SMC2906

cemiplimab concentrate for solution for infusion (Libtayo®)

Regeneron UK Limited

09 October 2026

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 full submission assessed under the end of life medicine process

cemiplimab (Libtayo®) is accepted for restricted use within NHSScotland.

Indication under review: In combination with platinum-based chemotherapy for the first-line treatment of adult patients with non-small cell lung cancer (NSCLC) expressing PD-L1 (in ≥1% of tumour cells) with no EGFR, ALK or ROS1 aberrations, who have:

- locally advanced NSCLC who are not candidates for definitive chemoradiation, or
- metastatic NSCLC

SMC restriction: Treatment with cemiplimab is subject to a stopping rule of a maximum of 36 three-weekly cycles.

Evidence from a double-blind, phase III study demonstrated that cemiplimab plus chemotherapy improved overall survival (OS) compared with placebo plus chemotherapy. Indirect comparisons suggest similar OS and progression-free survival (PFS) compared with pembrolizumab plus chemotherapy, which is a relevant treatment for metastatic NSCLC.

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.

Co Vice Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Cemiplimab is a monoclonal antibody which binds to the programmed cell death-1 (PD-1) receptor and blocks its interaction with the programmed cell death ligand 1 (PD-L1). Some cancers produce PD-L1 which combines with PD-1 to switch off activity of T cells of the immune system, preventing them from attacking the cancer. By blocking PD-1, cemiplimab increases the immune system's ability to kill cancer cells.[1, 2] The recommended dose of cemiplimab is 350 mg every 3 weeks administered as an intravenous infusion over 30 minutes. Treatment may be continued until disease progression or unacceptable toxicity.[1]

1.2. Disease background

Lung cancer is the most common cause of cancer death in Scotland, accounting for 22% of all cancer deaths in Scotland in 2024.[3] It was the third most common malignancy in Scotland in 2023 with 5,324 diagnoses. Rates have fallen over the past decade, and this reflects success in reducing the prevalence of smoking which is the largest risk factor for lung cancer.[4] Non-small cell lung cancer (NSCLC) accounts for 80% to 85% of all lung cancers. For most patients, first diagnosis of NSCLC is made at an advanced stage of disease which is not amenable to curative treatment or has spread to other organs. Prognosis is poor for patients with locally advanced or metastatic NSCLC; median OS estimates from recent studies range from 12.1 months to 22.0 months.[5-7]

1.3. Company proposed position

The submitting company has requested that the duration of treatment with cemiplimab is restricted to 36 three-weekly cycles.

1.4. Treatment pathway and relevant comparators

The most relevant comparator for the first-line treatment of patients with locally advanced NSCLC (who are not candidates for definitive chemoradiation) expressing PD-L1 in ≥1% of tumour cells and with no EGFR, ALK or ROS1 aberrations, is chemotherapy. The most common regimens include carboplatin in combination with either gemcitabine, vinorelbine, or paclitaxel (in squamous NSCLC) or carboplatin in combination with pemetrexed (in non-squamous NSCLC).[8] Although not routinely available in Scottish clinical practice, some clinical experts consulted by SMC stated that there may be some patients who receive off-label pembrolizumab plus chemotherapy in this setting.

The most relevant comparator for the first-line treatment of patients with metastatic NSCLC expressing PD-L1 1% to <50% with no EGFR, ALK or ROS1 aberrations, is pembrolizumab in combination with chemotherapy (SMC2187 and SMC2207).[8]

The most relevant comparator for the first-line treatment of patients with metastatic NSCLC expressing PD-L1 ≥ 50% with no EGFR, ALK or ROS1 aberrations, is pembrolizumab monotherapy (SMC1239/17).[8] Atezolizumab monotherapy has also been accepted for use within NHSScotland (SMC2379); however, data from the Cancer Medicines Outcomes Programme-Public Health Scotland (CMOP-PHS) show that use is low.[9]

1.5. Category for decision-making process

Eligibility for a PACE meeting

Cemiplimab meets SMC end of life 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 cemiplimab plus chemotherapy for the treatment of adult patients with NSCLC with no EGFR, ALK or ROS1 aberrations, who have locally advanced NSCLC (who are not candidates for definitive chemoradiation) or metastatic NSCLC comes from EMPOWER-Lung 3. Details are summarised in Table 2.1.

Table 2.1. Overview of relevant study.[6, 10]

Criteria	EMPOWER-Lung 3
Study design	International, multicentre, randomised, double-blind, phase III study
Eligible patients	• Adult patients with histologically or cytologically documented squamous or non-squamous NSCLC with stage IIIB or IIIC disease who are not candidates for treatment with definitive concurrent chemoradiation, or patients with stage IV disease who have not received prior systemic treatment for recurrent or metastatic NSCLC. Patients who received adjuvant or neoadjuvant platinum-based doublet chemotherapy (after surgery and/or radiation therapy) and developed recurrent or metastatic disease more than 6 months after completing therapy were eligible. • Availability of a tumour tissue sample. • At least one radiographically measurable lesion per RECIST 1.1 criteria. • ECOG performance status ≤ 1.
Treatments	Cemiplimab 350 mg via intravenous infusion every 3 weeks for up to 108 weeks (36 cycles) plus chemotherapy or placebo plus chemotherapy. Treatment with cemiplimab could be continued beyond RECIST 1.1 defined disease progression if the investigator judged the patient to be experiencing clinical benefit and if the patient had not completed the 108-week period. Chemotherapy was administered every 3 weeks for four cycles or until RECIST 1.1 defined disease progression or early treatment discontinuation for another reason. The chemotherapy regimen used was selected by the investigator prior to randomisation and in accordance with local standard of care; the options were paclitaxel plus carboplatin, paclitaxel plus cisplatin, pemetrexed plus carboplatin (plus pemetrexed maintenance treatment), or pemetrexed plus cisplatin (plus pemetrexed maintenance treatment).
Randomisation	Patients were randomised in a 2:1 ratio. Randomisation was stratified according to baseline histology (non-squamous versus squamous) and PD-L1 level (<1% versus 1% to 49% versus ≥ 50%).
Primary outcome	OS, defined as the time from date of randomisation to the date of death.
Secondary outcomes	PFS, ORR.
Statistical analysis	Efficacy analyses were performed in the full analysis set (as per the intention-to-treat principle), which included all patients who had been assigned study treatment by randomisation. The PD-L1 ≥ 1% subgroup analysis relevant to this submission were not statistically powered and were descriptive in nature.

Abbreviations: ECOG = Eastern Cooperative Oncology Group; NSCLC = non-small cell lung cancer; ORR = objective response rate; OS = overall survival; PD-L1 = programmed death ligand-1; PFS = progression-free survival; RECIST 1.1 = Response Evaluation Criteria in Solid Tumours version 1.1.

At data-cut June 2022 (final OS analysis), median OS was significantly longer in the cemiplimab plus chemotherapy group compared with placebo plus chemotherapy (intention-to-treat [ITT] population). The secondary outcomes PFS and ORR were also met in the ITT population. See Table 2.2 for details.

Table 2.2. Key efficacy results for EMPOWER-Lung 3.[6, 11, 12]

	FAS population		Licensed population (PD-L1 ≥ 1%)	
	Cemiplimab plus chemotherapy (n=312)	**Placebo plus chemotherapy (n=154)**	**Cemiplimab plus chemotherapy (n=217)**	**Placebo plus chemotherapy (n=110)**
Median follow-up	28.4 months		28.0 months	
Primary outcome: overall survival				
Events, n	180	111	114	77
Median OS	21.1 months	12.9 months	23.5 months	12.1 months
Hazard ratio (95% CI)	0.65 (0.51 to 0.82) p<0.001		0.51 (0.38 to 0.69)	
OS rate at 12 months	66%	54%	-	-
OS rate at 24 months	-	-	48%	28%
Key secondary outcome: PFS (BIRC, RECIST 1.1)				
Events, n	234	134	157	94
Median PFS	8.2 months	5.5 months	8.3 months	5.5 months
Hazard ratio (95% CI)	0.55 (0.44 to 0.68) p<0.001		0.48 (0.37 to 0.62)	
PFS rate at 12 months	39%	16%	-	-
PFS rate at 24 months	-	-	23%	4.8%
Key secondary outcome: ORR				
ORR	44%	22%	48%	23%
Odds ratio (95% CI)	2.82 (1.80 to 4.41) p<0.001		3.12 (1.86 to 5.25)	
CR	4.2%	0	5.1%	0
PR	39%	22%	43%	23%

Abbreviations: BIRC = blinded independent review committee; CI = confidence interval; CR = complete response; FAS = full analysis set; ORR = objective response rate; OS = overall survival; PD-L1 = programmed death ligand-1; PFS = progression-free survival; PR = partial response; RECIST 1.1 = Response Evaluation Criteria in Solid Tumours.

At 5-year follow-up, cemiplimab continued to show OS benefit versus placebo plus chemotherapy in the PD-L1 ≥ 1% subgroup (median OS 24.0 months versus 12.1 months; hazard ratio (HR) = 0.54 [95% CI: 0.41 to 0.70]).[5]

2.2. Health-related quality of life outcomes

Health-related quality of life was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Lung Cancer 13 (EORTC QLQ-LC13). Overall, patients in the cemiplimab plus chemotherapy group had numerically similar global health status/quality of life, function and symptom scores compared with patients treated with placebo plus chemotherapy.[6]

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

In the absence of direct evidence comparing cemiplimab plus chemotherapy with pembrolizumab (with or without chemotherapy) the submitting company presented indirect treatment comparisons. This has been used to inform the economic base case. An exploratory network meta-analysis in the PD-L1 1% to 49% population and an exploratory Matching-Adjusted Indirect Comparison (MAIC) in the PD-L1 ≥ 50% population were used as economic scenarios only; therefore, no further details are presented here.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview
Design	Time varying anchored MAICs PD-L1 ≥1% population: • Squamous NSCLC (economic base case) • Non-squamous NSCLC (economic base case) Time varying HRs were applied due to the treatment effects changing over time so a single HR would not adequately reflect the changes in the relative effectiveness throughout the follow-up period. The timepoints were reported every 3 months until month 12 and 6 monthly thereafter until 30 months.
Population	Patients with metastatic NSCLC expressing PD-L1 ≥ 1% who are previously untreated for metastatic disease
Comparators	Squamous NSCLC MAIC: pembrolizumab plus chemotherapy Non-squamous NSCLC MAIC: pembrolizumab plus chemotherapy
Studies included	Squamous NSCLC MAIC: IPD from EMPOWER-Lung-3 study for cemiplimab plus chemotherapy versus aggregate data from KEYNOTE-407[13] for pembrolizumab plus chemotherapy. Non-squamous NSCLC MAIC: IPD from EMPOWER-Lung-3 for cemiplimab plus chemotherapy versus aggregate data from KEYNOTE-189[14] for pembrolizumab plus chemotherapy.
Outcomes	OS and PFS
Results	**Squamous NSCLC MAIC** OS When compared with pembrolizumab plus chemotherapy a numerical benefit in favour of cemiplimab plus chemotherapy was reported until 18 months, thereafter the benefit is in favour of pembrolizumab plus chemotherapy. The HRs were generally close to one and credible intervals crossed one and were wide, which shows no evidence of a difference between the two treatments. PFS When compared with pembrolizumab plus chemotherapy a numerical benefit in favour of cemiplimab plus chemotherapy at the 3-month time point, thereafter the benefit is in favour of pembrolizumab plus chemotherapy. The HRs were generally close to one and credible intervals crossed one and were wide, which shows no evidence of a difference between the two treatments.

	Non-squamous NSCLC MAIC OS When compared with pembrolizumab plus chemotherapy a numerical benefit was reported in favour of cemiplimab plus chemotherapy across all time points. The HRs were generally close to one and credible intervals crossed one and were wide, which shows no evidence of a difference between the two treatments. PFS When compared with pembrolizumab plus chemotherapy, HRs numerically favoured cemiplimab plus chemotherapy for the first year and numerically favoured pembrolizumab plus chemotherapy thereafter. The HRs were generally close to one and credible intervals crossed one and were wide, which shows no evidence of a difference between the two treatments.

Abbreviations: HR = hazard ratio; IPD = individual patient data; MAIC = matching adjusted indirect comparison; NSCLC = non-small cell lung cancer; OS = overall survival; PD-L1 = programmed death ligand-1; PFS = progression-free survival.

3. Summary of Safety Evidence

Evidence from EMPOWER-Lung 3 supports the relative safety of cemiplimab plus chemotherapy compared with placebo plus chemotherapy for the treatment of patients with locally advanced (who are not candidates for definitive chemoradiation) or metastatic NSCLC. Chemotherapy is a relevant comparator for patients with locally advanced NSCLC. Data presented are the from the PD-L1 ≥ 1% subgroup analysis at June 2022 data-cut; median duration of exposure was 47 weeks with cemiplimab plus chemotherapy and 21 weeks with placebo plus chemotherapy.[12]

In the cemiplimab plus chemotherapy (n=217) and placebo plus chemotherapy (n=109) groups respectively, 96% and 93% had any treatment-emergent adverse event (TEAE); 48% and 28% had any TEAE grade ≥ 3; 6.5% and 3.7% had a TEAE that led to discontinuation of study treatment; 6.5% and 7.3% had a TEAE that led to death. The most commonly reported TEAEs reported with an incidence of ≥ 15% were anaemia (47% versus 36%), alopecia (37% versus 44%), nausea (25% versus 13%), hyperglycaemia (19% versus 13%), increased alanine transaminase (19% versus 14%), neutropenia (18% versus 12%), increased aspartate transaminase (17% versus 10%), arthralgia (17% versus 9.2%), decreased appetite (16% versus 9.2%), constipation (16% versus 9.2%), thrombocytopenia (16% versus 11%), dyspnoea (15% versus 4.6%), increased blood creatinine (15% versus 6.4%). Immune-mediated adverse events of any grade occurred in 32% of the patients in the cemiplimab plus chemotherapy group.[12]

Overall, the addition of cemiplimab to chemotherapy resulted in increased toxicity, especially haematological and immune-mediated adverse events. However, no new safety signals were identified, and regulators considered the safety profile was acceptable in this setting. Patients should be monitored for signs and symptoms of immune-mediated adverse reactions and infusion-related reactions.[1, 6]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- Cemiplimab in combination with chemotherapy would be the first immunotherapy to be made routinely available for patients with locally advanced NSCLC who are not candidates for definitive chemoradiation.
- EMPOWER-Lung 3 was a double-blind, phase III study which provides direct evidence versus placebo plus chemotherapy. Chemotherapy is the most relevant comparator for patients with locally advanced NSCLC.
- In the PD-L1 ≥ 1% subgroup (licensed population), median OS in the cemiplimab plus chemotherapy group was 23.5 months compared with 12.1 months in the placebo plus chemotherapy group (June 2022 data-cut). These data were sufficiently mature and can be considered clinically meaningful.[6] At 5-year follow-up, cemiplimab continued to show OS benefit versus placebo plus chemotherapy. Secondary outcomes including PFS and ORR were also supportive.

4.2. Key uncertainties

- There are no direct data comparing cemiplimab plus chemotherapy with:
    - pembrolizumab plus chemotherapy, which is the most relevant comparator for patients with metastatic NSCLC PD-L1 1% to <50% or
    - pembrolizumab monotherapy, which is the most relevant comparator for patients with metastatic NSCLC PD-L1 ≥50%.
- The indirect treatment comparisons (ITCs) had the following limitations; there was clinical and methodological heterogeneity between included studies; rates of subsequent immunotherapy received off study were not reported for the target population in any of the comparator studies; credible intervals were wide reflecting uncertainty in the results. The company considered it reasonable to assume similar clinical efficacy between cemiplimab plus chemotherapy and pembrolizumab plus chemotherapy from the ITC. SMC clinical experts concurred with this view.
- Results from the PD-L1 ≥ 1% subgroup (approximately 70% of the total study population) in EMPOWER-Lung 3 were not powered to detect statistical differences and should therefore be interpreted with some caution.
- Patients in EMPOWER-Lung 3 were able to continue cemiplimab plus chemotherapy following disease progression if the investigator judged the patient to be experiencing clinical benefit and if the patient had not completed the 108-week treatment period. This differs to Summary of Product Characteristics (SPC) dosing recommendations, that state treatment may be continued until disease progression or unacceptable toxicity.[1] At data-cut June 2021 (FAS population), 105/154 (68%) continued treatment with cemiplimab plus chemotherapy following BIRC-confirmed disease progression.[6]

- The 5-year follow-up results presented by the company should be interpreted with some caution. Patients in the EMPOWER-Lung 3 control group could not crossover to receive cemiplimab plus chemotherapy following progression, and in some of the countries the study was conducted in, patients were not able to routinely access immunotherapy treatment post-progression. This may represent a generalisability issue, since the expected rates of subsequent immunotherapy treatment may be higher in Scottish practice.

4.3. Clinical expert input

Clinical experts consulted by SMC considered that cemiplimab plus chemotherapy fills an unmet need in this therapeutic area, particularly for patients with locally advanced disease (who at present only receive chemotherapy) and for some patients with metastatic disease whose tumours express PD-L1 ≥ 50% since some patients would benefit from the addition of chemotherapy to immunotherapy.

4.4. Service implications

For patients with locally advanced disease, the addition of cemiplimab to chemotherapy would require an increase in resource from the service to deliver. When compared with pembrolizumab, cemiplimab is administered every 3 weeks via intravenous infusion and pembrolizumab can be administered intravenously every 6 weeks, which has benefits for the service. Additionally, a new subcutaneous formulation of pembrolizumab has been recently approved.

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

5. Patient and clinician engagement (PACE)

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of cemiplimab, as an end of life medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- Locally advanced or metastatic NSCLC is a devastating diagnosis with a poor prognosis if untreated. It is an incurable illness that has a debilitating effect on both the person and their family. The symptoms are difficult to manage and patients often live with other symptomatic comorbidities adding to symptom burden. Patients may develop breathlessness, fatigue, chronic troublesome cough, loss of appetite, weight loss, and pain. These symptoms impact on mobility, confidence, and simple activities of daily living and many may become housebound, becoming dependent on others. This can cause low mood, anxiety and depression. It may also be associated with a considerable financial strain if they are unable to work or need to fund transport for appointments. Patients may have dependents relying on their pay, they may be carers for children or elderly parents, and they may need to buy clothes due to weight loss, and energy bills are increased as they often feel the cold more. Patients suffer the stigma which is still present with smoking, and it can be particularly hard for them to accept or understand their diagnosis if they have never smoked.

- Patients with locally advanced NSCLC and PD-L1 ≥1% or with metastatic NSCLC and PD-L1 ≥50% are currently ineligible for chemotherapy plus immunotherapy due to licensing and SMC restrictions. Currently, if clinicians wish to use chemo-immunotherapy in these groups, for example, for those with very aggressive metastatic disease, individual patient requests are required before treatment can begin, and this can lead to anxiety around delays or possible decline of the request and the potential for unequal access across Scotland.
- Cemiplimab in combination with chemotherapy would widen the availability of chemo-immunotherapy to include these groups of patients. Cemiplimab plus chemotherapy may increase overall survival and may also provide benefits in PFS, improve response rates, and provide longer disease control, improving symptom control including pain and thus would allow patients to maintain their independence for longer. Any offer of a treatment that can potentially provide a bit more time and improved quality of life whilst regaining their independence cannot be underestimated. It would provide hope for patients and their loved ones.
- Clinicians are experienced at prescribing chemo-immunotherapy for lung cancer and noted the side effect profile is expected to have a similar toxicity profile to other immunotherapies and is manageable.

Additional Patient and Carer Involvement

We received a patient group submission from Roy Castle Lung Cancer Foundation, which is a registered charity. Roy Castle Lung Cancer Foundation has received 10% pharmaceutical company funding in the past two years, including from the submitting company. A representative from the patient group participated in the PACE meeting. The key points of their submission have been included in the full PACE statement considered by SMC.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

The economic case is summarised in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis in the locally advanced NSCLC, PD-L1 ≥1% population. Cost-minimisation analysis in the metastatic NSCLC, PD-L1 ≥1% population.
Time horizon	30 years.
Population	The cost-effectiveness of cemiplimab plus chemotherapy was evaluated in patients with locally advanced or metastatic, squamous or non-squamous NSCLC who were previously untreated with systemic therapy for their advanced or metastatic disease with PD-L1 ≥1%, and no EGFR, ALK or ROS1 aberrations.
Comparators	In the locally advanced NSCLC, PD-L1 ≥1% population, chemotherapy was the comparator. In the metastatic NSCLC, PD-L1 ≥1% population, pembrolizumab plus chemotherapy was the comparator.
Model description	A three-state partitioned survival model was used, with health states of pre-progression, post-progression, and death. Patients entered in the pre-progression health state and received either cemiplimab plus chemotherapy or a comparator. From this health state, patients could transition to the post-progression health state or death. Patients in the post-progression

	health state could transition to death. Subsequent treatments were administered in the post-progression health state.
Clinical data	In the locally advanced NSCLC, PD-L1 ≥1% population, clinical data for cemiplimab plus chemotherapy and chemotherapy were from EMPOWER-Lung 3.[6, 11, 12] In the metastatic NSCLC, PD-L1 ≥1% population, clinical data were sourced from the squamous and non-squamous time varying MAICs. EMPOWER-Lung 3 was the source for cemiplimab plus chemotherapy. KEYNOTE-189 (non-squamous) and KEYNOTE-407 (squamous) were the sources for pembrolizumab plus chemotherapy.
Extrapolation	In the locally advanced NSCLC, PD-L1 ≥1% population, PFS data for both cemiplimab plus chemotherapy and chemotherapy were extrapolated using log-normal distributions. OS data were adjusted for subsequent immunotherapy in EMPOWER-Lung 3 and extrapolated using log-normal distributions in both treatment arms. In the metastatic NSCLC, PD-L1 ≥1% population, chemotherapy PFS data were extrapolated using generalised gamma distributions for both squamous and non-squamous populations. Relative treatment effects from the MAIC were then applied to derive PFS curves for cemiplimab plus chemotherapy and pembrolizumab plus chemotherapy. For OS, chemotherapy data were extrapolated using a Weibull distribution in the non-squamous population and a log-normal distribution in the squamous population. MAIC-derived relative treatment effects were applied to generate OS curves for cemiplimab plus chemotherapy and pembrolizumab plus chemotherapy. Across PFS and OS, extrapolated curves for squamous and non-squamous populations were combined into weighted measures of progression and mortality risk. In the economic model, pembrolizumab plus chemotherapy was assumed to have equivalent efficacy to cemiplimab plus chemotherapy, based on the indirect evidence, which indicated no meaningful PFS and OS differences in these treatments, and expert opinion. A treatment waning assumption was included in the model, where treatment benefits for cemiplimab plus chemotherapy and pembrolizumab plus chemotherapy waned between 3 and 5 years. After this point, hazards were assumed to be equal to those for chemotherapy alone.
Quality of life	Health state utility values were derived from EORTC QLQ-C30 data from EMPOWER-Lung 3 mapped to the EQ-5D-3L.[16] The progression-free utility value was 0.757 and the progressed disease utility value was 0.728. Utility decrements were included for adverse events. Utility values were adjusted for age.
Costs and resource use	Costs included medicine acquisition, administration, subsequent treatments, adverse events, disease management, and end of life care. Cemiplimab had a 36 cycle (equivalent to 108 weeks when dosing every 3 weeks) stopping rule. In the metastatic NSCLC, PD-L1 ≥1% population, for acquisition costs of pembrolizumab with chemotherapy, the cost of pembrolizumab monotherapy was applied as a simplifying and conservative assumption.
PAS/contract price	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 was offered on the list price. PAS discounts are in place for pembrolizumab and atezolizumab (which was used in subsequent lines of therapy) and these were included in the results used for decision-making by using estimates of the comparator PAS price.

6.2. Results

SMC considered results for decision-making that took into account all relevant PAS and contract prices.
SMC is unable to present these results due to competition law issues.

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

6.3. Sensitivity analyses

A range of sensitivity analyses were presented. Key descriptions of the scenario analysis are presented below.

Table 6.3.1: Scenario analysis - Locally advanced NSCLC, PD-L1 ≥1%

	Parameter	Base case	Scenario	ICER (£/QALY)
	Base case			CiC
1a	OS and PFS curves	PFS and OS = log-normal	OS and PFS = log-logistic	CiC
1b			PFS and OS = Gamma	CiC
2	OS adjustment subsequent treatments	Adjusted OS curves	Unadjusted OS curves	CiC
3a	Waning PFS and OS	3-5 years	5 years	CiC
3b			Excluded	CiC
4a	ToT	ToT=PFS	Applying HRs to PFS to estimate ToT	CiC
4b			TTD from EMPOWER-Lung 3	CiC
5	Utility values	EMPOWER-Lung 3. PFS = 0.757. PD = 0.728	NICE TA584 IMpower 150. PFS = 0.71. PD = 0.69.	CiC
6	Wastage	No vial sharing	Vial sharing	CiC
7	Chemo regimens	Clinical opinion	EMPOWER-Lung 3	CiC
8	Time horizon	30 years	10 years	CiC
C1	1b and 5. Gamma extrapolation and Impower 150 utility values.			CiC

Abbreviations: C = combination scenario; ICER = incremental cost-effectiveness ratio; Incr = incremental; OS = overall survival; PFS = progression-free survival; PD = progressed disease; QALYs = quality-adjusted life years; ToT = time on treatment; TTD = time to treatment discontinuation.

Table 6.3.2: Scenario analysis - Metastatic NSCLC, PD-L1 ≥1%

	Parameter	Base case	Scenario	Incr. costs (£)
	Base case			CiC
1a	Waning PFS and OS	3-5 years	5 years	CiC
1b			Excluded	CiC
2a	ToT	ToT=PFS	Applying HRs to PFS to estimate ToT	CiC
2b			TTD from EMPOWER-Lung 3 and KEYNOTE-024	CiC
3	Wastage (i.e. no vial sharing)	Included	No wastage	CiC
4	Chemo regimens	Clinical opinion	EMPOWER-Lung 3	CiC
5	Time horizon	30 years	10 years	CiC

Abbreviations: OS = overall survival; PFS = progression-free survival; ToT = time on treatment; TTD = time to treatment discontinuation.

6.4. Key strengths

- Data in the locally advanced PD-L1 ≥1% economic analysis comparing cemiplimab plus chemotherapy to chemotherapy were from a phase III randomised study.

- The model structure was appropriate.
- The sources used to value costs in the economic model were appropriate.
- The one-way deterministic sensitivity analysis varied parameters through an appropriate range.

6.5. Key uncertainties

- In the locally advanced PD-L1 ≥1% population, alternative plausible extrapolations were available within selection criteria. The use of the Gamma distribution for PFS and OS in both arms resulted in a change to the ICER (Table 6.3.1, Scenario 1b).
- Pembrolizumab + chemotherapy was applied as the comparator across the whole of the metastatic NSCLC PD-L1 ≥1% population. However, the SMC-accepted therapy in patients with PD-L1 ≥50% would be pembrolizumab monotherapy. The company reported that any introduced bias would favour the comparator arm, and so the approach was conservative. This view appeared reasonable.
- There was uncertainty over the time on treatment for cemiplimab plus chemotherapy in the model. The base case set time on treatment equal to PFS to align with the SPC, where treatment may be continued until disease progression or unacceptable toxicity. The submitting company noted clinical expert support for this assumption. However, in EMPOWER-Lung 3 patients were allowed to continue treatment beyond progression. To consider this, scenario analysis explored alternatives where time on treatment was not equal to PFS. These considered applying hazard ratios to PFS to estimate time on treatment and using TTD data from clinical studies (Table 6.3.1, Scenarios 4a and 4b. Table 6.3.2, Scenarios 2a and 2b). The Committee viewed the scenarios utilising study data directly as a suitable way to explore this uncertainty, and these had a modest impact on the ICER.

7. Conclusion

After considering all the available evidence and the output from the PACE process, the Committee accepted cemiplimab for restricted use in NHSScotland.

8. Guidelines and Protocols

National Institute for Health and Care Excellence (NICE) published guidelines on 28 March 2019 (last updated 08 March 2024) titled “Lung cancer: diagnosis and management”.[17]

European Society for Medical Oncology (ESMO) have a living guideline titled “ESMO Living Guideline: Early and Locally Advanced NSCLC”. Current version is 1.2, last updated June 2026.[18]

European Society for Medical Oncology published guidelines in 2023 titled “Non-oncogene-addicted metastatic non-small-cell lung cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up”.[19]

9. Additional Information

9.1. Product availability date

02 February 2024

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per cycle (£)
Cemiplimab	**350 mg every 3 weeks via intravenous infusion until disease progression or unacceptable toxicity**	**£4,650**

Costs from BNF online on 06 July 2026. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

Locally advanced NSCLC, PD-L1 ≥1%: The submitting company estimated there would be 124 patients eligible for treatment with cemiplimab in year 1 rising to 167 in year 3.

Metastatic NSCLC, PD-L1 ≥ 1% population: The submitting company estimated there would be 884 patients eligible for treatment with cemiplimab in year 1 rising to 1,192 in year 3.

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/contract price discounts associated with comparator medicines or PAS/contract prices 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 10 September 2026.

**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 includes Scottish national contract prices in its decision-making. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document.

Patient Access Schemes (PAS): A PAS 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. The Patient Access Scheme Assessment Group (PASAG), established under the auspices of Public Services Delivery Scotland, reviews and advises NHS Scotland on the feasibility and acceptability on implementing proposed schemes. PASAG operates separately from SMC to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a PAS that has been considered acceptable for implementation by PASAG, a set of guidance notes on the operation of the scheme will be circulated to health boards' Area Drugs and Therapeutics Committees 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.