SMC2909

lisocabtagene maraleucel dispersion for infusion (Breyanzi®)

Bristol Myers Squibb

09 October 2026

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, 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

lisocabtagene maraleucel (Breyanzi®) is accepted for use within NHSScotland.

Indication under review: Treatment of adult patients with diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma (HGBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B), who relapsed within 12 months from completion of, or are refractory to, first-line chemoimmunotherapy.

In an open-label, phase III study, lisocabtagene maraleucel statistically significantly improved event-free survival compared with salvage chemoimmunotherapy, followed by high-dose chemotherapy and autologous stem cell transplantation. This approach may now be relevant only to a small subset of patients. Indirect evidence suggests no meaningful difference in efficacy between lisocabtagene maraleucel and axicabtagene ciloleucel, the most relevant treatment, although some safety outcomes may favour lisocabtagene maraleucel.

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.

Co Vice Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Lisocabtagene maraleucel is a CD19-directed autologous chimeric antigen receptor (CAR) T-cell therapy comprising genetically modified CD4+ and CD8+ T lymphocytes. After binding to CD19-expressing B cells, the CAR T cells become activated, proliferate, release cytokines and mediate cytotoxic killing of target cells.

Lisocabtagene maraleucel is administered as a single dose for intravenous infusion at a target dose of 100×10^6 CAR-positive viable T cells (range 44 to 120×10^6). Further information on pre-treatment with lymphodepleting chemotherapy, administration of lisocabtagene maraleucel, and monitoring is included in the Summary of Product Characteristics (SPC).[1] Lisocabtagene maraleucel is an advanced therapy medicinal product (ATMP).

1.2. Disease background

Diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma (HGBCL) and primary mediastinal large B-cell lymphoma (PMBCL) are aggressive subtypes of large B-cell lymphomas (LBCL), while follicular lymphoma grade 3B (FL3B) is an aggressive form of follicular lymphoma with features that overlap with DLBCL. DLBCL is the most common subtype and accounts for approximately a third of newly diagnosed non-Hodgkin lymphomas. Patients may experience a range of symptoms, including painless enlarged lymph nodes, fever and fatigue. Relapsed or refractory disease is associated with a poorer prognosis.[2-6]

1.3. Treatment pathway and relevant comparators

The CAR T-cell therapy axicabtagene ciloleucel has been accepted for use in Scotland and is now a recommended second line treatment option for selected adult patients with relapsed or refractory DLBCL or HGBCL whose disease is refractory to first-line chemoimmunotherapy or relapses within 12 months (SMC2695).

Prior to the availability of CAR T-cell therapy, the standard of care for patients with LBCL was salvage immunochemotherapy followed by high-dose chemotherapy and ASCT (autologous stem cell transplant) in eligible chemosensitive patients. ASCT remains a treatment option for eligible patients.

Other options for LBCL include glofitamab plus gemcitabine and oxaliplatin (SMC2846), polatuzumab vedotin plus bendamustine and rituximab (SMC2524), further chemoimmunotherapy such as rituximab-gemcitabine-oxalaplatin, or best supportive care.

For patients with PMBCL, salvage chemoimmunotherapy and ASCT are options for eligible patients with chemosensitive disease. Experts suggest that axicabtagene ciloleucel may also be used off-label.

For patients with FL3B, second line treatment may include rituximab-based chemoimmunotherapy, obinutuzumab plus bendamustine followed by obinutuzumab maintenance therapy (SMC 1219/17), or ASCT in eligible patients with chemosensitive disease.[7-9]

The submitting company considered axicabtagene ciloleucel to be the only relevant comparator for this submission.

Clinical experts consulted by SMC considered that lisocabtagene maraleucel could displace some use of axicabtagene ciloleucel and may also displace some use of ASCT in selected patients with FL3B and PMBCL.

1.4. Category for decision-making process

Eligibility for a PACE meeting

Lisocabtagene maraleucel meets SMC orphan equivalent criteria.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

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

Table 2.1. Overview of relevant studies [10-13]

Criteria	TRANSFORM
Study design	International, randomised, open-label, parallel group, phase III study.
Eligible patients	• Aged ≥18 years and ≤75 years with an ECOG PS ≤1 • Histologically proven DLBCL NOS (de novo or transformed from indolent non-Hodgkin lymphoma), high grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements with DLBCL histology (double-hit lymphoma/triple-hit lymphoma), primary mediastinal large B-cell lymphoma, T-cell/histiocyte rich B-cell lymphoma or follicular lymphoma grade 3B • Patients with secondary CNS involvement were eligible if the investigator assessed that the potential benefit outweighed the risk • Refractory disease (SD, PD, PR or CR with relapse before 3 months) or relapsed disease (defined as CR with relapse on or after lasting at least 3 months but <12 disease under study) • Eligible for ASCT
Treatments	Patients received: • SOC arm: three 21-day cycles of salvage immune-chemotherapy with one of the protocol-defined regimens (rituximab, dexamethasone, cytarabine, and cisplatin [R-DHAP], rituximab, ifosfamide, carboplatin and etoposide [R-ICE], or rituximab, gemcitabine, dexamethasone, and cisplatin [R-GDP]), followed in responders (with CR or PR) by high-dose chemotherapy and ASCT, or • Lisocabtagene maraleucel arm: Bridging therapy (with one of the protocol-defined SOC regimens or local radiotherapy), if needed, followed by lymphodepleting chemotherapy (LDC) with fludarabine and cyclophosphamide prior to lisocabtagene maraleucel (100×10^6 CAR+ viable T cells on Day 29 [2 to 7 days after completion of LDC]) Cross-over to lisocabtagene maraleucel was permitted for patients in the SOC arm who did not achieve a CR or PR by 9 weeks post-randomisation, experienced disease progression at any time, or required further antineoplastic therapy due to efficacy concerns after 18 weeks post-randomisation; and bridging with non-investigational therapy was allowed for those who crossed over to lisocabtagene maraleucel. Intrathecal methotrexate and/or cytarabine for CNS prophylaxis or treatment was permitted in both arms.

Randomisation	Equal randomisation, stratified according to best overall response to first-line therapy (refractory versus relapsed); Secondary Age-Adjusted International Prognostic Index (0 or 1 versus 2 or 3).
Primary outcome	EFS defined as the time from randomisation to death from any cause, PD, failure to achieve CR or PR by 9 weeks post-randomisation, or start of new antineoplastic therapy due to efficacy concerns, whichever occurred first. Failure to achieve CR or PR was evaluated after three cycles of SOC for the SOC arm (expected 9 weeks post-randomisation) and 5 weeks after the infusion for lisocabtagene maraleucel arm. Primary efficacy was assessed according to the Lugano criteria by an IRC based on radiographic tumour evaluation.
Key secondary outcomes	• CRR, defined as the proportion of subjects achieving a CR (based on IRC assessment using Lugano criteria) from randomisation. • PFS, defined as the time between date of randomisation to the date of progression (based on IRC assessment using Lugano criteria) or death due to any cause, whichever occurred first. • OS, defined as the time between date of randomisation and death due to any cause.
Statistical analysis	Efficacy analyses were performed in the intention-to-treat population, which included all patients who underwent randomisation. A hierarchical statistical testing strategy was applied in the study for the primary and key secondary endpoints (CR rate, PFS and OS) with no formal testing of outcomes after the first non-significant outcome in the hierarchy.

Abbreviations: ASCT, autologous stem cell transplant; CAR, chimeric antigen receptor; CNS, central nervous system; CR, complete response; CRR, complete response rate; DLBCL, diffuse large B-cell lymphoma; NOS, not otherwise specified; EFS, event-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; IRC, independent review committee; LDC, lymphodepleting chemotherapy; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; SOC, standard of care.

Lisocabtagene maraleucel was associated with a statistically significant improvement in event-free survival (EFS) compared with standard of care (SOC). Key efficacy results are detailed in Table 2.2.

Table 2.2. Key efficacy results for TRANSFORM (primary analysis data cut: 13 May 2022) (ITT). [10, 12, 14]

	Liso-cel (n=92)	SOC (n=92)
Primary outcome: EFS by IRC		
Events, n	44	71
Median EFS, months	NE	2.4
Hazard ratio (95% CI), p-value	0.36 (0.24 to 0.52), <0.001	
EFS rate at 24 months	50%	21%
Key secondary outcome: CRR by IRC		
Responders, %	74%	43%
p-value	<0.001	
Key secondary outcome: PFS by IRC		
Events, n	37	52
Median PFS, months	NE	6.2
Hazard ratio (95% CI), p-value	0.40 (0.26 to 0.62), <0.001	
PFS rate at 24 months	56%	29%
Key secondary outcome: OS		
Deaths, n	28	38
Median OS	NE	29.9
Hazard ratio (95% CI), p-value	0.72 (0.44 to 1.18), 0.0987	
OS rate at 24 months	65%	55%

Abbreviations: CI = confidence interval; CRR, complete response rate; EFS, event-free survival; HR, hazard ratio; IRC, independent review committee; ITT, intention-to-treat; liso-cel, lisocabtagene maraleucel; NE, not estimable; OS, overall survival; PFS, progression-free survival; SOC, standard of care.

Updated results from the final data cut (23 October 2023), with a median follow-up of 33.9 months, were consistent with the primary analysis. Median overall survival (OS) had not yet been reached in either treatment arm (HR 0.757, 95% CI 0.481 to 1.191). [15]

2.2. Health-related quality of life outcomes

Health-Related Quality of Life (HRQoL) was assessed using the European Organisation for Research and Treatment of Cancer–Quality of Life C30 Questionnaire (EORTC QLQ-C30), the Functional Assessment of Cancer Therapy–Lymphoma "Additional concerns" subscale (FACT-LymS) and the EQ-5D-5L questionnaire. [11, 14]

Descriptive HRQoL analyses suggest that lisocabtagene maraleucel did not appear to adversely affect HRQoL compared with the SOC arm during the observed follow-up period, although interpretation is limited by low compliance rates, the open-label study design and the absence of multiplicity adjustment. [10, 14, 15]

2.3. Supportive studies

The PILOT study was a phase II, multicentre, single-arm study in 61 adults with relapsed or refractory LBCL who had received one previous line of therapy and met at least one criterion indicating they were not intended for haematopoietic stem cell transplantation (HSCT).

Patients received lisocabtagene maraleucel (total target dose of 100×10^6 CAR+ T cells) following lymphodepleting chemotherapy. Optional bridging therapy was permitted before leukapheresis and/or while lisocabtagene maraleucel was being manufactured to maintain disease control, using low-dose salvage chemotherapy or non-curative standard of care chemotherapy.

The primary outcome was overall response rate (ORR), defined as the proportion of patients achieving a complete or partial response. At the final analysis with median follow-up of 18.2 months (data cut: 1 December 2022), the ORR was 80% (49/61 patients), with a complete response (CR) rate of 54%. The median duration of response was 23.3 months, median progression-free survival (PFS) was 9.0 months, and median OS was not reached. The 18-month PFS and OS rates were 43% and 59%, respectively.[16, 17]

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

In the absence of direct comparative evidence between lisocabtagene maraleucel and axicabtagene ciloleucel, a matching-adjusted indirect treatment comparison (MAIC) was conducted. Efficacy was assessed using an anchored MAIC, with SOC serving as the common comparator across studies. Due to limitations in the availability and suitability of safety data, safety outcomes were assessed using an unanchored MAIC. These analyses only included the stem cell transplant (SCT) eligible population. Several outcomes were assessed; EFS was the primary efficacy outcome, and other outcomes are detailed in table 2.3 below. The EFS result (IRC-assessed) and OS results informed the economic base case. The submitting company explored options for conducting a robust indirect treatment comparison (ITC) in the SCT-ineligible population; however, this was not considered feasible because of limited data availability.

Table 2.3: Summary of indirect treatment comparison

<table>
<tr><th>Criteria</th><th>Overview</th></tr>
<tr><td>Design</td><td>Efficacy: Anchored MAIC
Safety: Unanchored MAIC</td></tr>
<tr><td>Population</td><td>Adult patients with SCT-eligible LBCL who have received one prior line of therapy</td></tr>
<tr><td>Comparators</td><td>lisocabtagene maraleucel and axicabtagene ciloleucel</td></tr>
<tr><td>Studies included</td><td>lisocabtagene maraleucel: TRANSFORM, an international, multicentre, open-label, phase 3 RCT (IPD)[18]
axicabtagene ciloleucel: ZUMA-7, an international, multicentre, open-label phase 3 RCT (published summary level data)[19-21]</td></tr>
<tr><td>Outcomes</td><td>Efficacy: IRC-assessed EFS, INV-assessed EFS, PFS, OS, ORR, CRR
Safety: any grade and Grade ≥ 3: TEAEs, TESAEs, most common TEAEs and TESAEs, and AESIs including: CRS[a] and NT.</td></tr>
<tr><td>Results</td><td>The MAIC results suggest that there was generally no evidence of difference in efficacy outcomes between lisocabtagene maraleucel and axicabtagene ciloleucel. The IRC-assessed EFS, OS and PFS results are presented in Table 2.3.1.

Table 2.3.1: Selected MAIC efficacy results
<table>
<tr><th>Liso-cel versus axi-cel:</th><th>HR</th><th>95% CI</th></tr>
<tr><td>IRC-assessed EFS[22, 23]</td><td>0.75</td><td>0.43 to 1.33</td></tr>
<tr><td>OS results[23]</td><td>0.62</td><td>0.30 to 1.27</td></tr>
<tr><td>PFS results[23]</td><td>0.68</td><td>0.37 to 1.23</td></tr>
</table>

Following matching and adjusting of TEAEs and TESAEs, only one outcome saw a statistically significant result suggesting lisocabtagene maraleucel may be associated with lower odds of developing a TESAE of grade 3 or above. Improved safety was also evident from the lower rates of study-defined CRS and NT, both for grade and those of grade ≥3.All differences were statistically significant following matching and adjustment.

Table 2.3.2: Selected ITC safety results[23]
<table>
<tr><th rowspan="2">Liso-cel versus axi-cel</th><th colspan="2">Unmatched and unadjusted</th><th colspan="2">MAIC</th></tr>
<tr><th>Any Grade</th><th>Grade ≥3</th><th>Any Grade</th><th>Grade ≥3</th></tr>
<tr><td colspan="5">TESAEs</td></tr>
<tr><td>OR (95% CI)</td><td>0.88 (0.53 to 1.46)</td><td>0.66 (0.39 to 1.12)</td><td>0.62 (0.35 to 1.09)</td><td>0.49 (0.27 to 0.90)</td></tr>
<tr><td colspan="5">CRSs[a]</td></tr>
<tr><td>OR (95% CI)</td><td>0.08 (0.04 to 0.16)</td><td>0.16 (0.02 to 1.25)</td><td>0.09 (0.04 to 0.18)</td><td>0.09 (0.01 to 0.75)</td></tr>
<tr><td colspan="5">Study defined NTs</td></tr>
<tr><td>OR (95% CI)</td><td>0.08 (0.04 to 0.17)</td><td>0.17 (0.06 to 0.49)</td><td>0.08 (0.03 to 0.18)</td><td>0.21 (0.06 to 0.68)</td></tr>
</table></td></tr>
</table>

[a] CRS defined by Lee 2014 criteria[24]

Abbreviations: AESI: adverse events of special interest; axi-cel: axicabtagene ciloleucel; CI: confidence interval; CRS: Cytokine release syndrome; EFS: event-free survival; ESS: effective sample size; HR: hazard ratio; IPD: individual patient data; IRC: Independent review committee; INV: investigator assessed; liso-cel: lisocabtagene maraleucel; MAIC: matching-adjusted indirect comparison; N: sample size; NT: Neurological Toxicities; OR: odds ratio; OS: overall survival; PFS: Progression-free survival; RCT: randomised control trial; TESAE: treatment-emergent serious adverse event.

3. Summary of Safety Evidence

At the final data cut of TRANSFORM (23 October 2023), the median duration of follow-up was 33.9 months.[15]

Any treatment-emergent adverse event (AE) was reported by 100% (N=92) of patients in the lisocabtagene maraleucel group and 99% (N=91) in the SOC group. In the lisocabtagene maraleucel and SOC groups respectively, patients reporting a grade 3 or 4 AE were 92% versus 89%, patients with a reported serious AE were 47% versus 49%. [15]

The most frequently reported grade 3 or 4 AEs with an incidence ≥10% in the lisocabtagene maraleucel group versus the SOC group were: neutropenia (82% versus 52%), anaemia (52% versus 56%), thrombocytopenia (50% versus 68%), lymphopenia (26% versus 10%), leukopenia (16% versus 13%), febrile neutropenia (12% versus 23%). [15]

In the lisocabtagene maraleucel group, any grade cytokine release syndrome (CRS) was reported in 49% of patients and any grade Neurological Toxicity Immune Effector Cell-associated Events were reported in 11% of patients. [15, 25]

The safety profile of lisocabtagene maraleucel was considered manageable and consistent with previous experience with LBCL in third or later line setting, with no new safety concerns identified. [10]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- In TRANSFORM, lisocabtagene maraleucel demonstrated a statistically significant improvement in the primary endpoint of EFS compared with salvage immunochemotherapy followed by high-dose chemotherapy and ASCT in responders. Regulators considered the magnitude of the EFS benefit to be clinically meaningful. [10]
- Results for the key secondary endpoints of complete response rate (CRR) and PFS also demonstrated statistically significant improvements which were supportive of the EFS findings and provided additional evidence of clinical benefit. [10]
- The PILOT study provided supportive evidence of the efficacy of lisocabtagene maraleucel in an older population of patients with LBCL who were considered ineligible for ASCT.
- Lisocabtagene maraleucel is the first CAR T-cell therapy licensed in adults with PMBCL and FL3B, who relapsed within 12 months from completion of, or are refractory to, first-line chemoimmunotherapy.

4.2. Key uncertainties

- The TRANSFORM study compared lisocabtagene maraleucel with salvage immunochemotherapy followed by high-dose chemotherapy and ASCT in responders. While this approach represented historical SOC for most patients, clinical experts indicated CAR T-cell therapy is the preferred second line treatment for suitable patients with relapsed or refractory

LBCL. Experts noted, however, that lisocabtagene maraleucel may displace some ASCT use in patients with FL3B and PMBCL.

- In the absence of direct evidence comparing lisocabtagene maraleucel with axicabtagene ciloleucel, the most relevant comparator in current Scottish clinical practice, the submitting company conducted an anchored and an unanchored MAIC. These were associated with a number of limitations.. There were clinical and methodological differences in the studies that could not be accounted for and there was a substantial loss of sample size during the matching and adjustment process.

  The MAICs only included SCT-eligible patients; the submitting company suggests findings are generalisable to the entire population based upon clinical expert opinion, however, this remains uncertain. In the SCT-ineligible population, a population-adjusted ITC was not feasible because of substantial differences between the PILOT and ALYCANTE studies. Consequently, only a naïve comparison was conducted. Due to these limitations, the findings of the ITCs were considered uncertain.

- Some patients considered ineligible for ASCT may still be suitable candidates for CAR T-cell therapy. However, evidence in this population is limited to PILOT, a small, single-arm, uncontrolled study with relatively short follow-up. SMC clinical experts considered it was reasonable to assume the clinical effectiveness of second line CAR T-cell therapy in ASCT ineligible patients would be similar to ASCT eligible patients with relapsed or refractory large B-cell lymphoma.

- Although a numerical improvement in OS was observed in TRANSFORM, a statistically significant benefit was not demonstrated. There is further uncertainty due to the high rate of crossover from the SOC arm to lisocabtagene maraleucel (66%), making the magnitude of any survival advantage uncertain, although this may be reflective of NHSScotland clinical practice. Regulators noted that OS results should be interpreted with caution but considered there was no clear detrimental effect. [10]

4.3. Clinical expert input

Clinical experts consulted by SMC considered lisocabtagene maraleucel a therapeutic advancement because it provides an additional CAR T-cell therapy with a potentially more favourable safety profile than axicabtagene ciloleucel and enables access to CAR T-cell treatment for patients with FL3B and PMBCL, for whom no on-label CAR T-cell treatment option is currently available in the second line setting.

4.4. Service implications

Clinical experts consulted by SMC were mixed in their views on whether the introduction of this medicine may impact service delivery. They noted existing capacity pressures within ASCT/CAR T services and the management of treatment related toxicities including ICU, which may constrain implementation. However, it was also noted that lisocabtagene maraleucel may be suitable for outpatient administration and could have a positive service impact due to its potentially more favourable toxicity profile.

5. Summary of Patient and Carer Involvement

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

- We received a patient group submission from Lymphoma Action, which is a registered charity.
- Lymphoma Action has received 7.2% pharmaceutical company funding in the past two years, including from the submitting company.
- Large B-cell lymphoma is an aggressive cancer with a considerable impact on patients and their families, particularly when the lymphoma relapses or does not respond to treatment. Symptoms often include rapidly enlarging lymph nodes, fatigue, night sweats, weight loss, loss of appetite and itching. Fatigue is one of the most debilitating symptoms affecting daily activities, work and relationships.
- Current treatment options have a substantial side effect profile, which impacts quality of life. Having access to additional treatment options provides reassurance, hope and a greater sense of control to patients.
- Lisocabtagene maraleucel has the potential to provide effective results with fewer treatment related toxicities than existing second line CAR T-cell therapy. Patients would value a treatment that reduces the chance of severe complications, intensive care admissions and prolonged hospitalisation.
- The possibility of a treatment that may support more outpatient based care could improve the quality of life of patients and their carers. Patients place high value on treatments that offer the possibility of durable remission, potential cure, fewer severe side effects and reduced disruption to family life.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

The details of the economic evaluation are provided below

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost utility analysis
Time horizon	Lifetime (50 years)
Population	Adult patients with DLBCL, HGBCL, PMBCL or FL3B, who have relapsed within 12 months of completion of, or are refractory to, first-line immunochemotherapy.
Comparators	The comparator is axicabtagene ciloleucel, accepted for use following assessment SMC2695 for the treatment of adult patients with DLBCL and HGBL that relapses within 12 months from completion of, or is refractory to, first-line chemoimmunotherapy.
Model description	The model is a partitioned state survival model with three health states of interest (event-free survival, progressed disease and death).
Clinical data	Clinical data for came from the TRANSFORM study comparing lisocabtagene maraleucel with a standard of care defined as three cycles of re-induction therapy delivered intravenously followed by high-dose chemotherapy and autologous SCT in responders.

	For axicabtagene ciloleucel the ZUMA-7 study was used via the ITC. The standard of care was similar in these studies but there were differences in bridging therapy and cross-over. An anchored MAIC from the ITC was used to inform hazard ratios for efficacy outcomes of EFS and OS, while the unanchored MAIC helped inform the model differences in safety outcomes. Mixture cure models were applied by identifying the probability that a patient would be cured, and standard mortality ratios that were age-adjusted and gender matched were applied to this proportion. For the remaining patients, standard parametric distributions were fitted to the TRANSFORM study data, with the EFS and OS for axicabtagene ciloleucel applied based on the hazard ratio identified from the MAIC. Results from the safety comparisons suggested a potentially favourable safety profile with lower odds of experiencing treatment-emergent serious adverse events at grade 3 or above, CRS and neurological toxicities. The ITC was performed only for the SCT-eligible population using data from the TRANSFORM and ZUMA-7 studies. An attempt was made to compare treatments in the SCT-ineligible population using the PILOT (lisocabtagene maraleucel) and ALYCANTE (axicabtagene ciloleucel) studies, but this was not possible due to differences between the two studies. Instead, for the economic model an assumption was made that the SCT-ineligible population data will be generalisable to the SCT-eligible population and therefore the model applies to both populations. Experts consulted by SMC felt that this was a reasonable assumption under the circumstances.
Extrapolation	The mixture cure models were used to extrapolate data beyond the follow-up period of the studies based on goodness of fit to the Kaplan-Meier data and clinical expert opinion regarding the longer-term prognosis for patients. Distributional choices were conservative but even so, did not entirely fit with the ITC conclusion that there was no evidence of difference in efficacy outcomes between the treatments. The Bucher ITC method was used in scenario analysis and provided results with reduced differences in EFS and OS. As the Bucher method provides an unadjusted comparison between the two trials it is prone to greater uncertainty, but in this case with the results being suggestive of a less pronounced difference between the treatments this could be considered a more conservative estimate of efficacy and therefore useful. Adverse events were considered in detail given the severity of the disease and also the ITC findings regarding differences in the safety profile of treatments, meaning the probability of adverse events and disutilities applied over the duration expected for recovery disproportionately affected axi-cel patients in the model, and Grade 1 and 2 events are considered for specific serious adverse events that incur both considerable disutilities and costs. Time to next treatment was equivalent to EFS owing to data from the TRANSFORM study. A cut-off was applied at 5 years, beyond which the cycle length changes to 1 year, end of life costs are no longer expected to apply as the submitting company argued that after year 5, event rates would be expected to be substantially lower and health status relatively stable among long-term survivors, so survival outcomes are expected to converge over time, resulting in only a small difference in the number and timing of deaths between treatment arms in the extrapolated period. This seems reasonable, albeit in the absence of long-term evidence on the effectiveness of CAR T-cell.
Quality of life	Utilities were taken from the TRANSFORM study and with event-free, long-term remission, post-event utility values of 0.852, 0.853 and 0.808 respectively. Alternative values were tested in scenario analysis.

Costs and resource use	Medicines costs included acquisition costs, administration costs, bridging therapy costs, leukapheresis costs, lymphodepleting chemotherapy costs, subsequent therapy costs and the costs of treating adverse events (e.g. including IVIg treatment for hypogammaglobulinemia). Non-medicines resource use included monitoring visits and tests and costs associated with treating adverse events, particularly CRS and neurotoxicity, and end of life costs.
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. A PAS discount is in place for axicabtagene ciloleucel and this was included in the results used for decision-making by using estimates of the comparator PAS price.

6.2. Results

SMC would wish to present the with-PAS cost-effectiveness results that were used for decision-making. However, SMC is unable to publish these results due to commercial in confidence concerns regarding the PAS.

6.3. Sensitivity analyses

A range of sensitivity and scenario analyses were considered and descriptions of these key scenarios are provided in table 6.3 below.

Table 6.3.1: Scenario analysis results

Scenario analyses	
1	Subsequent treatment methodology based on TTNT
2	Use of unadjusted ZUMA-7 data based on Bucher ITC for axi-cel efficacy
3	Alternative OS extrapolations
4	Bridging therapy distributions informed by TRANSFORM
5	Subsequent treatment bucket distribution: TRANSFORM for liso-cel and axi-cel
6	Subsequent treatment bucket distribution: liso-cel (TRANSFORM), axi-cel (ZUMA-7)
7	Patients requiring ICU stay: liso-cel: TRANSFORM, axi-cel: ZUMA-7
8	Pre-treatment period source: liso-cel TRANSFORM, axi-cel: ZUMA-7
9	Health state utility: TA895
10	General population utility cure time point: 2 years

Abbreviations: axi-cel = axicabtagene ciloleucel; ICER = incremental cost-effectiveness ratio; ITC = indirect treatment comparison; liso-cel = lisocabtagene maraleucel; OS = overall survival; QALYs = quality-adjusted life-years; TTNT = time to next treatment.

6.4. Key strengths

- Data were available for both CAR T-cell therapies of interest via the TRANSFORM and ZUMA-7 studies for lisocabtagene maraleucel and axicabtagene ciloleucel respectively, and an ITC was possible for the SCT-eligible patients.
- EQ-5D data were available from the TRANSFORM study and from the literature (for scenario analysis) to test utility estimates.

6.5. Key uncertainties

- The economic results rely on an ITC that did not show a statistically significant difference in EFS or OS and the assumptions regarding these outcomes were not adequately tested in the model. The company subsequently provided results using more conservative assumptions for these outcomes, which did not change the overall conclusion of the results.
- There were differences in the safety profile found in the ITC, and this is an indication where there are high costs and disutilities associated with the treatment of adverse events. There was a concern that costs had been double counted and/or disutilities may have been applied for durations longer than might be expected. However, when these were accounted for in the model the conclusion remained unchanged.
- There was a concern that the assumption about outpatient administration of CAR T cell therapies for 50% of lisocabtagene maraleucel patients compared with 0% of axicabtagene ciloleucel patients may not be feasible in clinical practice and further advice from experts was sought. This confirmed that the provision of outpatient or day case administration of CAR T-cell therapies is feasible. Furthermore, a scenario that assumed inpatient delivery for all CAR T medicines did not change the conclusion of the model.

7. Conclusion

After considering all the available evidence, the Committee accepted lisocabtagene maraleucel for use in NHSScotland.

8. Guidelines and Protocols

The European Society for Medical Oncology (ESMO) published the guideline 'Lymphomas: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up' in 2025. [27]

ESMO last updated the 'ESMO Living Guideline: Lymphomas' in February 2026. [28]

The British Society for Haematology published the guideline 'Management of relapsed or refractory large B-cell lymphoma' in 2025.[9]

9. Additional Information

9.1. Product availability date

19 May 2025

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per course (£)
lisocabtagene maraleucel	**single intravenous infusion at a target dose of 100 × 10^6 CAR-positive viable T cells (range 44 to 120 × 10^6)**	**£297,000**

Costs from eMC Dictionary of Medicines and Devices Browser on 3 August 2026. 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

The submitting company estimated there would be 27 patients eligible for treatment with lisocabtagene maraleucel each year, to which confidential uptake rates were applied.

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.

*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.