Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2840

serplulimab concentrate for infusion (Hetronifly®)

Accord Healthcare Ltd

05 December 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 full submission assessed under the end of life and orphan equivalent medicine process

serplulimab (Hetronifly®) is not recommended for use within NHSScotland.

Indication under review: in combination with carboplatin and etoposide for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

In a randomised, double-blind, phase III study in patients with previously untreated ES-SCLC serplulimab plus carboplatin and etoposide significantly improved overall survival compared with placebo plus carboplatin and etoposide.

The submitting company did not present a sufficiently robust economic analysis to gain acceptance by SMC.

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

Vice Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Serplulimab is a humanised monoclonal immunoglobulin G4 (IgG4) antibody that binds to the programmed cell death-1 (PD-1) receptors and blocks its interaction with the programmed death-ligand-1 (PD-L1) and programmed death-ligand-2 (PD-L2); this potentiates T-cell responses, including anti-tumour responses.[1, 2]

Serplulimab is administered as an intravenous (IV) infusion at a dose of 4.5 mg/kg every 3 weeks. Treatment is continued until disease progression or unacceptable toxicity. See Summary of Product Characteristics (SPC) for more details.[1]

1.2. Disease background

Small cell lung cancer (SCLC) is a very aggressive form of lung cancer that represents about 15% of all lung cancers.[3-5] SCLC can be classified into two stages of disease: limited-stage (LS) and extensive-stage (ES); approximately 70% of patients with SCLC present with ES-SCLC.[5] ES-SCLC is generally considered to be incurable and is managed palliatively with therapies aimed at prolonging survival and reducing symptoms associated with the disease.[6] Despite high response rates (60% to 70%) to first-line treatment, median overall survival (OS) is approximately one year[7, 8], with a 5-year survival of less than 5%.[9, 10] Additionally, more than 90% of patients with ES-SCLC relapse within 2 years of treatment.[11]

1.3. Treatment pathway and relevant comparators

In NHSScotland, the preferred first-line treatment for ES-SCLC is carboplatin plus etoposide in combination with either atezolizumab (SMC2279) or durvalumab (SMC2734); however, some patients unsuitable for immunotherapy may receive carboplatin plus etoposide alone or single agent platinum chemotherapy as an alternative.[12] Atezolizumab in combination with carboplatin plus etoposide was deemed to be the most relevant comparator by clinical experts contacted by SMC.

1.4. Category for decision-making process

Eligibility for interim acceptance decision option

Serplulimab received an Innovation Passport allowing entry into the Innovative Licensing and Access Pathway.

Eligibility for a PACE meeting

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

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

The evidence to support the use of serplulimab for this indication comes from the ASTRUM-005 study. Details are summarised in Table 2.1

Table 2.1. Overview of relevant study

Criteria	ASTRUM-005[13]
Study design	Multicentre, randomised, double-blind, phase III study.
Eligible patients	• Aged ≥ 18 years, with an ECOG PS of 0 or 1. • Histological or cytological diagnosis of ES-SCLC (as per the VALG staging system) with ≥ one measurable lesion as assessed by the IRRC according to RECIST 1.1 within 4 weeks prior to randomisation. • No prior systemic therapy for ES-SCLC. • Patients with asymptomatic and stable brain metastases were permitted.
Treatments and Randomisation	Patients were randomised 2:1 to receive serplulimab 4.5 mg/kg or placebo intravenously on day 1 of a 21-day treatment cycle. All patients also received chemotherapy for up to a maximum of four (21-day) treatment cycles which consisted of: intravenous carboplatin within the AUC of 5 mg/mL/min (up to 750 mg) on day 1 and, etoposide 100 mg/m^2 on days 1, 2, and 3. Treatment continued until disease progression, death, unacceptable toxicity, withdrawal of consent, or other reasons specified in the study protocol. At the investigator's discretion, patients who discontinued initial treatment due to disease progression could continue with blinded serplulimab or placebo in addition to second-line chemotherapy, until the second disease progression, intolerable toxicity, death, withdrawal of consent, or lost to follow-up. Randomisation was stratified according to: PD-L1 expression level (TPS < 1% or ≥ 1% or not available/evaluable); brain metastasis (yes or no); and age (≥ 65 years or < 65 years).
Primary outcome	OS was defined as the time from randomisation to death due to any cause.
Selected Secondary outcomes	PFS, assessed by IRRC according to RECIST v1.1.
Statistical analysis	Only OS was tested for statistical significance. No other outcomes were adjusted for multiplicity and PFS was considered exploratory.

AUC = area under the serum drug concentration time curve; ECOG PS = eastern cooperative oncology group performance status; ES-SCLS = extensive-stage small cell lung cancer; IRRC = Independent Radiology Review Committee; OS = overall survival; PFS = progression-free survival; RECIST 1.1 = Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1; TPS = tumour proportion score; VALG = Veterans Administration Lung Study Group

At the October 2021 data cut-off (primary analysis), serplulimab plus carboplatin and etoposide resulted in a statistically significant improvement in OS compared with placebo plus carboplatin and etoposide. The submitting company also provided results of the final end-of-study exploratory analysis (data cut-off May 2024), after unblinding; the OS and PFS results of this final analysis were consistent with the primary analysis and were used to inform the economic model. Results from both data cut-offs are presented in Table 2.2, where possible.

Table 2.2 Results of the primary and selected secondary outcomes from the ASTRUM-005 study (intention-to-treat population).

	Serplulimab + carboplatin + etoposide (n=389)	Placebo + carboplatin + etoposide (n=196)	Serplulimab + carboplatin + etoposide (n=389)	Placebo + carboplatin + etoposide (n=196)
Data cut-off	October 2021[2, 13]		May 2024[14]	
Primary outcome: OS				
Median OS follow-up	12.5 months	12.3 months	42.4 months	
Deaths	146	100	*	*
Median OS	15.4 months	10.9 months	15.8 months	11.1 months
Hazard ratio (95% CI), p-value	0.63 (0.49 to 0.82), p<0.001		0.60 (0.49 to 0.73)	
KM estimated OS at 12 months	61%	48%	*	*
KM estimated OS at 24 months	43%	7.9%	*	*
KM estimated OS at 48 months	Not recorded	Not recorded	22%	7.2%
Secondary outcome: PFS by IRRC				
Median PFS follow-up	9.5 months	8.4 months	Not available	
PFS events	223	151	*	*
Median PFS	5.7 months	4.3 months	5.8 months	4.3 months
Hazard ratio (95% CI)	0.48 (0.38 to 0.59)		0.47 (0.38 to 0.57)	
KM estimated PFS at 12 months	24%	6.0%	*	*
KM estimated PFS at 24 months	Not recorded	Not recorded	*	*

CI = confidence interval; IRRC = Independent Radiology Review Committee; KM = Kaplan-Meier; OS = overall survival; PFS = progression-free survival; * = company considers results confidential.

In ASTRUM-005, 69% of patients in the study were Asian (401/585) whilst 31% were non-Asian (184/585); all non-Asian patients were white. At the October 2021 data cut-off, pre-specified efficacy analysis of the non-Asian subgroup showed OS results that trended in favour of the serplulimab group (median OS follow-up of 9.1 months); hazard ratio (HR) = 0.70 (95% CI: 0.43 to 1.13).[2] Updated results at the May 2024 data cut-off also confirmed this trend.

2.2. Health-related quality of life (HRQoL) outcomes

HRQoL was assessed in ASTRUM-005 using the using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30), EORTC 13-item lung cancer module (EORTC QLQ-LC13) and the EuroQol 5-dimension 5-level questionnaire (EQ-5D-5L). These scales were evaluated prior to the first dose and at every other subsequent dosing cycle. Overall, the changes in all domains were comparable between the two treatment groups.[15]

2.3. Supportive studies

The ASTRIDE study (NCT05468489) is a randomised, open-label, phase III study evaluating the efficacy and safety of serplulimab plus carboplatin and etoposide in comparison with atezolizumab plus carboplatin and etoposide in previously untreated US patients with ES-SCLC.[16] The study is currently in progress with a reported primary completion date of December 2025.[17] Since atezolizumab is the most relevant comparator, and the US population may be more representative of patients in Scotland, then these results may be informative. The European regulator has recommended that the submitting company report the results of this study to clarify the size of the treatment effect of serplulimab.[2]

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

In the absence of direct evidence comparing serplulimab plus carboplatin and etoposide with atezolizumab plus carboplatin and etoposide, the submitting company presented an anchored matching-adjusted indirect comparison (MAIC). The results of the MAIC were used directly in the cost-effectiveness model.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview
Design	Matching-adjusted indirect comparison.
Population	Adult patients with previously untreated ES-SCLC.
Comparators	Atezolizumab in combination with carboplatin and etoposide.
Studies included	ASTRUM-005[14] and IMpower133.[16]
Outcomes	OS and investigator-assessed PFS.
Results	For both the unadjusted (Bucher) and matching adjusted analyses: improvements in OS and investigator-assessed PFS were found in favour of serplulimab plus carboplatin and etoposide; the OS confidence intervals all crossed 1, meaning the results were not significant. The PFS differences were significant, although the confidence intervals were wide so should be interpreted with caution. The company consider the results confidential.

CI = confidence interval; ES-SCLC = extensive-stage small cell lung cancer; HRs = hazard ratios; PFS = progression-free survival; OS = overall survival

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

3. Summary of Safety Evidence

Evidence from ASTRUM-005 supports the relative safety of serplulimab plus carboplatin and etoposide compared with placebo plus carboplatin and etoposide.

In ASTRUM-005, at the June 2022 data cut-off, the median number of treatment cycles in the serplulimab group was 8 (range: 1 to 32) and 6 (range: 1 to 36) in the placebo group; the median total numbers of treatment cycles of carboplatin and etoposide were both 4 cycles in both treatment groups as specified per the protocol.[15] The mean (SD) relative dose intensity was 92% (8.9%) for serplulimab and 91% (9.2%) for placebo; the mean relative dose intensities of carboplatin and etoposide were similar between the serplulimab and placebo treatment groups.[2] In the serplulimab (n=389) and placebo (n=196) groups respectively, patients reporting a treatment-related: grade ≥3 adverse event (AE) were 33% versus 28%; serious AE were 17% versus 14%; and the proportion of patients discontinuing their study treatment due to a treatment-related AE was 4.9% versus 4.1%.[15]

The safety profile of serplulimab was deemed to be similar to other immune checkpoint inhibitors approved for this indication. It is noted that the safety data is mainly obtained in an Asian population, but is not expected to be substantially different in the non-Asian population.[2]

The incidence of the most common grade ≥ 3 treatment-emergent AEs (occurring in ≥ 2% in either treatment group) were similar in both treatment groups; these data were included in the economic model. There was also a higher incidence of immune-related AEs (any grade) in the serplulimab group compared with the placebo group (38% versus 19%); this included

hypothyroidism (11% versus 1.5%) and hyperthyroidism (9.0% versus 3.1%). Whilst some of these can be serious, most are considered manageable with adequate warnings and precautions including dose reduction and interruption as reflected in the SPC.[2] The SPC provides recommendations for the management of immune-related reactions.[1]

There are no data comparing the safety of serplulimab plus carboplatin and etoposide with atezolizumab plus carboplatin and etoposide.

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- ASTRUM-005 was a double-blind, randomised, controlled, phase III study that appears to have been well-conducted; stratification and most baseline characteristics were balanced between the two treatment groups in the full ITT population. These design aspects make it likely that there is a low risk of bias and provide reassurance about the internal validity of the study.
- In ASTRUM-005, patients with previously untreated ES-SCLC who received serplulimab plus carboplatin and etoposide had statistically significant improvements in OS compared with placebo plus carboplatin and etoposide; the improvement in the median OS by 4.5 months was deemed to be clinically meaningful by the regulator.[2] OS results at the final data cut-off (May 2024) after approximately 3.5 years of follow-up were also consistent with the earlier data cuts which is reassuring.[14]
- Serplulimab is the first PD-1 inhibitor licensed for the treatment of ES-SCLC in the UK. However, clinical experts contacted by SMC were unsure if this mode of action would translate into a difference in clinical efficacy compared with the PD-L1 inhibitors currently used in practice.

4.2. Key uncertainties

- There were several key differences in the baseline characteristics of the ITT population of ASTRUM-005 compared to the SCLC population in Scotland, particularly with regards to the proportion of Asian participants, sex and never-smokers. This raises concerns about whether the study population is representative of that in Scotland; a concern that was also noted by some experts contacted by SMC.
- The interpretation of the OS results, and its applicability to the Scottish population, is complicated by the proportion of patients who continued serplulimab following progressive disease and by the variety of subsequent treatments that do not align with Scottish clinical practice.
- There are no direct data comparing serplulimab plus carboplatin and etoposide with the most relevant comparator to this submission (atezolizumab plus carboplatin and etoposide). The submitting company provided an anchored MAIC which had several limitations, including differences in baseline characteristics of included patients (proportions of females and those of Asian ethnicity), prior anti-cancer treatments and subsequent treatments. The submitting company concluded that the results of the MAIC demonstrate that serplulimab plus carboplatin and etoposide improved both OS and PFS compared with atezolizumab plus

carboplatin and etoposide. Only the PFS results were significantly differentand based on the limitations above, the results of the MAIC are uncertain.

- There were substantial differences in the median bodyweights of the ITT population (66.5 kg) and the non-Asian subgroup (77.0 kg); this meant more non-Asian patients likely received a higher dose of serplulimab compared with the Asian population.[2] Higher doses of serplulimab will likely be used in Scottish clinical practice than were used in ASTRUM-005; the impact that these higher doses would have on efficacy and safety (higher exposure) are unknown.

4.3. Clinical expert input

Most clinical experts consulted by SMC considered that serplulimab would not fulfil an unmet need and there were mixed views on whether it was a therapeutic advancement given the other immunotherapy options for this indication.

4.4. Service implications

Clinical experts contacted by SMC mentioned that there could be some impact for patients and the service if serplulimab is used over alternative immunotherapy options that are available as a subcutaneous formulation (for example atezolizumab).

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 **serplulimab (Hetronifly®), 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:

- ES-SCLC is an aggressive malignancy where many patients relapse and rarely live beyond one year. The condition is usually diagnosed at a late stage when many patients and families are given the devastating news at diagnosis that they only have weeks or months to live.
- Following diagnosis, the condition usually progresses rapidly with patients experiencing many debilitating symptoms that can cause patients to lose their mobility and confidence. This results in huge emotional distress, for both the person and their loved ones. Patients can feel guilt from being a smoker and feel their lives spiralling out of control as the symptoms worsen and the condition progresses.
- Families may also find themselves in a caring role very quickly due to the rapid increase in symptoms and find themselves overwhelmed with the increased dependence of their loved ones. As well as the intense caregiving demands, families also face impending bereavement.
- ES-SCLC is generally considered to be incurable and despite recent approvals of immunotherapies like atezolizumab and durvalumab, the survival benefit is still only measured in additional weeks when compared to chemotherapy. Patients can often experience an improvement in quality of life when starting first-line treatment, but most will then suffer a relapse, and a large proportion will not be fit enough to receive second-

line treatment.

- Serplulimab plus chemotherapy offers the potential for a longer survival of approximately 4 to 5 months beyond traditional chemotherapy. This treatment regimen may also prolong control of cancer, improve symptoms (such as dyspnoea, pain and fatigue) and performance status. Improved progression-free survival would also delay the use of less effective and less tolerable second-line treatment options that would require more visits to hospital. Optimising first-line treatment provides the best chance for patients to remain well.
- This treatment combination could allow patients to live longer, feel better and reduce stress on carers stress as patients maintain their independence for longer and regain some control of their life again.
- The safety profile of serplulimab plus chemotherapy appears to be similar to other immunotherapies that are already used in clinical practice. The monitoring and side effect management are well known to clinical teams and services.
- There are no major service implications expected with this medicine.

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 9.6% pharmaceutical company funding in the past two years, with none from the submitting company. A representative from Roy Castle Lung Cancer Foundation 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

An economic case was presented and is summarised in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis
Time horizon	20 years
Population	Adult patients with ES-SCLC with no prior treatment
Comparators	Atezolizumab plus carboplatin and etoposide (chemotherapy) or chemotherapy alone
Model description	A cohort-based partitioned survival model was used with three health states: progression-free (PF), progressed disease (PD) and death.
Clinical data	Data on PFS, OS, time to off treatment (TTOT), baseline patient characteristics and adverse events (AEs) for the serplulimab and chemotherapy arms of the model were from ASTRUM-005.[14] Hazard ratios from the MAIC were applied to extrapolated serplulimab data to estimate PFS, overall survival and treatment duration with atezolizumab.
Extrapolation	The company extrapolated long-term PFS, overall survival and TTOT for serplulimab and chemotherapy for use in the economic model using parametric survival modelling with independently fitted loglogistic distributions selected for each. Curve selection was based on goodness of fit statistics and clinical expert opinion. The relative efficacy of atezolizumab was estimated by applying the MAIC hazard ratios for overall

	survival and PFS to the respective serplulimab survival curves. Treatment duration for atezolizumab was estimated by applying the overall survival hazard ratio from the MAIC to the serplulimab extrapolated TTOT curve. This approach was selected as there were no data to inform this parameter and the analysis assumed that patients could be treated with serplulimab or atezolizumab beyond the point of disease progression.
Quality of life	EQ-5D-3L data from ASTRUM-005 were used to derive utility values for use in the economic model for the PF (0.830) and PD (0.796) health states. These data were also analysed to explore utility values that varied by on/off treatment status and proximity to death in scenario analysis. Utility values were adjusted for age. AE disutilities were included according to their frequency observed in the respective arms of the ASTRUM-005 study for serplulimab and chemotherapy. The frequency of AEs in the atezolizumab arm were from the rate of AEs observed in the atezolizumab arm of IMpower133 adjusted using the ratio of AEs in the placebo arms of the IMpower133 and ASTRUM-005 studies. AE disutilities were applied according to a constant probability per cycle.
Costs and resource use	Costs included in the model were for medicine acquisition, administration, subsequent treatments, AEs, disease management, terminal care and prophylactic cranial irradiation. Relative dose intensities from ASTRUM-005 were applied to serplulimab and chemotherapy medicines, and from IMpower133 for atezolizumab.
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 was offered on the list price. A PAS discount is in place for atezolizumab and this was included in the results used for decision-making by using an estimate of the comparator PAS price.

6.2. Results

The company presented results comparing serplulimab plus carboplatin and etoposide to atezolizumab plus carboplatin and etoposide, and carboplatin plus etoposide. The results of these analyses are presented in Table 6.2. The key drivers of the cost-effectiveness results were medicine acquisition costs and post-progression survival. SMC considered results for decision-making that took into account all relevant PAS. SMC is unable to present these results due to competition law issues.

Table 6.2: Base case results (PAS for serplulimab and atezolizumab)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incr. costs (£)	Incr. LYG	Incr. QALYs	ICER (£/QALY)
Serplulimab	CIC	2.47	1.73	-	-	-	-
Atezolizumab	CIC	1.74	1.24	CIC	0.74	0.49	CIC
Carboplatin-etoposide	21,869	1.38	1.00	CIC	1.09	0.74	CIC

Abbreviations: CIC = commercial in confidence, ICER = incremental cost-effectiveness ratio, Incr. = incremental, LYG = life years gained, PAS = patient access scheme, QALY = quality-adjusted life year

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

6.3. Sensitivity analyses

A range of sensitivity and scenario analysis were considered for the comparators described in section 6.2 and description of key scenarios are provided in Table 6.3.

The company provided probabilistic sensitivity analysis, deterministic sensitivity analysis (DSA) and scenario analysis. In the DSA, the parameters with the greatest impact on the incremental cost-effectiveness ratio were the overall survival hazard ratio from the MAIC, medicine acquisition cost and the selection of overall survival extrapolations for serplulimab.

Table 6.3 Key scenario analysis

	Parameter	Base case	Scenario
1a	Time horizon	20	5
1b			10
1c			15
2a	OS parametric model for serplulimab	Loglogistic	Weibull
2b			Gamma
2c			Exponential
3	PFS parametric model for serplulimab	Loglogistic	Gamma
4	TTOT parametric model for serplulimab	Loglogistic	Lognormal
5a	Relative efficacy for atezolizumab	MAIC HRs for OS and PFS (after matching)	HRs from MAIC (before matching)
5b			Independent model fitted to pseudo-IPD from IMpower133
5c			OS HR = 1
5d			Lower bound of the OS HR 95% CI
5e			Upper bound of the OS HR 95% CI
6a	Utilities	Progression status	Time to death
6b			Progression status by on/off treatment
7	Adverse events	Include	Exclude
8a	Treatment waning	Excluded	Immediate loss of treatment effect

			at 5 years
8b			Gradual loss of treatment effect from 5-10 years
9	Administration of etoposide	Intravenous	Oral
10a	Patient weight	ASTRUM-005 ITT population = 68.4kg	Non-Asian subgroup (13% female) = 78.8kg
10b			Non-Asian subgroup reweighted for 50% female = 76.4kg
11	Treatment beyond progression	Included	Excluded
12	Comparator	Atezolizumab	Durvalumab
C1	Combined scenario analysis	Log logistic distribution for serplulimab OS + ASTRUM-005 ITT population weight	2d + 10 Gamma distribution for serplulimab OS + non-Asian subgroup weight
C2		Serplulimab vs atezolizumab OS HR + ASTRUM-005 ITT population weight	5c + 10 Serplulimab vs atezolizumab OS HR = 1 + non-Asian subgroup weight
C3			5e + 10 Lower bound of MAIC OS HR 95% CI
C4		20-year time horizon + ASTRUM-005 ITT population weight	1c + 10 15-year time horizon + ASTRUM-005 non-Asian subgroup weight

Abbreviations: AE = adverse event; CI = confidence interval; CIC = commercial in confidence; HR = hazard ratio; IPD = individual patient data; ITT = intention to treat; kg = kilograms; MAIC = matched adjusted indirect comparison; OS = overall survival; PFS = progression-free survival; TTOT = time to off treatment

6.4. Key strengths

- The model structure was typical of oncology appraisals and felt appropriate for the decision problem.
- The availability of randomised, double-blinded, evidence from ASTRUM-005, which showed a benefit for OS and PFS with serplulimab plus carboplatin and etoposide compared to chemotherapy alone.

6.5. Key uncertainties

- There was uncertainty regarding the extrapolation of serplulimab plus carboplatin and etoposide OS, PFS and TTOT data from the ASTRUM-005 study. Though the company explored

a variety of approaches, none of the standard parametric models nor more flexible models had a good fit to the study KM data or produced plausible long-term outcomes. Alternative parametric models were explored in sensitivity analysis which highlighted the sensitivity of the cost-effectiveness results to alternative extrapolations for serplulimab OS. OS models that were better aligned with OS estimates for patients treated with serplulimab elicited from experts by the submitting company, including the Weibull (Scenario 2a), Gamma (Scenario 2b) and exponential distributions (Scenario 2c), resulted in higher estimates of cost-effectiveness.

- There was an absence of direct data comparing serplulimab to atezolizumab which necessitated a MAIC to provide estimates of relative efficacy for the economic analysis. There were uncertainties with the MAIC which in turn created uncertainty in the PFS and OS hazard ratios used to estimate the relative efficacy of atezolizumab compared to serplulimab in the economic evaluation. Additionally, the OS HR confidence intervals for serplulimab versus atezolizumab from the MAIC lacked statistical significance, whereas the point estimate of the hazard ratio applied in the economic evaluation maintained a significant survival benefit for serplulimab over the duration of the model time horizon. In a scenario where the OS HR for serplulimab versus atezolizumab was set to 1 (no difference) there was a large increase in the estimate of cost-effectiveness (Scenario 5c). The Committee noted that some of the uncertainties associated with the comparison with atezolizumab may be resolved following the completion of the phase III comparative ASTRIDE study.
- The health state utility values used in the company's base case analysis seemed high for the disease area and may not have fully captured the negative impact of later stages of ES-SCLC which generated a face validity concern. There was a paucity of data to provide external validation for the health state utilities. Alternative approaches were explored, including a time to death approach, on/off treatment status and the lower bounds of the confidence intervals for the health state utility analysis used for the base case. The results of the analysis were stable to varying health state utilities (Scenarios 6a and 6b).
- The average bodyweight of patients in the ASTRUM-005 ITT population was much lower than that of the non-Asian population; the non-Asian population bodyweight seemed more likely to be representative of the SCLC population in Scotland. As the dose of serplulimab is calculated according to bodyweight, the company's selection of the ITT population weight for the base case analysis was likely to underestimate medicine acquisition costs in the serplulimab arm of the model and bias the results of the analysis in its favour. A scenario analysis that used the ASTRUM-005 non-Asian population average bodyweight resulted in a higher estimate of cost-effectiveness (Scenario 10a). The company provided an additional scenario which used patient weight from the non-Asian subgroup of ASTRUM-005 reweighted to assume 50% female patients (Scenario 10b). A range of scenarios were explored that combined the ASTRUM-005 non-Asian population average bodyweight with other alternative assumptions (Scenarios C1 – C4).
- Treatment beyond progression was included in the model for serplulimab and atezolizumab as this reflected the protocol in the ASTRUM-005 and IMpower133 studies. In Scottish clinical practice patients are not likely to be treated with serplulimab or atezolizumab beyond disease progression. This made treatment duration for serplulimab and atezolizumab, and their

associated costs, highly uncertain. A scenario analysis that capped treatment duration at disease progression was explored (Scenario 12). This scenario had the additional uncertainty that efficacy in the model was not based on treatments costed for in the analysis.

- Serplulimab treatment duration required extensive extrapolation beyond the available ASTRUM-005 TTOT data. Most alternative parametric distributions explored in scenario resulted in higher estimates of cost-effectiveness (Scenario 4).

7. Conclusion

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

After considering all the available evidence and the output from the PACE process, the Committee was unable to accept serplulimab for use in NHSScotland.

8. Guidelines and Protocols

The National Institute for Health and Care Excellence (NICE) published Lung cancer: diagnosis and management guidelines in 2019; updated in March 2024.[18]

In 2021, the European Society for Medical Oncology (ESMO) published the guideline - SCLC: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.[6]

9. Additional Information

9.1.
Product availability date

21 November 2025

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per 21-day cycle (£)
Serplulimab 10 mg/mL concentrate for solution for infusion	**4.5 mg/kg every 3 weeks until disease progression or unacceptable toxicity**	**5,287**

Costs from NHS dm+d browser on 25 November 2025. Costs calculated using the full cost of vials assuming wastage. Costs do not take any patient access schemes into consideration. The median number of cycles of serplulimab used in ASTRUM-005 was 8; the median weight in the non-Asian subgroup was 77.0 kg.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The submitting company estimated there would be 178 patients eligible for treatment with serplulimab each year. The uptake rate was estimated to be 5% (9 patients) in years 1, 2 and 3.

SMC is unable to publish the budget impact due to commercial in confidence issues.

References

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This assessment is based on data submitted by the applicant company up to and including **17 October 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:

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.