

tarlatamab powder for solution for infusion (Imdylltra[®])

Amgen Ltd

10 October 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

tarlatamab (Imdylltra[®]) is not recommended for use within NHSScotland.

Indication under review: treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) with disease progression on or after at least two prior lines of therapy including platinum-based chemotherapy.

In a single-arm, open-label, phase II study in patients with ES-SCLC who had received at least two prior lines of therapy, tarlatamab resulted in an objective response rate of 40%.

The submitting company's justification of the treatment's cost in relation to its health benefits was not sufficient and in addition the company did not present a sufficiently robust economic analysis to gain acceptance by SMC.

Chair

Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Tarlatamab is a bispecific T-cell engager (BiTE) that binds to delta-like ligand 3 (DLL3) expressed on the surface of tumour cells and CD3 expressed on the surface of T cells. This bispecific binding triggers T-cell activation, the production of inflammatory cytokines, and the release of cytotoxic proteins; all of which results in lysis of tumour cells.¹

Tarlatamab is administered as an intravenous (IV) infusion at a dose of 1 mg on day 1, followed by a 10 mg dose on days 8, 15, and every 2 weeks thereafter. 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.²⁻⁴ 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.^{2, 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.^{5, 6}

1.3. Treatment pathway and relevant comparators

Current preferred first-line treatment for ES-SCLC consists of atezolizumab in combination with carboplatin and etoposide (SMC2279) or durvalumab in combination with etoposide and either carboplatin or cisplatin (SMC2734).⁷ However, despite high response rates (60% to 70%) to first-line treatment, median overall survival is approximately one year^{8, 9}, with more than 90% of patients with ES-SCLC relapsing within two years of treatment.^{5, 10} Preferred second-line treatment options for ES-SCLC in NHSScotland include re-challenge with carboplatin and etoposide (after being more than 90 days progression free); combination therapy with cyclophosphamide, doxorubicin and vincristine (CAV); or oral topotecan.⁷

Other than tarlatamab, there are no licensed treatments in the UK for ES-SCLC following two prior lines of treatment (that is third line and beyond). Only 20% to 30% of patients diagnosed with SCLC receive third-line therapy.^{5, 11} Treatment options are limited to re-challenge with previous second-line therapies, even if this means re-treatment with the same or a similar treatment option⁷. Median overall survival (OS) is approximately 4 months with response rates as low as 21%.⁵

1.4. Category for decision-making process

Eligibility for interim acceptance decision option

Tarlatamab has conditional marketing authorisation from the Medicines and Healthcare Products Regulatory Agency (MHRA). Tarlatamab also received an Innovation Passport allowing entry into the Innovative Licensing and Access Pathway (ILAP).

Eligibility for a PACE meeting

Tarlatamab meets SMC end of life and orphan 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 tarlatamab for this indication comes from the DeLLphi-301 study. Details are summarised in Table 2.1.

Table 2.1. Overview of relevant study

Criteria	DeLLphi-301 study (parts 1 and 2). ¹²
Study design	Multicentre, open-label, phase II study with three parts: a dose evaluation phase (part 1), a dose expansion phase (part 2) and a phase with a modified safety protocol/reduced inpatient monitoring (part 3). Only results from part 1 and part 2 have been included in this submission.
Eligible patients	- Aged ≥ 18 years with an ECOG PS of 0 to 1. - SCLC with $\geq$ one measurable lesion as defined by RECIST v1.1. - Histologically or cytologically confirmed SCLC with disease progression that had relapsed after, or was refractory to, one platinum-based treatment regimen and at least one other line of therapy. - Re-treatment with a platinum-based regimen was considered a second line of therapy. - A platinum-based regimen followed by a checkpoint inhibitor/anti-PD-L1 as maintenance therapy was considered one line of therapy. - In countries where standard of care first-line systemic treatment includes platinum containing chemotherapy in combination with a PD-L1 inhibitor, these patients must have failed PD-L1 inhibitor treatment as part of their first-line systemic treatment or were ineligible to receive PD-L1 inhibitor therapy. - Positivity for DLL3 expression on tumour cells was not required for study entry.
Treatments	In part 1 of DeLLphi-301, patients were randomised to receive 10 mg or 100 mg of tarlatamab. However, only the cohort of patients who received the licensed 10 mg dose in parts 1 and 2 will be discussed hereafter, as this is the relevant population for the submission. It should be noted that the 10 mg group included patients in part 2 who enrolled after dose selection and did not participate in part 1. In parts 1 and 2 of DeLLphi-301, patients received a step dose of 1 mg of tarlatamab on day 1 of cycle 1, after which they received 10 mg on day 8 and day 15 of cycle 1 and every 2 weeks thereafter in 28-day cycles (two doses per cycle) until disease progression occurred.
Primary outcome	ORR, defined as the proportion of patients achieving a best overall response of CR or PR as determined by BICR according to RECIST version 1.1. Patients without a post-baseline tumour assessment were considered non-responders. Up until the June 2023 data cut-off (primary efficacy analysis), efficacy analyses were all conducted in the BICR FAS population (except for OS which was conducted in the SAS). After the June 2023 data cut-off, all efficacy analyses were conducted in the SAS (as per FDA request). It should be highlighted that the BICR FAS and SAS populations contain the same 99 patients.
Secondary outcomes	These included but were not limited to: PFS by BICR, and OS.
Statistical analysis	DeLLphi-301 was a single-arm study. No adjustment for multiplicity was pre-specified.

BICR = blinded independent central review; CR = complete response; DLL3 = delta-like ligand 3; ECOG PS = Eastern Cooperative Oncology Group performance status; FAS = full analysis set; FDA = Food and Drugs Administration; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; PR = partial response; RECIST v1.1 = Response Evaluation Criteria in Solid Tumours version 1.1; SAS = safety analysis set; SCLC = small cell lung cancer.

Results from the latest formal October 2023 data cut-off were used to inform the economic model^{13, 14}; updated results from the later exploratory January 2024 (ORR by BICR and PFS only) and May 2024 (OS only) data cut-offs are also available.¹⁵ Detailed results from both data cut-offs are presented in Table 2.2.

Table 2.2. Primary and selected secondary outcomes from the DeLLphi-301 study (safety analysis set).

	Tarlatamab 10 mg (n=99)	Tarlatamab 10 mg (n=99)
Data cut-off (unless otherwise specified)	October 2023 ^{13, 14}	January 2024 ^{13, 15}
Primary outcome: ORR by BICR		
Median ORR follow-up	AIC	16.6 months
Overall response rate, % (n)	40% (40)	40% (40)
CR, % (n)	2.0% (2)	2.0% (2)
PR, % (n)	38% (38)	38% (38)
Secondary outcome: PFS by BICR		
Median PFS follow-up	13.6 months	16.4 months
PFS events	AIC	AIC
Median PFS (95% CI), months	4.3 (3.0 to 5.6)	4.3 (2.9 to 5.6)
KM estimated PFS at 12 months	25%	24%
Secondary outcome: OS		
Median OS follow-up	13.8 months	20.7 months (May 2024 data cut-off) ¹⁵
Deaths	AIC	AIC
Median OS (95% CI), months	15.2 (10.8 to NE)	15.2 (10.8 to NE)
KM estimated OS at 12 months	57%	57%

AIC = academic in confidence; BICR = blinded independent central review; CI = confidence interval; CR = complete response; KM = Kaplan-Meier; NE = not estimable; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; PR = partial response.

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

HRQoL was assessed in DeLLphi-301 using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30), the EuroQoL 5-dimension 5-level questionnaire (EQ-5D-5L), and the 13-item lung cancer module (QLQ-LC13). From baseline up to cycle 12, tarlatamab resulted in improved dyspnoea, and maintained cough and chest pain symptoms as observed in EORTC QLQ-C30 and QLQ-LC13 questionnaires. There was also a consistent trend towards improvement for global health status, while physical functioning remained similar to baseline (EORTC QLQ-C30).¹⁶

2.3. Supportive studies

DeLLphi-304 (NCT05740566) is a multinational, open-label, phase III study comparing tarlatamab (n=254) with chemotherapy (n=255) in patients with relapsed SCLC after receiving platinum-based chemotherapy as first-line treatment.¹⁷

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

In the absence of direct evidence with relevant comparators including topotecan, cyclophosphamide plus doxorubicin and vincristine (CAV) and carboplatin plus etoposide, the submitting company conducted an unanchored matching-adjusted indirect treatment comparison (MAIC). The MAIC used Individual Patient Data (IPD) from the DeLLphi-301 study, and pseudo-IPD from a UK real-world evidence (RWE) study that combined registry data from adults who had treatment for SCLC in the NHS in England (UK Cancer Analysis System [CAS] study). The base case results from the MAIC have been used to inform the economic analysis. See Table 2.3 for details.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview
Design	Unanchored MAIC.
Population	Adult patients with advanced SCLC with disease progression on or after platinum-based chemotherapy receiving treatment in the third line and beyond.
Comparators	Available treatment options received by patients initiating third-line therapy (UK CAS) which includes: topotecan (40%); CAV or other chemotherapy regimens (35%); carboplatin in combination with etoposide (20%); and other platinum containing regimens (5%).
Studies included	DeLLphi-301 study ¹² ; UK CAS RWE study.
Outcomes	OS and PFS (TTD was used as a proxy for PFS in the UK CAS RWE study).
Results	For both OS and PFS, all HRs (unadjusted and adjusted) were < 1 and the 95% CIs did not contain 1, indicating that tarlatamab is superior to the basket of comparators for both of these outcomes.

CAV = cyclophosphamide plus doxorubicin and vincristine; CAS = Cancer Analysis System; CI = Confidence Interval; HRs = Hazard ratios; MAIC = Matching-adjusted indirect treatment comparison; OS = overall survival; PFS; progression free survival; RWE= Real-world evidence; SCLC = small cell lung cancer; TTD = time to treatment discontinuation; UK = United Kingdom.

The submitting company also conducted an additional indirect treatment comparison (ITC) using RWE from the US-based Flatiron database, in which IPD and direct PFS data were available; this additional analysis was explored as a scenario in the economic analyses. The results are consistent with the MAIC used for the base case analysis (using the UK CAS study).

[*Other data were also assessed but remain confidential.**](#)

3. Summary of Safety Evidence

Evidence from the DeLLphi-301 study supports the safety of tarlatamab for the treatment of patients with ES-SCLC. However, there are no comparative safety data available.

In the DeLLphi-301 study at the October 2023 data cut-off, all patients (133/133) who received the licensed 10 mg dose in parts 1, 2, and 3 reported a treatment-emergent adverse event (AE); these were considered treatment-related in most patients. Treatment-related AEs led to dose interruption in 15% of patients and discontinuation in 3% of patients.¹⁸ Any grade ≥ 3 treatment-emergent AE was reported by 63% (84/133) of patients, the most common grade ≥ 3 treatment-emergent AEs (occurring in ≥ 2% of these patients) were: lymphopenia and lymphocyte count decreased (14%); anaemia (7.5%); hyponatraemia (6.0%); neutropenia (6.0%); asthenia (5.3%); fatigue (5.3%); pneumonia (4.5%); decreased appetite (3.0%); hypertension (3.0%); general physical health deterioration (2.3%); hypokalaemia (2.3%); nausea (2.3%); and respiratory tract infection (2.3%).¹⁸ The economic analysis includes safety data from parts 1 and 2 only, the rates of grade ≥ 3 AEs were similar in this population.

Cytokine release syndrome (CRS), which was an AE of special interest, is a potentially life-threatening condition associated with symptoms including: pyrexia, hypotension, fatigue, hypoxia, tachycardia, headache, chills, nausea, and vomiting.¹ It was reported in 53% (70/133) of patients with most events occurring after the first or second dose; these were mostly grade 1 (60%) or grade 2 (39%) in severity, though one patient with concurrent grade 3 CRS died from respiratory failure. The majority of cases were managed with supportive care, however 11% (8/70) of patients with CRS required additional intervention with tocilizumab. In parts 1 and 2 (48 hours of

mandatory monitoring after the first dose) 22% (22/99) of patients required hospital admission for serious CRS (median duration of 4 days) after the first or second dose. The median time to resolution for all grade CRS was 3 days.¹⁸

Immune effector cell-associated neurotoxicity syndrome (ICANS), which was also an AE of special interest, is a potentially life-threatening condition with symptoms including: headache, encephalopathy, confusion, delirium, seizure, ataxia, neurotoxicity, and tremor.¹ It was reported in 10% (13/133) of patients, mostly after the first or second dose and all events were grade 1 or 2 in severity. Hospitalisation for at least one serious ICANS event (median duration of 5 days) was required for 3.0% (4/133) of patients. The median time to resolution for all-grade ICANS was 33 days.¹⁸

The SPC specifies a need for hospital admission to administer the first two infusions (day 1 and day 8); additionally, patients require to be monitored post-infusion for at least 16 hours (day 1), 6 to 8 hours (day 8), and 2 to 4 hours (third infusion onwards as per healthcare professional). It is also recommended that patients (accompanied by a caregiver) remain within 1 hour of the treatment hospital (or appropriate healthcare setting) for 24 hours after each tarlatamab infusion.¹

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- Tarlatamab is a first-in-class treatment for this indication^{5, 19} because it also targets DLL3 which is believed to be expressed in at least 85% of SCLCs.^{5, 12} Most patients with an evaluable sample (96% [80/83]) had DLL3 expression in DeLLphi-301 though positivity for DLL3 expression on tumour cells was not required for study entry.¹²
- Results for ORR, PFS, and OS at earlier data cut-offs are broadly consistent with results at later data cut-offs which is reassuring.¹⁵ The results for PFS and OS were deemed clinically relevant by the regulator.⁵
- The study population is broadly generalisable to patients likely to receive tarlatamab in Scottish clinical practice based on prior therapy and ECOG performance status. In the DeLLphi-301 study all patients (in part 1 and 2) had prior platinum chemotherapy, 73% had prior PD-1/PD-L1 therapy, 20% had prior topotecan therapy¹², and 10% had prior CAV as a second-line treatment¹³; these are the preferred prior first and second-line treatments for patients with ES-SCLC in NHSScotland.⁷

4.2. Key uncertainties

- DeLLphi-301 is a single-arm, phase II study with a small sample size (99 patients). Therefore, the relative efficacy versus other treatment options is uncertain. The open-label design may have biased patient-reported outcomes including safety outcomes and HRQoL.
- There were patients who were treated with tarlatamab beyond BICR-assessed disease progression in the DeLLphi-301 study; these patients don't appear to have been censored from the analyses of the SAS cohort of 99 patients (parts 1 and 2) relevant to the submission. This means that the results for some outcomes (for example OS) may not translate to those observed in clinical practice where patients would not continue on tarlatamab beyond

progression as per the UK conditional marketing authorisation.¹ However, the company implemented a censoring rule for these patients in the MAIC.

- There are no direct data comparing tarlatamab with the relevant comparators to this submission (topotecan, CAV, and carboplatin in combination with etoposide). The submitting company provided an unanchored MAIC using RWE from the UK CAS study, which had several limitations, including a substantially reduced effective sample size, heterogeneity of baseline characteristics, time to treatment discontinuation (TTD) used as a proxy for PFS in the UK CAS study and the censoring rule used.
- The submitting company concluded that the results indicate that tarlatamab significantly improved OS and PFS compared with standard of care. Given these limitations noted, the results of the MAIC base case analysis are uncertain. However, when considering all the available evidence presented in the submission, the company's conclusion seems plausible.

4.3. MHRA conditional marketing authorisation specific obligations

Tarlatamab has a conditional marketing authorisation from the MHRA with specific obligations; however, these are primarily focused on the provision of annual safety updates. Therefore, it is unlikely that the specific obligations will address the key uncertainties in the clinical evidence presented.

4.4. Clinical expert input

Clinical experts consulted by SMC considered that tarlatamab fills an unmet need and is a therapeutic advancement; this is due to the lack of effective third-line treatment options for ES-SCLC. They considered it would be used in the third line setting and would be initiated at a cancer centre to allow monitoring for CRS events. Experts also highlighted that the shortages of topotecan capsules increase the need for more treatment options like tarlatamab in this setting.

4.5. Service implications

Clinical experts contacted by SMC highlighted the significant service implications for tarlatamab treatment based on the strict monitoring requirements. Solid tumour inpatient facilities have reduced in recent years with a move to day-case management; tarlatamab represents a shift in treatment location requirements and is likely to have a significant demand on inpatient services. Given that tarlatamab is the first in a new class of medicines to treat lung cancer, additional oncology staff resource may be required to monitor and treat side effects.

[Other data were also assessed but remain confidential.*](#)

5. Summary of Patient and Carer Involvement

While tarlatamab meets SMC orphan and end of life criteria in this indication, the company did not request a Patient and Clinician Engagement (PACE) meeting to consider the added value of tarlatamab, in the context of treatments currently available in NHSScotland.

The following information reflects the views of the specified Patient Groups.

- We received patient group submissions from Roy Castle Lung Cancer Foundation and the Scottish Lung Cancer Nurses Forum. Roy Castle Lung Cancer Foundation is a registered charity, and the Scottish Lung Cancer Nurses Forum is an unincorporated organisation.
- 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.
- Lung cancer patients have a high level of symptom distress due to their co-morbidities and multiple symptoms from their cancer. SCLC is an aggressive and highly progressive type of lung cancer, often diagnosed at a late stage with brain and bone metastases. Patients with ES SCLC have an even poorer prognosis.
- Patients with SCLC whose disease has progressed following two lines of therapy face a shortage of third-line treatment options.
- Tarlatamab offers a different and unique way of working to destroy the cancer cells, therefore, rather than being treated with the same type of medication which has not been very effective, this may provide hope of extension of life for that bit longer for both the patient and their loved ones, and the possibility of a reduction in their symptoms.
- Having an overnight stay for the first two doses may be an inconvenience for the patient, however, this may also be reassuring for them, and they may be willing to accommodate it if there is a potential to have an overall positive benefit to them long term.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

A summary of the economic analysis is provided in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost utility analysis.
Time horizon	10 years.
Population	Tarlatamab is indicated for the treatment of adult patients with ES-SCLC with disease progression on or after at least two prior lines of therapy, including platinum-based chemotherapy.
Comparators	A basket comparator was considered relevant for this population, reflecting standard of care (SOC) in Scotland. The basket comparator comprised of CAV, platinum plus etoposide chemotherapy, and topotecan. The proportions of patients receiving each component within the basket were based on data from the UK CAS dataset.
Model description	The economic analysis utilised a partitioned survival model with three health states: Progression free (PF), progressed disease (PD) and death. Cycle length was 1 week with a half-cycle correction applied. All patients enter the PF health state, and could remain, or transition to another health state.

Clinical data	Clinical data for the economic model were primarily sourced from the DeLLphi-301 phase II, single-arm study.¹² Only patients who received at least two lines of prior therapy and 10 mg tarlatamab during Part 1 and Part 2 of the study were included in the economic analysis. Given the single-arm nature of the DeLLphi-301 study, comparative effectiveness estimates versus SOC were derived using an unanchored MAIC. This used retrospective observational data from the CAS dataset. As IPD from the CAS dataset were not available, Kaplan-Meier curves were digitised and propensity score weighting was applied to align DeLLphi-301 patient-level data to the aggregated CAS cohort baseline characteristics. In the comparator arm, TTD was used as a proxy for PFS, as progression data was not available in CAS. In DeLLphi-301 analysis, patients continuing tarlatamab beyond progression were censored at time of progression. AE rates were based on the DeLLphi-301 study for tarlatamab, and AEs rates for the SOC arm were drawn from other literature sources.²⁰⁻²²
Extrapolation	Extrapolations of outcomes beyond the observed study period was based on the MAIC-weighted, post-progression-adjusted Kaplan-Meier curves for OS, PFS, and TTD. These curves were overlaid with a range of parametric survival functions, and the final distributions were selected based on statistical and visual fit. For OS, an exponential distribution was selected for the tarlatamab arm and a gamma distribution for the SOC arm. For PFS, a log-normal distribution was selected for tarlatamab, while generalised gamma was applied to SOC TTD (used as a proxy for PFS). For TTD in the tarlatamab arm, an exponential distribution was used.
Quality of life	HRQoL was measured using EQ-5D-5L data collected from DeLLphi-301 study. These were mapped to EQ-5D-3L utilities using Hernandez-Alava algorithm.²³ Utilities were applied by health state and assumed to be treatment-independent. An age-and sex-adjusted utility decrement was applied. Disutilities associated with AEs were modelled separately. Grade ≥ 3 AEs occurring in 3% of patients were included, as well as grade 1 and 2 CRS and ICANS events specific to tarlatamab. Duration of disutility was assumed to be 28 days for grade ≥ 3 AEs and 33 days for CRS/ICANS events. Disutility values were sourced from literature.²⁴⁻²⁶
Costs and resource use	The economic model included medicine acquisition costs for tarlatamab, the basket comparators, subsequent treatments and pre-treatments, monitoring, administration, AEs, resource use and end-of-life costs. Dosing schedules and relative dose intensities were taken directly from DeLLphi-301 study for tarlatamab, and respective study publications or assumptions for SOC. TTD curves were used to model treatment duration. The frequencies of medical resource use for monitoring were primarily sourced from the NICE submission for atezolizumab in SCLC patients (TA638).²⁰ It was assumed that patients who received tarlatamab or SOC incurred medical resource use and monitoring costs and that the costs were identical for both arms.
PAS	There is no Patient Access Scheme (PAS).

6.2. Results

The base case economic analysis indicated that tarlatamab was associated with increased health outcomes, as measured by quality adjusted life years, but also higher healthcare costs. Results for the comparison between tarlatamab and SOC cannot be presented here as they are considered commercial in confidence (CiC) by the submitting company.

6.3. Sensitivity analyses

A range of sensitivity and scenario analyses were considered and descriptions of these key scenarios are provided in Table 6.2.

Table 6.2: Sensitivity and Scenario Analysis results

	Parameter	Base case	Scenario	ICER (£/QALY)
	Base case			CiC
1	Time horizon	10 years	5 years	CiC
2			15 years	CiC
3	OS distribution selection	Tarlatab: exponential	Tarlatab: Weibull	CiC
4			Tarlatab: log-normal	CiC
5		SOC: gamma	SOC: log-logistic	CiC
6	PFS distribution selection	Tarlatab: log-normal	tarlatab: exponential	CiC
7			tarlatab: gamma	CiC
8		SOC: generalised gamma	SOC: gompertz	CiC
9	Tarlatab TTD distribution selection	Exponential	Weibull	CiC
10			Log-normal	CiC
11			Log-logistic	CiC
12			Generalised Gamma	CiC
13	Source of comparative effectiveness estimates	MAIC estimates	Flatiron ITC analysis	CiC
14	Censoring of post-progression tarlatab use	Included	Excluded	CiC
15	Utilities	Independent of treatment, health state values sourced from DeLLphi-301	Treatment-specific health state utility values used in the PFS state	CiC

Abbreviations: ICER = incremental cost-effectiveness ratio; OS = Overall survival; PFS = progression free survival; SOC = standard of care; TTD = time to treatment discontinuation; CAS = Cancer Analysis system; AE = adverse events; BNF = British national formulary; eMIT = electronic market information tool; SE = standard error

6.4. Key strengths

- The use of a partitioned survival model was a reasonable and widely accepted approach in oncology submissions.
- Health state utility values were derived directly from EQ-5D-5L data collected in DeLLphi-301 study and mapped to EQ-5D-3L using the preferred SMC methods.
- Modelling costs included the inpatient monitoring requirements for tarlatab.

6.5. Key uncertainties

- The DeLLphi-301 study is a Phase II, open-label, single-arm study with no direct comparator, so the economic analysis relied entirely on an unanchored MAIC to estimate comparative effectiveness against the SOC basket.
- There were several weaknesses associated with the MAIC. A comparison between clinical study data and real-world observational data, may have introduced bias. Additionally, after matching, the effective sample size for tarlatamab was small, and further reduced by censoring patients who continued treatment post-progression, increasing uncertainty around the relative treatment effect estimates. Scenario analysis showed a large impact on the incremental cost-effectiveness ratio (ICER) when censoring was not applied (see Scenario 14 in Table 6.2).
- The use of the TTD as a proxy for PFS in the SOC arm introduced uncertainty, as treatment discontinuation may occur for reasons unrelated to disease progression. However, scenario analyses varying the curve choice for TTD/PFS in the SOC arm did not indicate this was a key driver of the cost-effectiveness results (Scenario 8). Similarly, a scenario using the US Flatiron dataset (Scenario 13), which included PFS data, also suggested limited impact on the ICER.
- There is inherent uncertainty in the extrapolation of OS, PFS and TTD. Scenario analyses indicated that alternative curve choices for tarlatamab TTD (Scenarios 9 to 12) can meaningfully increase the ICER.

[Other data were also assessed but remain confidential.](#)*

7. Conclusion

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

After considering all the available evidence, the Committee was unable to accept tarlatamab for use in NHSScotland.

8. Guidelines and Protocols

The National Institute of Health and Care Excellence (NICE) published Lung cancer: diagnosis and management guidelines in 2019; updated in March 2024.²⁷

In 2021, the European Society for Medical Oncology (ESMO) published the guideline – Small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.⁶

9. Additional Information

9.1. Product availability date

19 March 2025

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per month (£)
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Tarlatamab	1 mg on day 1, then 10 mg dose on days 8, and 15, and every 2 weeks thereafter. Treatment should be continued until disease progression or unacceptable toxicity.	Month 1: 20,055 Month 2 onwards: 19,100
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Costs from BNF online on 24 June 2025. Costs calculated using the full cost of vials assuming wastage. 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 budget impact due to commercial in confidence issues.

*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 15 August 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/](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.