekly

treatment cycles (9.14 months).[11] The PBAC noted this resulted in an average of 5.67 vials of amivantamab per three weekly treatment cycle. The PBAC noted the drug cost per 3 weekly treatment cycle for amivantamab was $[redacted] compared to $4,019.53 for atezolizumab plus bevacizumab using the assumed effective price of atezolizumab.

Table 15: Drug cost per 3 weekly treatment cycle

	Amivantamab	Atezolizumab	Bevacizumab
Ex-manufacturer price	$[redacted] per 350 mg vial	$3,373.68 per 1,200 vial	$215.28 per 400 mg vial
Number of vials per 3 weekly cycle	5.67	1	3[1]
Cost per 3 weekly cycle	$[redacted]	$3,373.68	$645.84
Total cost per 3 weekly cycle	$[redacted]	$4,019.53	

1. Dose of 15 mg/ kg and assuming a mean weight of 65 kg, rounded to 3 vials

Drug cost/patient/course

Table 16: Drug cost per patient for proposed and comparator drugs

	AmiCP (amivantamab only)			Comparators					
				CP			ABCP		
	Trial	Model	Financial estimates	Trial	Model	Financial estimates	Trial	Model	Financial estimates
Mean duration (months)	6.49 [a]	9.14 [b]	9.14 [b]	4.20 [a]	6.84 [b]	6.84 [b]	12.41 [g]	6.84 [b]	6.84 [b]
Cost/patient/ month	$[redacted] [c]	$[redacted] [c]	$[redacted] [e]	$279 [h]	$279 [c]	$289 [e]	$4,534 [i]	$6,067 [c]	$6,137 [e]
Cost/patient/ course	$[redacted] [h]	$[redacted] [d]	$[redacted] [f]	$1,172 [h]	$1,909 [d]	$1,980 [f]	$56,237 [i]	$41,495 [d]	$42,003 [f]

Source: Compiled based on MARIPOSA-2 trial data, Attachment 3.1 (economic model) and Attachment 4.1 (financial estimates) of the submission.

Abbreviations: NR=not reported; NC=not calculatable.

Notes: The AmiCP columns report the amivantamab component only; dose intensity and weight/BSA assumptions follow those applied in the submitted economic model (MARIPOSA-2 for AmiCP and CP; ATTLAS-derived for ABCP), including the MARIPOSA-2 weight split (86% <80 kg; 14% ≥80 kg). ABCP costs were calculated assuming atezolizumab at 50% of its published price;

[a] As reported in MARIPOSA-2 trial at the primary analysis (clinical cutoff July 2023)

[b] Calculated based on mean TTD (years) obtained from economic model. The same mean duration was applied in financial estimates.

[c] Calculated based on cost per course (d) by mean duration.

[d] Obtained directly from the economic model.

[e] Calculated based on cost per course (f) by mean duration.

[f] Total drug cost across the initial and continuing phases (extracted from submission's financial estimates workbook), assuming 81.1% compliance.

[g] Estimated from ATTLAS mean number of atezolizumab cycles during induction (n=151) and maintenance (n=131), weighted by the proportion of patients who received maintenance (131/151). Each cycle was assumed to be 21 days. Mean duration (months) = total cycles × 21 / 30.4375 (365.25/12).

[h] Trial costs for AmiCP and CP estimated by multiplying the model-based cost/patient/month by the mean duration reported in MARIPOSA-2.

[i] Trial costs for ABCP estimated by scaling the model cost/patient/course (d) by the ratio of cumulative dose-intensity-adjusted cycles between ATTLAS and the model (mean cycles and relative dose intensity from Park et al. 2023 Table A4). Relative dose intensity for carboplatin was not reported in Table A4 and was assumed to be 100% for this approximation.

[11] 73 vials for patients weighing less than 80 kg (14%) and 88 vials for patients weighing 80 kg or more (86%), see AmiCP Dosing worksheet in Attach 4.1 UCM Ami 2 cEGFR Nov-25 (BASE).xls provided with submission

Estimated PBS usage & financial implications

6.68 This submission was not considered by DUSC.

6.69 The submission used an epidemiological approach to estimate the financial implications of listing amivantamab, used in combination with PDC, for the treatment of EGFRm locally advanced/metastatic NSCLC where the condition has progressed on or after osimertinib.

6.70 The submission used the PBS 100% data provided by the DUSC Secretariat as their starting source to estimate the number of patients that would be eligible for treatment with AmiCP. The PBS data included patients who had progressed on osimertinib and had gone on to receive subsequent therapy from the 2018-19 financial year to 2024-25. The submission estimated that there would be 860 incident patients in Year 1 (2026), growing to 1,409 patients in Year 6 (2031) using a linear extrapolation function. Although the linear function was fitted to historical data, it is uncertain if the trend in clinical practice would continue in the same way with a 10.5% increase annually which exceed the average increase of age-standardised incidence rate of lung cancer of 1.2% per year.[12]

6.71 The 100% PBS data included all patients who initiated subsequent therapy post-osimertinib. Although this is consistent with the requested listing (see paragraph 3.3), it is broader than the population studied in the MARIPOSA-2 trial by including patients treated with osimertinib in the adjuvant and the earlier stages of NSCLC. A

6.72 A summary of the key inputs in the financial analysis is presented in Table 17.

[12] Lung cancer statistics and trends. Cancer Council Victoria. https://www.cancervic.org.au/about-cancer/types/statistics/lung-cancer.html

Table 17: Key inputs for financial estimates

Parameter	Value applied and source	Comment
Incident patients (projected)	860 in Year 1 to 1,409 in Year 6; 100% PBS data provided by DUSC (data range from 2018/19 till 2024/25).	Year 1 estimates (2026) projected using linear function based on historical data. Includes all patients who initiated subsequent therapy post-osimertinib (irrespective of treatment line).
% with a WHO status of 0-2 (incident)	83.0%; post-1L osimertinib patient demographics reported in AURORA study.	Reasonable.
Uptake rate (incident)	[redacted]% in Year 1, [redacted]% in Year 2, [redacted]% in Year 3 and [redacted]% in subsequent years	The evaluation considered the proposed uptake rates are uncertain and appear high given the inferior safety profile.
Prevalent pool	1,474; 100% PBS data.	Based on the total number of patients who initiated subsequent therapy post-osimertinib (with no death record) recorded between 2018 to 2024.
% with a WHO status of 0-2 (prevalent)	79.7%; post-2L osimertinib patient demographics reported in AURORA study.	Reasonable.
Uptake rate(prevalent)	[redacted]% in Year 1, [redacted]% in Year 2 and [redacted]% in Year 3	The evaluation considered the proposed uptake rates are uncertain and appear high given the inferior safety profile. The PBAC considered it is unclear if AmiCP will be used in patients who have previously received osimertinib in combination with CP.
Treatment duration (amivantamab)	9.14 months (39.75 weeks). Based on mean TTTD curve from the economic model	Consistent with economic model
Compliance rate	MARIPOSA-2 trial Ami: 81.28% (<80 kg), 80.11% (≥80 kg) C:91.90% P: 80.78%,	This appears reasonable and in line with the MARIPOSA-2 trial and economic model.
Comparator split displacement	ABCP: 83.1%; PDC: 16.9%. Submission's assumption based on DUSC data	
MBS Item 13950	$126.00 per administration	

Source: Compiled during the evaluation using information from Section 4 of the submission
Abbreviation: 1L= first line treatment; 2L= second line treatment; ABCP= atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; Ami= amivantamab; AmiCP= amivantamab in combination with carboplatin and pemetrexed; C= carboplatin; DUSC= drug utilisation subcommittee; MBS=Medicare benefits schedule; P=pemetrexed; PBS = pharmaceutical benefit scheme; WHO= world health organisation.

6.73 The number of patients treated, estimated use and financial implications for the proposed PBS listing of amivantamab are summarised in Table 18.

Table 18: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of patients treated	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Number of amivantamab scripts dispensed[a]	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Estimated financial implications of amivantamab						
Cost to PBS/RPBS less copayments ($)	[redacted][4]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][6]	[redacted][6]
Estimated financial implications for CP (as part of AmiCP)						
Cost to PBS/RPBS less copayments ($)	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]
Estimated financial implications for PDC[a] (substituted medications)						
Cost to PBS/RPBS less copayments ($)	-[redacted][8]	-[redacted][8]	-[redacted][8]	-[redacted][8]	-[redacted][8]	-[redacted][8]
Estimated financial implications for ABCP (substituted medications) [b]						
Cost to PBS/RPBS less copayments ($)	-[redacted][8]	-[redacted][8]	-[redacted][8]	-[redacted][8]	-[redacted][8]	-[redacted][8]
Net financial implications[b]						
Net cost to PBS/RPBS ($)	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]
Net cost to MBS ($)	-[redacted][8]	-[redacted][8]	-[redacted][8]	-[redacted][8]	-[redacted][8]	-[redacted][8]
Net cost to Australia health budget ($)	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]

Source: Table 4.3, 4.4, 4.9, 4.12, 4.17, 4.23, p289- 310 of the submission and recalculated during the evaluation using Table 4.3, 4.4, 4.9, 4.12, 4.15, 4.17, and Table 4.23 in sheet 'TABLES' of the submitted financial model (Attachment 4.1),:

Abbreviations: AmiCP = amivantamab in combination with carboplatin and pemetrexed; ABCP = atezolizumab plus bevacizumab plus carboplatin plus paclitaxel; CP= carboplatin plus pemetrexed; PDC= platinum-based doublet chemotherapy; MBS= Medicare benefits schedule; PBS= pharmaceutical benefit scheme; RPBS= repatriation pharmaceutical benefits scheme;

[a] Represented by carboplatin and pemetrexed

[b] Based on 50% of published price of atezolizumab. Atezolizumab has an SPA

The redacted values correspond to the following ranges:

[1] *500 to < 5,000*

[2] *5,000 to < 10,000*

[3] *10,000 to < 20,000*

[4] *$30 million to < $40 million*

[5] *$40 million to < $50 million*

[6] *$50 million to < $60 million*

[7] *$0 to < $10 million*

[8] *net cost saving*

6.74 The submission estimated the net cost of listing amivantamab to the PBS+RPBS to be $30 million to < $40 million in year 1, increasing to $50 million to < $60 million in year 6, totalling $200 million to < $300 million across 6 years. The submission estimated (using 50% of published price of atezolizumab) that the proposed listing of amivantamab would result in a net cost to the Australian health budget of $0 to < $10 million in Year 1, increasing to $0 to < $10 million in Year 6, totalling $10 million to < $20 million across six years.

6.75 These estimated net cost savings may be overestimated because:

- The submission assumed a CP/ABCP comparator split of 16.92%/83.08%. As discussed in paragraph 5.4, the submission's approach results in an overestimation of the number (and proportion) of patients that would be treated with ABCP.

- The number of eligible patients for AmiCP is likely overestimated due to the broad coverage of the source data for incident patients, high uptake rates for both incident and prevalent patients and uncertainty in the duration of amivantamab treatment applied in financial estimates (mean TTTD sourced from the economic model).
- The PBAC noted the uptake of AmiCP for patients with EGFR exon20ins NSCLC in the first year of listing has been much lower than anticipated.

Quality Use of Medicines

6.76 The submission noted that quality use of amivantamab will rely on clinicians being informed about the appropriate patient population and clinical circumstances for its use. This includes ensuring clinicians understand each patient's characteristics, clinical status, treatment risks and benefits, appropriate dosing and duration, and any relevant comorbidities.

6.77 The submission outlined four groups of stakeholders who play a fundamental role in the appropriate use of amivantamab in combination with chemotherapy: patients, prescribers, nursing staff, and dispensers. Each of these stakeholder groups will be provided with appropriate education, resources and support from the sponsor to promote appropriate prescribing and use of amivantamab in combination with chemotherapy. Education materials will include information for the patient/carer and treating HCPs.

For more detail on PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

7.1 The PBAC recommended the listing of amivantamab, in combination with platinum-based doublet chemotherapy (PDC), for the treatment of patients with epidermal growth factor receptor gene mutated (EGFRm) locally advanced/metastatic non-small cell lung cancer (NSCLC), where the condition has progressed on or after osimertinib, on the basis that it should be available only under special arrangements under Section 100 - Efficient Funding of Chemotherapy (EFC) Public/Private hospitals. The PBAC noted the submission nominated PDC and atezolizumab plus bevacizumab in combination with carboplatin and paclitaxel (ABCP) as the main comparators. The PBAC considered patients likely to be treated with amivantamab in combination with PDC would be similar to patients that are currently treated with ABCP (specifically, fit patients with a high burden of disease); therefore, the PBAC considered ABCP was the appropriate comparator. The PBAC noted there was insufficient clinical data available to assess if there is an incremental benefit for amivantamab in combination with PDC compared to ABCP. In this context, the PBAC considered that it would be reasonable for the cost-effective price of amivantamab in EGFRm patients to be informed by the price of atezolizumab plus bevacizumab in the non-squamous NSCLC population. The PBAC considered amivantamab would be cost effective with a cost per 3-week treatment cycle no higher than that for atezolizumab plus bevacizumab. The PBAC

considered the estimated number of eligible patients presented in the submission was reasonable, but uptake was substantially overestimated.

7.2 The PBAC welcomed input from individuals, health professionals and organisations, which noted the limited treatment options and high unmet clinical need for effective treatments for patients who have previously received osimertinib.

7.3 With regards to the restriction criteria, the PBAC advised:

- The clinical criterion 'Patient must have disease progression on or after osimertinib' was appropriate. The PBAC noted this would allow amivantamab to be used in a patient population broader than included in the MARIPOSA-2 trial (see paragraph 3.3) but considered that was reasonable;
- It was appropriate to require patients to have received osimertinib (including patients in the access program outlined in paragraph 3.6) prior to accessing AmiCP;
- The clinical criterion 'Patient must have/have had a WHO performance status of no greater than 2 at treatment initiation with this drug for this condition' was reasonable;
- It was reasonable to not specify the mutation types; however, it proposed inclusion of the clinical criterion 'Patient must have evidence of an activating epidermal growth factor receptor (EGFR) gene mutation known to confer sensitivity to treatment with amivantamab in tumour material'; and
- The criterion 'The treatment must be/have been initiated in combination with platinum-based doublet chemotherapy (PDC)' was appropriate.

7.4 The submission nominated PDC and ABCP as the main comparators, with a comparator split of 16.92% for PDC and 83.08% for ABCP, based on an analysis of PBS data, with 'higher' cost treatments (see paragraph 5.4) redistributed to ABCP. In clinical practice the PBAC considered patients likely to be treated with either amivantamab in combination with PDC or ABCP are likely to be similar in terms of disease burden and fitness to receive additional lines of therapy. Therefore, the PBAC considered ABCP alone is the appropriate main comparator and that there is no basis for a weighted comparator.

7.5 The PBAC noted the submission claimed amivantamab in combination with PDC was superior in terms of effectiveness and inferior in terms of safety compared to PDC and superior in terms of effectiveness and non-inferior in terms of safety compared to ABCP. The PBAC noted the submission assumed carboplatin plus pemetrexed (CP) was a proxy for PDC.

7.6 To support the clinical claim versus PDC, the submission presented data from MARIPOSA-2, a head-to-head, open-label, randomised trial comparing amivantamab in combination with CP (AmiCP) (n=131) and CP (n=263). To support the clinical claim versus ABCP, the submission presented data from a subgroup of patients from ATTLAS,

a head-to-head, open-label, randomised trial comparing ABCP (n=12) and PDC (n=9). The submission did not present a formal indirect treatment comparison of AmiCP and ABCP but relied on the ATTLAS trial to claim that ABCP is of limited efficacy with no efficacy assumed in the economic model.

7.7 The PBAC noted that based on the MARIPOSA-2 trial, treatment with AmiCP resulted in a modest improvement over CP in progression free survival (6.28 months vs 4.17 months; HR = 0.48; 95% CI: 0.36, 0.64, p<0.0001) and overall survival (17.74 months vs 15.34 months; HR = 0.73; 95% CI: 0.54, 0.99, p=0.0386). The PBAC noted AmiCP was associated with more Grade ≥3 treatment-emergent adverse events compared to CP (72.3% vs. 48.1%) and more serious adverse events (32.3% vs. 20.2%). The PBAC considered the claim AmiCP was superior in terms of effectiveness and inferior in terms of safety compared to PDC was reasonable.

7.8 The PBAC considered an indirect comparison of AmiCP and ABCP using the subgroup of patients from the ATTLAS trial was not informative given the small patient numbers in ATTLAS with EGFRm NSCLC and prior osimertinib treatment and transitivity issues between the trials (see paragraph 6.22). The PBAC considered the data presented was insufficient to assess if there is an incremental benefit for AmiCP compared to ABCP. The PBAC considered the claim AmiCP was superior in terms of effectiveness and non-inferior in terms of safety compared to ABCP was not supported.

7.9 The PBAC considered the economic model comparing AmiCP and ABCP (the main comparator) was uninformative as the clinical claim of superiority was not accepted.

7.10 The PBAC considered that it would be reasonable for the cost-effective price of amivantamab in EGFRm patients to be informed by the price of atezolizumab plus bevacizumab in the non-squamous NSCLC population, noting this included patients with EGFRm. In this context, the PBAC considered amivantamab (in combination with PDC) would be cost effective with a drug cost for a 3 weekly treatment cycle no higher than the cost of atezolizumab plus bevacizumab (in combination with carboplatin and paclitaxel). The PBAC considered it would be appropriate for the 3 weekly cycle cost to be calculated based on ex-manufacturer prices (including the effective price of atezolizumab) and an average of 5.67 vials of amivantamab (see Table 15).

7.11 The PBAC considered the estimated number of eligible patients in the submission was reasonable, but uptake rates assumed for the prevalent and incident populations were substantially overestimated. The PBAC considered that given the moderate clinical benefit and high toxicity of AmiCP, uptake will be limited to a small population of selected patients with a high disease burden able to tolerate the increased risk of adverse events. The PBAC advised uptake rates should be reduced by 50% and the financial estimates would need to be updated to include the revised price of amivantamab as outlined in paragraph 7.10. The PBAC considered a majority of use of AmiCP would be offset by ABCP.

7.12 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.

Specifically, the PBAC found that in the circumstances of its recommendation for amivantamab:

a) The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy, over alternative therapies as the clinical benefit is expected to be modest;

b) The treatment is not expected to address a high and urgent unmet clinical need as alternative treatments are available as standard care (PDC and ABCP);

c) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed.

7.13 The PBAC noted that this submission is not eligible for an Independent Review as it is a positive recommendation.

Outcome:
Recommended

8 Recommended listing

8.1 Add new item:

Initial treatment

MEDICINAL PRODUCT Form	**PBS item code**	**Max. Amount**	**№.of Rpts**
AMIVANTAMAB Solution concentrate for I.V. infusion, 350 mg in 7 mL	{NEW (Public)} {NEW (Private)}	2100 mg	5
Available brands			
Rybrevant amivantamab 350 mg/7 mL injection, 7 mL vial			
Restriction Summary [] / Treatment of Concept: []			
Concept ID (for internal Dept. use)	**Category / Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals		
	Prescriber type: ☒Medical Practitioners		
	Restriction type: ☒Authority Required (telephone/online PBS Authorities system)		
Prescribing rule level	**Administrative Advice:** Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.		
	Administrative Advice: No increase in the maximum amount or number of units may be authorised.		
	Administrative Advice: No increase in the maximum number of repeats may be authorised.		
	Administrative Advice: Special Pricing Arrangement apply.		
	Indication: Stage IIIB/ IIIC (locally advanced) or Stage IV (metastatic) non-small cell lung cancer (NSCLC)		
	Treatment Phase: Initial treatment – For patients whose condition progressed on or after osimertinib therapy		
	Clinical criteria:		
	Patient must have disease progression on or after osimertinib.		
	AND		
	Clinical criteria:		
	Patient must have evidence of an activating epidermal growth factor receptor (EGFR) gene mutation known to confer sensitivity to treatment with amivantamab in tumour material.		
	AND		
	Clinical criteria:		
	Patient must have/have had a WHO performance status of no greater than 2 at treatment initiation with this drug for this condition;		
	AND		
	Clinical criteria:		
	Patient must not have previously received this drug for this condition; OR		
	Patient must be each of: (i) currently receiving non-PBS-subsidised supply for this drug for this PBS indication, (ii) free of disease progression since commencing non-PBS-subsidised supply.		
	AND		
	Clinical criteria:		
	The treatment must be/have been initiated in combination with platinum-based doublet chemotherapy		
	AND		
	Administrative Advice: A patient may only qualify for PBS-subsidised treatment under this restriction once. Following completion of the initial PBS-subsidised course, further applications for treatment will be assessed under the continuing treatment restriction.		

Continuing treatment

MEDICINAL PRODUCT Form	PBS item code	Max. amount	№. Of Repeats
AMIVANTAMAB Solution concentrate for I.V. infusion, 350 mg in 7 mL	New (Public) New (Private)	2100 mg	7
Available brands			
Rybrevant amivantamab 350 mg/7 mL injection, 7 mL vial			
Restriction Summary [new] / Treatment of Concept: [new]			
Concept ID (for internal Dept. use)	**Category / Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals		
	Prescriber type: ☒Medical Practitioners		
	Restriction Type ☒Authority Required – immediate/real time assessment by Services Australia (telephone/online application avenues)		
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.		
	Administrative Advice: No increase in the maximum amount or number of units may be authorised.		
	Administrative Advice: No increase in the maximum number of repeats may be authorised.		
	Administrative Advice: Special Pricing Arrangement apply.		
	Indication: Stage IIIB/IIIC *(*locally advanced*)* or Stage IV *(*metastatic*)* non-small cell lung cancer *(*NSCLC*)*.		
	Treatment Phase: Continuing treatment – For patients whose condition progressed on or after osimertinib therapy		
	Clinical criteria		
	Patient must have previously received PBS-subsidised treatment with this drug for this condition		
	AND		
	Clinical criteria		
	Patient must not have developed disease progression while receiving treatment with this drug for this condition		

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

The sponsor had no comment.