SMC2878

amivantamab concentrate for solution for infusion (Rybrevant®)

Janssen-Cilag Ltd

07 November 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a resubmission assessed under the end of life and orphan equivalent medicine process

amivantamab (Rybrevant®) is accepted for use within NHSScotland.

Indication under review: in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) Exon20 insertion mutations.

In a phase III study of patients with locally advanced or metastatic NSCLC with EGFR Exon20 insertion mutations, the addition of amivantamab to carboplatin plus pemetrexed significantly improved progression-free survival.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Amivantamab is a IgG1-based monoclonal antibody with specificity to epidermal growth factor receptor (EGFR) and mesenchymal-epithelial transition (MET) factor gene that targets tumours with activating EGFR mutations such as Exon20 insertion mutations. Amivantamab binds to EGFR and MET, inhibiting signalling and causing degradation of EGFR and MET, thereby slowing the growth and spread of cancer. It also helps targeting of cancer cells for destruction by immune cells.[1]

For this indication (in combination with chemotherapy), the recommended starting dose of amivantamab is 1,400 mg for patients <80 kg and 1,750 mg for patients ≥80 kg by intravenous infusion once weekly for the first 4 doses. At week 7 onwards, the dose of amivantamab is increased to 1,750 mg for patients <80 kg and 2,100 mg for patients ≥80 kg every 3 weeks. Treatment should continue until disease progression or unacceptable toxicity occurs.[1]

1.2. Disease background

Lung cancer is the most common cancer in Scotland with 5,391 new diagnoses reported in 2022.[2] Most diagnoses of lung cancer in Scotland are at an advanced stage.[3] Non-small cell lung cancer (NSCLC) is one of two main subtypes of lung cancer and accounts for 85% of all lung malignancies. NSCLC is further differentiated into three subtypes: squamous-cell carcinoma, adenocarcinoma and large-cell carcinoma.[4-6] In patients with NSCLC adenocarcinoma, EGFR is one of the most prevalent driver mutations. The most common EGFR mutations are Exon 19del and L858R (80 to 85% of patients with EGFR mutations). EGFR Exon20 are identified in up to 10% of patients with EGFR mutations: mainly females, non-smokers, with adenocarcinoma and of Asian origin.[6-9] EGFR Exon20 insertion mutations are associated with poorer outcomes for patients with NSCLC compared with other EGFR mutations.[7]

1.3. Treatment pathway and relevant comparators

There are no approved targeted therapies for the first-line treatment of patients with EGFR Exon20 insertion-mutated advanced NSCLC. Standard of care in this setting is platinum-based doublet chemotherapy, namely carboplatin plus pemetrexed.[9, 10]

1.4. Category for decision-making process

Eligible for a PACE meeting

Amivantamab meets SMC end of life and orphan equivalent criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of amivantamab for this indication comes from PAPILLON. Details are presented in Table 2.1.

Table 2.1. Overview of relevant study

Criteria	PAPILLON [9, 11]
Study design	International, randomised, open-label, phase III study.
Eligible patients	• Adult patients ≥18 years of age. • Histologically or cytologically confirmed, locally advanced or metastatic, non-squamous NSCLC with documented primary EGFR Exon20 insertion activating mutations. • Measurable disease according to RECIST v1.1. • ECOG performance status of 0 or 1.
Treatments	Patients were randomised to receive carboplatin (via intravenous infusion; AUC 5; day 1 of each 21-day cycle for up to 4 cycles) plus pemetrexed (via intravenous infusion; 500 mg/m^2 BSA; day 1 of each 21-day cycle; continued until disease progression), with or without amivantamab. Amivantamab was administered as an intravenous infusion at a dose of 1,400 mg (1,750 mg for a body weight ≥80 kg) once weekly for the first 4 weeks. At cycle 3 (week 7), the dose of amivantamab was increased to 1,750 mg (2,100 mg for a body weight ≥80 kg), administered once every 3 weeks until disease progression confirmed by BICR or unacceptable toxic effects. Patients in the chemotherapy-only treatment group were permitted to crossover to receive amivantamab monotherapy (on a 3-weekly regimen) after documented disease progression according to BICR.
Randomisation	Patients were randomised equally. Randomisation was stratified according to ECOG performance status score (0 versus 1), history of brain metastases (yes versus no) and previous receipt of an EGFR tyrosine kinase inhibitor (yes versus no).
Primary outcome	PFS, defined as the time between date of randomisation to the date of first progression (assessed by BICR per RECIST v1.1 criteria) or death due to any cause, whichever occurred first.
Relevant secondary outcomes	• ORR assessed by BICR per RECIST v1.1 • OS • DoR assessed by BICR • Time to subsequent anticancer therapy
Statistical analysis	Efficacy analyses were performed in the FAS population, defined as all patients who underwent randomisation. A hierarchical statistical testing strategy was applied in the study with no formal testing of outcomes after the first non-significant outcome in the hierarchy. The following outcomes were tested sequentially: PFS, ORR, and OS. Other secondary outcomes were not included in the hierarchical testing strategy, therefore the results reported for these outcomes are descriptive only and not inferential (no p-values reported).

Abbreviations: AUC = area under the curve; BICR = blinded independent central review; BSA = body surface area; DOR = duration of response; ECOG = Eastern Cooperative Oncology Group; EGFR = epidermal growth factor receptor; FAS = full analysis set; NSCLC = non-small cell lung cancer; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; RECIST = Response Evaluation Criteria in Solid Tumours

At the interim analysis (data cut-off May 2023), after a median follow-up of 14.9 months, the addition of amivantamab to carboplatin plus pemetrexed resulted in a statistically significant improvement in PFS. See Table 2.2 for details.[11]

Table 2.2: Primary and selected secondary outcomes from PAPILLON (data-cut May 2023, FAS population).[9, 11]

	Amivantamab plus chemotherapy (n=153)	Chemotherapy (n=155)
Primary outcome: PFS (assessed by BICR per RECIST v1.1)		
Median follow-up, months	Confidential	Confidential
PFS events, n	84	132
Median PFS, months	11.4	6.7
HR (95% CI), p-value	0.40 (0.30 to 0.53), p<0.001	
KM-estimated PFS at 12 months	48%	13%
Secondary outcome: ORR (assessed by BICR per RECIST v1.1) [a,b]		
Measurable disease at baseline, n	152	152
ORR, %	73%	47%
CR, %	3.9%	0.7%
PR, %	69%	47%
Odds ratio (95% CI), p-value	2.97 (1.84 to 4.79), p<0.001	
Secondary outcome: overall survival		
Deaths, n	28	42
Median OS, months	NE	24.4
HR (95% CI), p-value	0.67 (0.42 to 1.09), p=0.11	
KM-estimated OS at 12 months	86%	82%
Secondary outcome: duration of response assessed by BICR [a]		
Measurable disease at baseline, n	152	152
Median DOR, months	10.1	5.6
Secondary outcome: time to subsequent anticancer therapy		
Events, n	58	109
Median time to subsequent therapy, months	17.7	9.9
HR (95% CI)	0.35 (0.25 to 0.49)	

Abbreviations: BICR = blinded independent central review; CI = confidence interval; CR = complete response; DOR = duration of response; FAS = full analysis set; HR = hazard ratio; KM = Kaplan-Meier; NE = not estimable; ORR = objective response rate; PR = partial response; PFS = progression-free survival; RECIST = Response Evaluation Criteria in Solid Tumours

[a] assessed in patients with measurable disease at baseline

[b] defined as achieving either complete response or partial response

Data from a later data cut-off (October 2023) was also presented for OS, the median duration of follow-up was 20.9 months. There were 40 deaths in the amivantamab plus chemotherapy group and 52 deaths in the chemotherapy group. Median OS was not reached in the amivantamab plus chemotherapy group and was 28.6 months in the chemotherapy group (HR: 0.76, 95% CI: 0.50 to 1.14).[9] Patients in the chemotherapy group were permitted to crossover to receive amivantamab monotherapy between 21 and 90 days after their last dose of chemotherapy, following confirmed disease progression by blinded independent central review. At the October 2023 data-cut off, 78 patients had crossed over to receive amivantamab monotherapy. After adjustment for crossover, the HR estimate for OS was used to inform the economic base case.[12]

2.2. Health-related quality of life outcomes

Health-related Quality of Life (HRQoL) was assessed using three patient reported questionnaires: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC-QLQ-C30), Patient-Reported Outcomes Measurement Information System–Physical

Function (PROMIS-PF) and EQ-5D-5L. Scores were measured at baseline, at each study visit and at the end of treatment. HRQoL was consistent across both treatment groups and maintained for the amivantamab plus chemotherapy group throughout treatment.[9]

2.3. Indirect evidence to support clinical and cost-effectiveness comparisons

In the absence of direct evidence comparing amivantamab plus chemotherapy with pembrolizumab plus chemotherapy, the submitting company conducted an indirect treatment comparison. This has been used to inform the economic base case. Further details are provided in Table 2.3.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview
Design	Population adjusted ITC
Population	Locally advanced or metastatic NSCLC with EGFR Exon20 insertion mutation
Comparators	Pembrolizumab in combination with chemotherapy (carboplatin and pemetrexed)
Studies included	PAPILLON [11], a phase III randomised open-label trial and NECTAR [13], a non-interventional, retrospective, observational cohort study with pooled data from the following sources: NCRAS; ESME; ConcertAI and COTA.
Outcomes	TTNT and OS
Results	The ITC suggested that amivantamab plus chemotherapy was superior to pembrolizumab in combination with chemotherapy, the company considered the results to be confidential. [11, 13]

Abbreviations: CI = confidence interval; EGFR = epidermal growth factor receptor; ESME = Epidemiological Strategy and Medical Economics; HR = hazard ratio; ITC = indirect treatment comparison; NCRAS = National Cancer Registration and Analysis Service; NSCLC = non-small cell lung cancer; OS = overall survival; TTNT = time to next treatment

*Other data were also assessed but remain confidential.**

3. Summary of Safety Evidence

In the PAPILLON study at data cut-off May 2023, the median duration of treatment in the amivantamab plus chemotherapy group was 9.7 months and in the chemotherapy group was 6.7 months. Any treatment-emergent adverse event (AE) was reported by 100% (151/151) of patients in the amivantamab plus chemotherapy group and 98% (152/155) in the chemotherapy group and these were considered treatment-related in 100% and 94% respectively. In the amivantamab plus chemotherapy and chemotherapy groups respectively, patients reporting a grade 3 or higher AE were 75% versus 54%, patients with a reported serious AE were 37% versus 31%, patients with a dose reduction due to treatment-emergent AEs were 48% versus 23%, the proportion of AEs that led to dose interruptions were 69% versus 36% and patients discontinuing therapy due to an AE was 24% versus 10%.[11]

The most frequently reported treatment-related AEs of grade 3 or higher in the amivantamab plus chemotherapy group versus the chemotherapy group were: neutropenia (32% versus 22%), rash (11% versus 0), leukopenia (11% versus 3%) and anaemia (9% versus 11%).[11]

Overall, the safety profile of amivantamab was similar to that previously reported in later treatment lines. Rash, dermatitis acneiform, hypoalbuminemia, hypokalaemia and infusion related

reactions were described as the most common safety risks. However, the risks were considered manageable with dose reductions and interruptions. See the Summary of Product Characteristics for further information including advice on monitoring, dose modifications, treatment interruption and withdrawal.[1, 9]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- Amivantamab is the first licensed treatment to target EGFR Exon20 insertion mutation positive advanced NSCLC in combination with carboplatin and pemetrexed.
- PAPILLON is a well-conducted phase III study that investigated the addition of amivantamab to carboplatin plus pemetrexed, which is the most relevant comparator in Scottish clinical practice.
- In PAPILLON, at the interim analysis with a median follow-up of 14.9 months, amivantamab in combination with chemotherapy was associated with a statistically significant and clinically relevant improvement in PFS compared with chemotherapy. Median PFS gain was 4.7 months (11.4 months versus 6.7 months). A statistically significant improvement was also observed in the hierarchically tested secondary outcome, objective response rate.[11]

4.2. Key uncertainties

- Scottish clinical pathways and clinical experts consulted by SMC consider that carboplatin plus pemetrexed is standard of care for patients in Scotland with advanced NSCLC with Exon20 insertion mutations, therefore the indirect treatment comparison comparing amivantamab plus chemotherapy with pembrolizumab plus chemotherapy is not relevant for decision making.[10, 14]
- OS results are not sufficiently mature to evaluate the effect of amivantamab on survival. At the October 2023 data-cut off, estimated median OS was not reached in the amivantamab plus chemotherapy group and was 28.6 months in the chemotherapy group. There were 40 deaths in the amivantamab plus chemotherapy group and 52 deaths in the chemotherapy group.[9]
- At the May 2023 data-cut off, subsequent anticancer therapy was received by 38% in the amivantamab plus chemotherapy group and 70% in the chemotherapy group (including 65 patients who crossed over to amivantamab monotherapy), this included treatment with tyrosine kinase inhibitors which may not be reflective of the treatment pathway in Scotland. This may confound overall survival and limits future data-cuts evaluating OS.[9]
- PAPILLON had an open-label design, this could introduce potential bias for subjective efficacy, safety and quality of life outcomes and these should be interpreted with caution. This risk was mitigated for PFS and ORR which were assessed by blinded independent central review as per RECIST criteria.

4.3. Clinical expert input

Clinical experts consulted by SMC considered that amivantamab is a therapeutic advancement and would be used in combination with carboplatin and pemetrexed chemotherapy.

4.4. Service implications

Amivantamab is administered in conjunction with current standard of care, therefore will require increased resource from chemotherapy day units and pharmacy aseptic services. However, patient numbers are small therefore no significant service implications are expected.

Diagnostic test required to identify patients eligible for treatment: contact local laboratory for information.

5. Patient and clinician engagement (PACE)

A PACE meeting with patient group representatives and clinical specialists was held to consider the added value of amivantamab, as an orphan equivalent and end of life medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- EGFR Exon20 insertion mutation NSCLC is a very rare subset of EGFR positive NSCLC, which is already a rare diagnosis. It is a life-threatening condition associated with devastating physical, emotional and financial consequences. Patients with this diagnosis have a very poor prognosis and worse outcomes than patients with more common EGFR positive mutations.
- Patients with EGFR Exon20 insertion mutation NSCLC experience significant psychological distress and negative quality of life. The symptoms associated with this diagnosis are distressing with patients unable to do daily tasks and unable to work. This negatively impacts their relationships, independence and places financial strain on family life. Patients and families of those with this diagnosis often feel overlooked and experience significant stress, anxiety and depression with the burden of disease, fear of progression and uncertainty around treatment options.
- PACE participants consider that there is an urgent and significant unmet need for a targeted treatment option for EGFR Exon20 insertion mutation NSCLC. There is no standard of care and, in contrast to other mutations, no targeted treatment options available for patients with this mutation.
- Patients with EGFR Exon20 insertion mutation NSCLC do not respond well to current chemotherapy treatments.
- Amivantamab will offer patients a targeted treatment option that significantly improves progression free survival and overall response, and this will have a positive impact on patient outcomes, wellbeing, quality of life and help to alleviate some of their distress. PACE participants note that while amivantamab is associated with some side effects, amivantamab is generally well tolerated and side effects are predictable and manageable, allowing patients to maintain a good quality of life while on treatment.

- PACE participants agreed that amivantamab should be used as per the licensed indication. Initial infusions require extended monitoring in hospital, however, this is not expected to have a significant impact on the service.

Additional Patient and Carer Involvement

We received patient group submissions from EGFR Positive UK, Roy Castle Lung Cancer Foundation and the Scottish Lung Cancer Nurses Forum. EGFR Positive UK and Roy Castle Lung Cancer Foundation are registered charities. The Scottish Lung Cancer Nurses Forum is an unincorporated organisation. EGFR Positive UK has received 8% pharmaceutical company funding in the past two years, including from the submitting company. Roy Castle Lung Cancer Foundation has received 7.6% pharmaceutical company funding in the past two years, including from the submitting company. The Scottish Lung Cancer Nurses Forum has not received any pharmaceutical company funding in the past two years. Representatives from EGFR Positive UK and the Scottish Lung Cancer Nurses Forum participated in the PACE meeting. The key points of the submissions from all three organisations have been included in the full PACE statement considered by SMC.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

The submitting company presented an economic case, summarised in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis
Time horizon	A lifetime horizon of 30 years with 1 week cycle length
Population	Adult patients with advanced NSCLC with activating EGFR Exon20 insertion mutations
Comparators	The company considered the two most relevant comparators to be: • Carboplatin with pemetrexed (chemotherapy) • Pembrolizumab in combination with carboplatin and pemetrexed A weighted comparator, representative of the proportional use of each of the two individual comparators in clinical practice, was applied in the base case analysis. It was assumed that 70% of patients would be treated with chemotherapy and 30% would be treated with pembrolizumab with chemotherapy.
Model description	A three-state partitioned survival model was used, with health states of progression-free survival (PFS), progressed disease (PD) and death. All patients entered the model in the PFS state and remained in this health state until disease progression, following which, patients either transitioned into the PD health state or entered the absorbing health state of death. The occupancy of health states over time was derived from the survival curves from the PAPILLON[11] study. The proportion of patients occupying each health state was calculated using the PFS and OS survival curves.
Clinical data	The key effectiveness data for amivantamab came from the PAPILLON[11] study. This included input parameters for PFS, OS, time to treatment discontinuation or death (TTDD) and patient utilities. Since there was no head-to-head data available for amivantamab plus chemotherapy versus pembrolizumab plus chemotherapy, an ITC was conducted using the NECTAR study and the PAPILLON[11] study.
Extrapolation	The model used independently fitted parametric curves to estimate PFS and OS as the proportional hazards assumption was violated.

	PFS data in the model are relatively mature, given that median PFS had been reached in the PAPILLON[11] study for the amivantamab treatment arm. All extrapolations featured similar statistical fits and similar long-term survival outcomes. Gamma parametric curves were applied in the base case to estimate PFS in both amivantamab and chemotherapy arms. The log-logistic extrapolation had the best statistical fit and was selected for PFS in pembrolizumab-chemotherapy. For amivantamab and chemotherapy, the long-term OS extrapolations in the base case were informed by OS data at the October 2023 data cut-off from PAPILLON, with the chemotherapy arm adjusted to account for treatment switching. For amivantamab OS, the exponential and Gompertz extrapolations had the best statistical fit but the base case assumed a Weibull distribution as it closely aligned with 5 and 10-year survival estimates validated by clinical experts consulted by the company. For chemotherapy, the best statistical fit was the log-logistic extrapolation, followed by the gamma and Weibull extrapolations which had comparable fits. After validation with clinical experts and assessment of the hazard plots, the base case assumed a gamma distribution for chemotherapy OS. The OS KM curve for pembrolizumab-chemotherapy was generated based on pooled efficacy data from the NECTAR study. OS data for pembrolizumab-chemotherapy was relatively mature. Therefore, curve selection was driven by statistical fit and the log-logistic extrapolation was selected in the base case.
Quality of life	Utility values were based on pooled EQ5D-5L data from the PAPILLON[11] study. The utility values were health state dependent and were the same for all treatments. Adverse event disutilities were applied and the utilities were adjusted for age.
Costs and resource use	Costs included in the model were medicine acquisition, administration, monitoring, adverse events and end of life. A price year of 2022/23 was used and costs and benefits were discounted at 3.5%
PAS	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount of was offered on the list price. A PAS discount is in place for pembrolizumab and this is included in the results used for decision-making by using estimates of the comparator PAS price. SMC considered results for decision-making that took into account all relevant PAS. SMC is unable to present the results comparing amivantamab plus chemotherapy against the weighted comparator, which contained pembrolizumab, due to competition law issues.

6.2. Results

This submission has been assessed under the fast-track resubmission process. Table 6.2 presents the base case economic results. Where the comparator is not subject to a confidential PAS discount, the incremental cost-effectiveness ratio (ICER) is shown. Where the comparator is subject to a confidential PAS discount, SMC is unable to present these results due to competition law issues. The main quality adjusted life year (QALY) driver was from improvements in OS for amivantamab compared to the comparators. The main cost driver was medicine acquisition cost.

Table 6.2 Base case results (PAS price)

Intervention	Total costs (£)	Total QALY	Incr. costs (£)	Incr. LYG	Incr. QALY	ICER (£/QALY)
Amivantamab plus chemotherapy	CiC	CiC	-	-	-	-
Chemotherapy	CiC	CiC	CiC	1.80	CiC	40,435
Weighted comparator	CiC	CiC	CiC	1.77	CiC	CiC

Abbreviations: CiC, commercial in confidence; ICER, incremental cost-effectiveness ratio; LYG, life years gained; QALY: quality adjusted life year.

6.3. Sensitivity analyses

The company provided probabilistic sensitivity analysis (PSA), deterministic sensitivity analysis (DSA) and scenario analysis. In the DSA, the parameter with the greatest impact on the ICER was the choice of OS parametric extrapolation for amivantamab.

The company also conducted scenario analyses to test the impact of several assumptions provided in table 6.3 below.

Table 6.3 Scenario analysis results (PAS Price)

	Parameter	Base Case	Scenario	ICER versus Chemotherapy (£/QALY)	ICER versus weighted comparator (£/QALY)
	Base case			*40,435*	CiC
1	Discount rate	3.5%	0%	36,561	CiC
2			5%	42,139	CiC
3	Treatment switch adjustment method	IPCW	TSE with re-censoring	36,206	CiC
4			TSE without re-censoring	44,434	CiC
5	Amivantamab PFS extrapolation	Gamma	Log - logistic	39,509	CiC
6	Chemotherapy PFS extrapolation	Gamma	Weibull	40,420	CiC
7	TTDD extrapolation	Weibull for amivantamab and Gamma for chemotherapy	Gamma for amivantamab and chemotherapy	42,221	CiC
8			Gamma for amivantamab, Weibull for chemotherapy	41,919	CiC
9			Weibull for amivantamab, Gamma for chemotherapy	40,753	CiC
10	Amivantamab OS extrapolation	Weibull	Gamma	36,264	CiC
11			Gompertz	79,040	CiC

12	Chemotherapy OS extrapolation	Gamma	Weibull	38,173	CiC
13			Log-logistic	45,147	CiC
14	EGFR Exon20 mutation testing costs	Excluded	Included	40,851	CiC
15	Price of pemetrexed	BNF price	Apply eMIT price (£40.77)	37,728	CiC

Abbreviations: BNF: British national formulary; CiC = commercial in confidence; eMIT: electronic medicines market information tool; ICER: incremental cost-effectiveness ratio; IPCW: inverse probability of censoring weighting; OS: overall survival; PAS: Patient Access Scheme; QALY: quality-adjusted life year; TSE: two stage estimation; TTDD: time to treatment discontinuation or death

6.4. Key strengths

- The economic model was comprehensive and structurally sound. Appropriate sources were selected to inform the model parameters and results were based on the latest available data-cut from the PAPILLON study.

6.5. Key uncertainties

- There is substantial uncertainty regarding the inclusion of pembrolizumab as a relevant comparator. The company estimated that the breakdown of treatment in practice was likely to be 70% chemotherapy and 30% pembrolizumab with chemotherapy based on clinical expert opinion from an advisory panel. This was included as a weighted comparator in the model. It is unclear whether using immunotherapies to treat exon20 insertion mutation-positive NSCLC can be considered standard practice and evidence of their efficacy in this population is limited at best. The inclusion of pembrolizumab with chemotherapy as a component in the weighted comparator used in the model is therefore not justified and does not appear to be consistent with standard practice in Scotland.
- The relative effectiveness of amivantamab on overall survival is yet to be established as the survival data from PAPILLON is still relatively immature. This raises questions about the plausibility of extrapolated outcomes.
- The choice of parametric curve selected to estimate overall survival with amivantamab is a key driver of cost effectiveness in the sensitivity analysis. In the base case, the company fitted a Weibull distribution to the OS data for amivantamab because it most closely aligned with 5-year survival estimates elicited from its clinical expert advisory board. It is plausible that the Weibull estimated survival is too optimistic. Applying the Gompertz distribution, which had the best statistical fit but predicts the most conservative median OS of all models, increased the ICER versus chemotherapy by 96% (see scenario 11, table 6.3).
- The majority of life-year and QALY gains for amivantamab occur in the progressed-disease health state. This is counterintuitive to the presumption that a greater proportion of incremental QALYs ought to accrue in the PFS state given that treatment with amivantamab is stopped at the stage of disease progression or unacceptable toxicity. It is unclear whether the accrual of a maintained treatment effect is due to a different mechanism of action of amivantamab or due to uncertainty of inputs and assumptions feeding into the model. Treatment effect waning was also not included in the model. The uncertainty surrounding the nature of a large post-progression benefit even after stopping

amivantamab treatment, casts doubt on the choice of OS parametric curves applied in the base case.

- There is some uncertainty regarding the base case utility values for health states which might lack face value. These appear to be higher than those used in other appraisals of NSCLC medicines. Given the poorer prognosis and greater severity of illness associated with exon20 insertion mutation positive NSCLC, it is counterintuitive that their utilities might be higher than those of other NSCLC patients. The company did not explore the use of alternate utility values in the scenario analysis.

*Other data were also assessed but remain confidential.**

7. Conclusion

The Committee considered the benefits of amivantamab in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as amivantamab is an orphan equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, and after application of the appropriate SMC modifiers, the Committee was accepted amivantamab for use in NHSScotland.

8. Guidelines and Protocols

The European Society for Medical Oncology (ESMO) published the clinical practice guideline for oncogene-addicted metastatic non-small-cell lung cancer: diagnosis, treatment and follow-up in April 2023.[14]

9. Additional Information

9.1. Product availability date

31 July 2024

Table 9.1 List price of medicine under review

Medicine	Dose regimen		Cost per 21-day cycle (£)
amivantamab	**Body weight**	**Dose and frequency**	**17,264 to 21,580 for first 4 doses then 5,395 to 6,474**
	<80 kg	**1,400 mg once weekly for first 4 doses** **1,750 mg every 3 weeks from week 7 onwards**	
	≥80 kg	**1,750 mg once weekly for first 4 doses** **2,100 mg every 3 weeks from week 7 onwards**	

Costs from BNF online on 20 February 2025. Costs calculated based on first 4 doses, then a 21-day cycle of maintenance treatment. Costs calculated using the full cost of vials assuming wastage. Amivantamab is used in combination with carboplatin and pemetrexed. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines or PAS associated with medicines used in a combination regimen.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 18 September 2025.

*Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.