Medical Services Advisory Committee (MSAC) Public Summary Document

Application No. 1771.1 – Axicabtagene ciloleucel therapy for patients with relapsed or refractory follicular lymphoma

Applicant: **Gilead Sciences Pty Limited**

Date of MSAC consideration: **31 July 2025**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, visit the MSAC website

1. Purpose of application

A re-application requesting public funding through the National Health Reform Agreement (NHRA), Highly Specialised Therapies (HST) program of axicabtagene ciloleucel (Yescarta®), henceforth referred to as AXI, for the treatment of patients with relapsed or refractory (r/r) follicular lymphoma (FL) after two or more lines of systemic therapy was received from Gilead Sciences Pty Limited by the Department of Health, Disability and Ageing.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, MSAC supported public funding of axicabtagene ciloleucel (AXI) as a Highly Specialised Therapy (HST) through the National Health Reform Agreement (NHRA) for the treatment of adult patients with relapsed or refractory (r/r) follicular lymphoma (FL) after two or more lines of systemic therapy. MSAC recalled it acknowledged the clinical need for the proposed treatment in this population and noted that while the updated clinical data demonstrated that AXI appeared to offer clinical benefit relative to the standard of care over a longer follow up period, the long-term clinical benefits remained uncertain as FL is a relatively indolent condition compared with other cancers with funded CAR-T therapies. MSAC considered AXI has an inferior safety profile compared to the current standard of care.

MSAC considered a price reduction was required for AXI to be cost-effective. This was due to likely higher real-world costs of administering CAR-T therapy as indicated in the state and territory feedback. Furthermore, MSAC considered the cure assumption in the economic model was not appropriate based on the available evidence and the generally indolent nature of FL. MSAC considered these factors had a significant impact on both the economic and financial implications. MSAC noted as joint funders of the HST, the jurisdictions were supportive of a risk sharing arrangement with a two-part pay for performance pricing structure. Therefore, MSAC support for public funding was contingent on a risk sharing arrangement that includes the following requirements:

- a 2-part pay-for-performance arrangement constructed with first payment of redacted% of the maximum price per responder of AXI ($redacted) and the remaining redacted% ($redacted) for the second payment if patients have clinical outcome of CR per clinical criteria and demonstrated by FDG PET-CT at 12 months; and

- pay for performance arrangement constructed to achieve an average price of $redacted per successfully infused patient that corresponds to an incremental cost effectiveness ratio of $redacted per quality-adjusted life year gained calculated using updated treatment cost estimates and removing assumption of disease cure; and
- limit of one successful CAR-T infusion per lifetime funded for this indication through the National Health Reform Agreement Addendum 2020-2025; and
- annual patient caps starting at redacted patients in Year 2026 increasing to redacted patients in Year 2031 with redacted% payment of the average price per successfully infused patient made for patients exceeding the annual caps.

Consumer summary

This re-application from Gilead Sciences Pty Ltd requested public funding under the National Health Reform Agreement (NHRA) of the cell-therapy axicabtagene ciloleucel (also known as Yescarta®) for patients with relapsed or refractory follicular lymphoma as third-line or later therapy (that is, if 2 or more previous courses of treatment have not been effective in treating the disease). MSAC had considered this application once previously in August 2024 and did not support it due to uncertainty about the clinical benefits and whether it was good value for money.

Follicular lymphoma is a blood cancer that arises from a type of white blood cell (specifically B-cells), which form part of the body's immune system to fight infections. Follicular lymphoma is a slow-growing cancer and patients may go through stages where they don't have any symptoms and don't need treatment. When symptoms appear, patients may typically present with painless swelling of lymph nodes, fatigue, shortness of breath, night sweats, fever and weight loss.

Axicabtagene ciloleucel is a chimeric antigen receptor T-cell (CAR-T) therapy that is produced using a patient's own T-cells (another form of immune cell), making the product unique to each patient. For CAR-T therapy, a patient's T-cells are collected and genetically modified in a laboratory to attack the cancer-causing lymphoma B-cells. The modified T-cells are multiplied and then infused back into the patient, where they target and kill the cancerous lymphoma B-cells, thereby treating the lymphoma.

MSAC noted the additional data provided in the re-application which followed patients for a longer time than in the original submission. Although some uncertainties remained, MSAC accepted that axicabtagene ciloleucel is an effective therapy for patients with relapsed or refractory follicular lymphoma, but that more data were needed before claims of 'cure' could be accepted. MSAC noted that while there appeared to be a high rate of adverse events associated with the treatment, they are known and managed for this class of treatments, which is already in use for some other blood cancers. MSAC also noted information provided by state and territory health authorities about the real-world hospital costs associated with this therapy, which were higher than the costs proposed by the applicant. MSAC noted that uncertainties relating to costs remained and the price of the therapy would need to be further reduced before the total cost of treatment (including hospital costs) could be considered good value for money. MSAC also noted the arrangements that the applicant had proposed to manage these risks and uncertainties.

MSAC supported public funding on the condition that the treatment be provided at a lower cost, and with the requirement for an appropriate risk sharing agreement.

MSAC's advice to the Commonwealth Minister for Health, Disability and Ageing

MSAC supported public funding of axicabtagene ciloleucel for the treatment of patients with relapsed or refractory follicular lymphoma as third-line or later therapy, on the condition that as part of a risk sharing agreement the applicant reduce the price. MSAC considered axicabtagene ciloleucel would address a clinical need for new treatments for these patients,

Consumer summary
however based on the evidence presented the magnitude and duration of clinical benefits and costs of the treatment were still uncertain. MSAC advised that risks and uncertainties could be managed with a risk sharing agreement, assuming that the cost is reduced, for the treatment to provide good value for money.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted that this re-application from Gilead Sciences Pty Limited sought public funding under the National Health Reform Agreement (NHRA) as a Highly Specialised Therapy (HST) for axicabtagene ciloleucel (AXI, also known as Yescarta®, a chimeric antigen receptor T-cell [CAR-T] therapy) for patients with relapsed or refractory (r/r) follicular lymphoma (FL) after 2 or more lines of systemic therapy.

MSAC recalled that it had previously considered this application at its August 2024 meeting (MSAC Application 1771[1]) and had not supported public funding at that time, due to uncertainty about the magnitude and duration of benefits, and therefore uncertainty about its likely cost-effectiveness. MSAC noted this re-application included longer-term follow-up data (increased from previous 48 months to 60 months), an updated analysis from the single arm ZUMA-5 study, amendments to the patient eligibility criteria, a price reduction for the therapy, and a proposed single upfront payment per patient successfully infused with AXI or an alternative risk sharing arrangement (RSA) payment structure incorporating a pay-for-performance (PfP). MSAC noted the re-application claimed that the longer-term follow-up data supported and maintained the same outcomes as the original application, with a clinical claim of superior effectiveness and inferior safety of AXI compared with standard of care (SOC).

MSAC noted that its advice and concerns regarding the proposed clinical and treatment criteria from the original application had been only partially addressed in the re-application. MSAC agreed with ESC that the funding indication for AXI should be restricted to adults with 'Classic Follicular Lymphoma' as defined by the World Health Organization (WHO) classifications of lymphoma. MSAC considered this was consistent with patient eligibility in the ZUMA-5 study, which included entities classified under the International Consensus Classification (ICC) system as Grade 1, 2 or 3A FL, and excluded patients with Grade 3B disease. MSAC further noted that Grade 3B FL (as per the ICC system or Follicular large B-cell lymphoma [FLBL] under the WHO classifications) is managed more like diffuse large B-cell lymphoma (DLCBL), which is regarded as a separate indication. MSAC reiterated that the indication criteria should include the wording "Prior therapy must have included an anti-CD20 monoclonal antibody along with an alkylating agent unless contraindicated", and that the treatment criteria should include that "Patients must not have a history or suspicion of central nervous system (CNS) involvement by lymphoma", as these conditions reflected the inclusion criteria for the study. MSAC noted and supported the eligibility for funding of AXI to include that patients must be treated in a tertiary hospital with appropriate credentials but considered equity concerns may arise due to significant access limitations, as treatment is restricted to tertiary hospitals only. However, MSAC considered that these issues were unavoidable and were the same for all currently funded CAR-T therapies.

[1] https://www.msac.gov.au/applications/1771

MSAC acknowledged that public funding of AXI for r/r FL would increase the number of patients treated using CAR-T, which would require additional staff and resources to deliver.

MSAC noted the feedback from states and territories indicated support for funding of AXI for r/r FL. However, MSAC noted their preference for a PfP arrangement and concerns around likely under-estimation of real-world treatment costs, uncertainties around estimated patient volumes and therefore the consideration and setting of annual patient caps. MSAC noted that state and territory feedback advised on a PfP model consisting of 2 payments, one at successful infusion and the other after 12 months including considerations for the percentage split between the payments and whether the 12-month timepoint should be extended. MSAC noted states and territories provided estimates for AXI treatment costs (based on real-world experience with CAR-T therapies) including hospital costs which were substantially higher than the hospital costs included by the applicant. MSAC also noted that feedback from 4 jurisdictions recommended a review of the clinical effectiveness, cost-effectiveness and budget impact of AXI in the currently approved indications to inform the assessment of AXI for additional indications.

MSAC noted all consultation feedback received was supportive of the application.

MSAC noted that bi-specific T-cell engagement therapies (BiTEs) and tri-specific therapies (TriTEs) may become treatment choices in the future. These medicines are alternative immunotherapeutic approaches to treatment of r/r FL that are simpler to prepare and administer compared to CAR-T therapies.

MSAC noted that the re-application had also requested public funding of AXI for r/r marginal zone lymphoma (MZL). However, MSAC agreed with ESC that as MZL is not included in the Therapeutic Goods Administration (TGA) indication, it would not be eligible for funding under the NHRA.

MSAC noted that the re-application did not introduce any changes to the comparator (SOC), the proposed clinical management algorithm or the clinical claim of superior effectiveness and inferior safety of AXI compared to SOC. MSAC noted the proposed clinical management algorithm was consistent with the National Comprehensive Cancer Network (NCCN) guidelines except NCCN specifies third-line (3L) therapy. For the unchanged clinical claim of inferior safety, MSAC noted that it was reasonable as the safety profile and toxicities were similar to AXI in other indications and similar to other CAR-T therapies.

Regarding comparative clinical effectiveness, MSAC noted the ADAR presented an indirect comparison between ZUMA-5 (AXI) and SCHOLAR-5 (3L SOC), using a propensity score-weighted methodology. MSAC noted the study was published in a peer-reviewed journal, with response rate as the primary outcome. Furthermore, MSAC noted that the re-application included longer-term follow-up data from the ZUMA-5 study which showed comparative clinical effectiveness of 60-month data from ZUMA-5 vs 48-month data from SCHOLAR-5. MSAC noted that the commentary and ESC had identified uncertainty in the extrapolations of longer-term outcomes due to limitations in the comparative clinical effectiveness analysis. However, overall MSAC considered that the updated analysis suggested that the survival benefits following treatment with AXI were maintained to 60 months and supported the clinical claim of superior effectiveness of AXI to SOC. Although MSAC reiterated that the magnitude of this benefit remained uncertain as the median overall survival (OS) was not reached.

MSAC noted that the applicant had proposed a price reduction for AXI in the re-application from $**redacted** to $**redacted** – a reduction of approximately **redacted**%. MSAC considered that this price remained high and inadequately justified. MSAC noted that the economic evaluation in the re-application retained the cure assumption. MSAC also noted it had previously advised that the economic evaluation should remove the cure assumption in the absence of longer term data. MSAC considered that the longer follow-up data in this re-application remained insufficient to

justify a cure assumption and advised that the cure assumption should be removed from the model. MSAC noted that removing the cure assumption increased the incremental cost effectiveness ratio (ICER) by 30% (from base case ICER of $redacted/per quality-adjusted life year (QALY) to $redacted/QALY) which made the ICER similar to that in the original application. MSAC also considered that the time horizon of 30 years in the model was not adequately justified. Given the median age of diagnosis of FL is approximately 60 to 65 years, MSAC considered the estimated proportion of patients surviving to age 90 years was not plausible. MSAC noted that reducing the time horizon to 20 years increased the ICER by 23%.

MSAC noted the financial impacts and considered that these remained high and highly uncertain. MSAC considered hospital cost estimates from the state and territory feedback which ranged from $redacted to $redacted per patient would be closer guides to real world adjunctive hospital costs. MSAC noted the assumptions and the simplified approach taken in the use of estimates for sensitivity analysis by the department, but considered these estimates suitable for informing the potential economic and financial impacts of funding AXI. MSAC noted that the overall net cost to government from Year 2026 to Year 2031 in the re-application ranged from $redacted to $redacted would increase with the $redacted (lowest jurisdictional estimate) hospital cost estimate to the range of $redacted to $redacted, and the $redacted (highest jurisdictional estimate) hospital cost estimate to the range of $redacted to $redacted which MSAC considered to be high.

MSAC considered removing the cure assumption and adjusting the hospital costs to $redacted (the second lowest estimate provided by the jurisdictions) would give a more plausible estimate of the clinical benefits and the hospital costs of AXI. MSAC considered AXI would be cost-effective at an ICER of $redacted per QALY gained. MSAC considered this would be high but within the range of ICERs for other CAR-T therapies that had previously been supported by MSAC. MSAC noted this would equate to achieving an average price of $redacted per successfully infused patient. MSAC noted the applicant's pre-MSAC response, which indicated that the price proposed in the re-application was the applicant's final price offer.

MSAC noted the proposed RSA and PfP structure proposed by the applicant as an alternative to a single payment on successful infusion model. MSAC noted that ESC considered that a PfP structure with 2-stage payment was preferred and was also supported by the jurisdictions. MSAC agreed with ESC and the jurisdictions to support a PfP structure with 2-stage payment with payment linked to treatment outcomes. MSAC noted that the applicant stated that the proposed PfP structure was consistent with current AXI funding for 2L and 3L+ Large B-cell Lymphoma (LBCL). MSAC noted the applicant used the 12-month complete response (CR) rate for FL patients in the ZUMA-5 study (CR= redacted%) for the weighted maximum price per responder. The department calculated that based on the MSAC suggested AXI price of $redacted, the maximum price per responder would be $redacted. MSAC further noted the applicant had suggested a first payment of redacted% of the maximum price per responder on successful infusion and then the remaining redacted% of that price for the second payment if patient has outcome of complete response as per clinical criteria as demonstrated by fluorodeoxyglucose (FDG) positron emission tomography with computed tomography (PET-CT) at 12 months. However, MSAC advised that redacted% payment should be made on successful infusion and redacted% payment on achieving a CR at 12 months. Therefore, based on MSAC's suggested AXI pricing and structure, the department calculated that the first payment price would be $redacted (redacted% of maximum price per responder) and second payment price would be $redacted (remaining redacted%). MSAC noted ESC's consideration and one state & territory feedback for a timepoint for the second payment to be longer than 12 months, but concluded that the data were insufficient to inform a different timepoint.

MSAC considered that an RSA with annual patient caps was appropriate and that cap values could reflect the expected utilisation in the financial estimates (redacted patients). For each patient in excess of the cap in each year, a single payment would be made on successful infusion that is redacted% of the average price per successfully infused patient for patients within the cap. MSAC considered that this was appropriate and consistent with arrangements for CAR-T therapies for third-line diffuse Large B-Cell Lymphoma (DLBCL) and second-line LBCL. However, MSAC noted advice from Queensland estimating that up to redacted patients per year could be treated in Queensland alone, which meant the annual cap could be reached quickly.

Overall, MSAC accepted that AXI is a clinically effective therapy, although with some uncertainty with the magnitude of long-term benefit over SOC. MSAC noted that uncertainties relating to costs remained and the price of AXI would need to reflect an average price of $redacted per successfully infused patient so that treatment with AXI could be considered cost-effective. Therefore, MSAC supported public funding through the NHRA of AXI in r/r FL after 2 or more lines of systemic therapy contingent on a risk sharing arrangement that includes the following requirements:

- a 2-part pay-for-performance arrangement constructed with first payment of redacted% of the maximum price per responder of AXI ($redacted) and the remaining redacted% ($redacted) for the second payment if patients have clinical outcome of CR per clinical criteria and demonstrated by FDG PET-CT at 12 months; and
- pay for performance arrangement constructed to achieve an average price of $redacted per successfully infused patient that corresponds to an incremental cost effectiveness ratio of $redacted per quality-adjusted life year gained calculated using updated treatment cost estimates and removing assumption of disease cure; and
- limit of one successful CAR-T infusion per lifetime funded for this indication through the National Health Reform Agreement Addendum 2020-2025; and
- annual patient caps starting at redacted patients in Year 2026 increasing to redacted patients in Year 2031 with redacted% payment of the average price per successfully infused patient made for patients exceeding the annual caps.

4. Background

Table 1 Summary of key matters of concern

Component	Matter of concern	How the current assessment report addresses it [Comment]
Population	The PSD outlines 3 domains relating to the criteria establishing the eligibility for patients being eligible for treatment with AXI: counting anti-CD20 monotherapy as a prior line of treatment; renal, cardiac and respiratory parameters; and history or suspicion of CNS involvement.	Revised criteria establishing eligibility for AXI proposed. [The Commentary considered that this requires consideration as some suggested amendments were addressed and others not.]
Comparator	No specific issues identified. MSAC considered that the proposed comparator (SOC, represented by a basket of PBS-funded therapies) was appropriate (p4 of PSD).	No change required.

Component	Matter of concern	How the current assessment report addresses it [Comment]
Outcomes: safety	No specific issues identified. MSAC concluded that the claim that AXI had inferior safety compared with SOC was likely reasonable (p5 of PSD).	No change required. Safety outcomes from updated analysis of ZUMA-5 with 60 months of follow-up presented. [The Commentary noted that no updated comparative data was presented. MSAC concluded that the claim that AXI had inferior safety compared with SOC was likely reasonable, but noted that comparative safety of AXI versus SOC was based on naive comparisons of various clinical studies with a high risk of bias, and the limited and low-certainty data resulted in overall uncertainty. The evidence presented does not address the overall uncertainty of the comparative safety claim.]
Outcomes: efficacy	MSAC concluded that longer-term follow-up data were required to be able to adequately assess any survival benefit (p5 of PSD).	Efficacy outcomes from updated analysis of ZUMA-5 with 60 months of follow-up presented. [The Commentary noted that no updated comparative effectiveness data was presented. MSAC acknowledged the clinical need for new therapies for this patient population, and considered that AXI appeared to offer clinical benefit, particularly in progression free survival. However, MSAC noted that due to the low certainty of evidence, the magnitude of benefit was highly uncertain (p1 of PSD).]
Cost-effectiveness	MSAC agreed with ESC that there was a need to consider a longer period of remission for FL (at least 10 years, given that some patients relapse at 10 years) before assuming that a patient with r/r FL may be cured (p5 of PSD). MSAC considered any future re-application would require longer-term follow-up data or, in the absence of longer-term data, an economic model that does not assume cure, and includes a reduced price for AXI (p6 of PSD).	Efficacy outcomes from updated analysis of ZUMA-5 with 60 months of follow-up presented. Evidence on the plausibility of cure assumption in some patients presented. Base case applies more conservative cure assumption. [The Commentary noted that the same 'cure' assumption was applied – 40% of progression free patients who received AXI from 5 years – as in the previous ADAR. The additional 60-month follow-up data is considered insufficient to support an assumption of 'cure', particularly as the ZUMA-5 study showed patients continued to progress and die over the additional 12 months of follow-up.]

Component	Matter of concern	How the current assessment report addresses it [Comment]
Financial impact	MSAC considered the financial impact was highly uncertain due to uncertainty in the estimated utilisation, adjunctive hospital costs being underestimated and potential cost-savings being overestimated (p6 of PSD). Neither PBS nor hospitalisation costs would be expected to be key drivers of the financial impact (p41 of PSD).	Estimated utilisation of AXI unchanged. 'Triangulation' of original estimates using PBS claims data corroborated the estimates in original ADAR. [The Commentary noted issues with the use of idelalisib to triangulate the estimates as idelalisib is not restricted to FL, but includes other non-Hodgkin lymphomas. Estimates are likely overestimated.] PBS costs revised to decrease weighting of more costly components of obinutuzumab and idelalisib. [The Commentary noted that adjunctive hospital costs associated with AXI remained unchanged from the previous ADAR.]
AXI price	MSAC noted the proposed price of AXI had not been adequately justified and considered a price reduction along with a risk sharing arrangement would be required for any future re-application (p1 of PSD).	A revised price of $**redacted** is proposed. This represents a **redacted**% reduction in the price requested in the original ADAR and is equivalent to the average net price agreed for 2L LBCL. [The Commentary noted that the proposed price in the previous ADAR was $**redacted**.] Parameters for a risk sharing arrangement outlined for MSAC consideration.

Source: Table 11, pp17-18 of the re-application ADAR + in-line commentary
ADAR = applicant-developed assessment report; AXI = axicabtagene ciloleucel; CNS = central nervous system; ESC = Evaluation Sub-Committee; FL = follicular lymphoma; LBCL = large B cell lymphoma; MSAC = Medical Services Advisory Committee; PBS = Pharmaceutical Benefits Scheme; PSD = Public Summary Document; r/r = relapse or refractory; SOC = standard of care.

5. Prerequisites to implementation of any funding advice

AXI was first included on the Australian Register of Therapeutic Goods (ARTG) on 11 February 2020 for r/r large B cell lymphoma (LBCL) (ARTG ID 329770). The indication was extended to include patients with r/r FL after two or more lines of systemic therapy on 12 December 2022 (ARTG ID 400895).

The approved therapeutic indication for AXI is as follows:

YESCARTA® is a genetically modified autologous immunocellular therapy for the treatment of:

- Large B-cell Lymphoma
  - Patients with relapsed or refractory large B-cell lymphoma (LBCL).
  - YESCARTA® is not indicated for the treatment of patients with primary central nervous system lymphoma.
- Follicular Lymphoma
  - Patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

6. Proposal for public funding

Public funding for AXI for the treatment of r/r FL in the 3L setting (or later) is sought through the NHRA.

Consistent with current practice, the proposed technology would be delivered in select tertiary hospital treatment centres that specialise in delivery of Chimeric Antigen Receptor T-cell (CAR T) therapy.

The ADAR stated that all referrals for AXI (and all CAR T-cell therapies) are presented to the National Patient Prioritisation Committee to review all referrals and confirm patient eligibility. New patient referrals are discussed nationally to ensure fair and equitable access to CAR T-cell therapies. The applicant stated that a clinical advisory board of four clinicians experienced in the management of patients with r/r FL and use of CAR T-cell treatments, convened for the ADAR, highlighted that eligibility criteria that is too restrictive can result in the committee being unable to confirm a patient is eligible to be treated with a CAR T-cell therapy even if there is consensus from the Committee that it would be clinically appropriate.

The domains of the eligibility criteria that were highlighted in the previous ADAR and how these were addressed in the re-application ADAR, upon consultation of the clinical advisory board, are presented in Table 2. The ADAR stated the proposed changes to the eligibility criteria were made with the intent to support clinically appropriate use of AXI and ensure fair and equitable access to treatment. The ADAR also stated that should ESC/MSAC be concerned with any of these changes, the applicant suggests the Committee first seek to consult with the clinicians experienced with AXI that attend the National Patient Prioritisation Committee.

Table 2 Domains relating to establishing patient eligibility for AXI

Domain	MSAC consideration outlined in PSD	How addressed in re-application ADAR [Comment]
Counting anti-CD20 monotherapy as a prior line of treatment	MSAC considered that it may be reasonable to specify in the indication that alkylating agents must be included along with anti-CD20 as prior therapy, unless contraindicated (p4 of PSD). MSAC considered that the extent to which the number of eligible patients would increase was uncertain but likely low, and that it would be inequitable to deny AXI treatment to patients for whom alkylating agents were contraindicated (p4 of PSD).	Partially agreed. Indication wording suggested by clinical advisory board has been included which removes any reference to use of an alkylating agent. Alternative wording as per MSACs advice is also provided which specifies that prior therapy must have included an anti-CD20 monoclonal antibody combined with an alkylating agent, unless contraindicated. [The Commentary considered that the proposed alternative wording suggests that patients are not required to have previously received an anti-CD20 antibody if contradicted, rather than the alkylating agent component of combination treatment which may be overlooked if contraindicated, as is interpreted to be the intent of MSAC from consideration of the original submission. The Commentary noted the pivotal ZUMA-5 study required patients to have had prior therapy with an anti-CD20 monoclonal antibody combined with an alkylating agent (single-agent anti-CD20 antibody did not count as line of therapy for eligibility)].
Renal, cardiac and respiratory parameters	MSAC noted the applicant's proposed changes to the treatment criteria regarding renal, cardiac and respiratory function parameters, and considered that these were reasonable to ensure consistency with organ function criteria established for AXI for the treatment of patients with LBCL in Australia (p4 of PSD)	Agreed. Renal, cardiac and respiratory parameters amended to be consistent with LBCL criteria. [Consistency with the renal, cardiac and respiratory parameters with LBCL criteria could not be independently verified during the evaluation].
History or suspicion of CNS involvement	MSAC noted ESC's proposed change to the treatment criteria to specify that the patient must not have a history or suspicion of central nervous system (CNS) involvement by lymphoma. MSAC noted that the study criteria for ZUMA-5 specified "Individual has no known presence or history of central nervous system (CNS) involvement by lymphoma". MSAC further noted that the Australian Register of Therapeutic Goods (ARTG) indication for AXI for LBCL states that it is not indicated for patients with primary central nervous system lymphoma. Therefore, MSAC agreed with ESC's proposed change to ensure alignment between the study and funding eligibility criteria as well as the ARTG indication (p4 of PSD).	Partially agreed. The original request to not include criteria preventing patients with a history or suspicion of CNS involvement was based on clinician feedback. Gilead would like to clarify that the TGA indication for AXI as treatment for r/r FL does not exclude patients with history or suspicion of CNS involvement. Gilead would not oppose a recommendation for funding that included the exclusion of patients with a history or suspicion of CNS involvement. However, such an exclusion does not align with the TGA approved indication and is understood to not have broad support among clinicians. As such, alternative wording provided by clinicians experienced with AXI and FL is provided for consideration.

Source: Table 12, p21 of the re-application ADAR + in-line commentary
ADAR = applicant-developed assessment report; ARTG = Australian Register of Therapeutic Goods; AXI = axicabtagene ciloleucel; CNS = central nervous system; ESC = Evaluation Sub-Committee; LBCL = large B cell lymphoma; MSAC = Medical Services Advisory Committee; TGA = Therapeutic Goods Administration

A summary of the proposed request for public funding of AXI in r/r FL showing the indication requested, and the proposed treatment and clinical criteria beside what was supported for AXI in r/r Large B-cell Lymphoma (LBCL) is presented in Table 3.

Table 3 Clinical, treatment and public funding criteria proposed for AXI in r/r FL versus criteria supported in r/r LBCL

Domain	Description proposed for AXI in r/r FL (1771.1)	Description supported for AXI in r/r LBCL (1722.1[2])
Indication	Adults with follicular lymphoma who are relapsed or refractory after two or more lines of systemic therapy and have disease requiring treatment. Prior therapy must have included an anti-CD20 monoclonal antibody*. *(*Alternative wording from MSAC: Prior therapy must have included an anti-CD20 monoclonal antibody, unless contraindicated) – note that actual wording from MSAC was: Prior therapy must have included an alkylating agent along with an anti-CD20 monoclonal antibody, unless contraindicated*	Adult patients with CD 19 positive LBCL who are relapsed or refractory no more than 12 months after first line chemoimmunotherapy • LBCL includes the following types defined by the WHO in 2016: o DLBCL, NOS (including ABC or GCB) o DLBCL arising from FL o DLBCL associated with chronic inflammation o DLBCL + EBV o HGBL with or without MYC and BCL2 and/or BCL6 rearrangement o T-cell/histiocyte-rich LBCL o Primary cutaneous DLBCL, leg type o PMBCL* • First-line therapy must include (at a minimum): o An anti-CD20 monoclonal antibody unless the investigator determined that the tumour was CD20 negative, and o An anthracycline-containing chemotherapy regimen
Treatment criteria	Patient must be treated in a tertiary hospital with appropriate credentials AND Patient must be treated by a haematologist working in a multidisciplinary team specialising in the provision of CAR T cell therapy AND Patient must not have uncontrolled infection, including uncontrolled HIV or active hepatitis B or C infection AND Patient must not have primary CNS lymphoma* AND Patient must not have Secondary CNS disease anticipated to be uncontrolled at the time of lymphocyte infusion*.	Patient must be treated in a tertiary hospital with appropriate credentials AND Patient must be treated by a haematologist working in a multi-disciplinary team specialising in the provision of CAR-T cell therapy AND Patient must not have uncontrolled infection, including uncontrolled HIV or active hepatitis B or C infection AND Patient must not have primary CNS lymphoma AND

[2] https://www.msac.gov.au/sites/default/files/documents/1722.1%2520Final%2520PSD%2520-%2520April2024%2520%28redacted%29.pdf

	*(*Alternative wording from MSAC: Patient must not have a history or suspicion of CNS involvement by lymphoma)*	Patient must not have uncontrolled secondary CNS disease, or secondary CNS disease anticipated to be uncontrolled at the time of lymphocyte infusion.
Clinical criteria	Patient must have a ECOG performance status of 0 or 1 AND Patient must have sufficient organ function, including: • Renal function: Creatinine clearance >40mL/min, serum ALT/AST <5 x ULN and total bilirubin <2 x ULN • Cardiac function: absence of symptomatic heart failure (i.e. NYHA grade <2), cardiac left ventricular ejection fraction (LVEF) ≥40%, or supplementary functional tests and cardiology assessment demonstrating adequate cardiopulmonary reserve • Pulmonary function: Baseline peripheral oxygen saturation > 91% room air, in the absence of anaemia AND The treatment team must consider the patient's condition can be effectively managed during lymphocyte collection and manufacturing, to allow for the absence of rapidly progressive disease at the time of lymphocyte infusion	FOR TFL: The condition must have relapsed after, or be refractory to, at least one prior chemoimmunotherapy administered after disease transformation. FOR ALL OTHER LBCL: The condition must have relapsed after, or be refractory to, at least one prior chemoimmunotherapy FOR ALL INDICATIONS: Patient must have a WHO performance status of 0 or 1 AND Patient must have sufficient organ function, including: • Renal function: Creatinine clearance >40mL/min, serum ALT/AST <5 x ULN and total bilirubin <2 x ULN • Cardiac function: absence of symptomatic heart failure (i.e. NYHA grade <2), cardiac left ventricular ejection fraction >/= 40%, or supplementary functional tests and cardiology assessment demonstrating adequate cardiopulmonary reserve. • Pulmonary function: Baseline peripheral oxygen saturation >91% on room air, in the absence of anaemia AND The treatment team must consider the patient's condition can be effectively managed during lymphocyte collection and manufacturing, to allow for the absence of rapidly progressive disease at the time of lymphocyte infusion.

Source: Table 13, p24 of the re-application ADAR + in-line commentary and Table 2, p10 of MSAC application 1722.1 PSD
ALT = alanine transaminase; AST = aspartate aminotransferase CAR T = Chimeric Antigen Receptor T-cell; CNS = central nervous system; ECOG = Eastern Cooperative Oncology Group; HIV = human immunodeficiency virus; LVEF = left ventricular ejection fraction; min = minute; mL = millilitre; NYHA = New York heart association; ULN = upper limit of normal
Blue font indicates additions by the department, Green font indicates clarification note made by department

Indication

The Commentary noted indication has changed compared with the previous ADAR (Table 1, p8, MSAC 1771 PSD, August 2024 MSAC meeting) that specified:

> Adults with Grade 1, Grade 2 or Grade 3a follicular lymphoma (based on the WHO classification) who are relapsed or refractory after two or more lines of systemic therapy and have symptomatic disease and/or high tumour burden following relapse. Prior therapy must have included an anti-CD20 monoclonal antibody combined with an alkylating agent (where single-agent anti-CD20 antibody (e.g. rituximab) would not count as a prior line of therapy for eligibility).

The ADAR stated that grading of FL by the 2016 World Health Organization (WHO) criteria was identified as being a domain that should be removed from the eligibility criteria. The applicant stated that clinicians advised them that the grading of lymphoma is conducted at the point of diagnosis of FL and is not relevant to the patient's eligibility of AXI in the relapse or refractory setting; rather, clinicians will consider the nature and biology of the patients' disease at the time of relapse.

In 2022 the 5th edition of the WHO classification (Kurz 2023[3]) significantly revised the classification of FL moving from classic grading to biological grouping, now termed as classic follicular lymphoma (cFL), follicular large B-cell lymphoma (FLBL) and follicular lymphoma with uncommon features (uFL). The ADAR stated that removing the definition of FL will ensure there is longevity in the eligibility criteria if guidelines are revised and remove the potential for misinterpretation of patient eligibility.

Treatment criteria

The Commentary noted the treatment criteria remained largely unchanged from that requested in the previous ADAR (Table 1, p8, MSAC 1771 PSD, August 2024 MSAC meeting), with the applicant requesting reconsideration of the changes suggested by MSAC to specify that "Patient must not have a history or suspicion of CNS [central nervous system] involvement by lymphoma". The ADAR noted that it would not oppose a recommendation for funding that included a criterion that excluded patients with a history or suspicion of CNS involvement, however, it claimed this does not have broad support among clinicians due to lack of a clinical justification for excluding patients access to AXI because of this rare clinical occurrence, particularly in FL patients. The ADAR stated as set out in Table 3, alternative wording has been provided by the clinical advisory board that is claimed to be consistent with the eligibility criteria for AXI for LBCL and provides a clear directive with regards to secondary CNS, which clinicians have advised is open to interpretation under the MSAC proposed criterion.

[3] Kurz KS et al. Follicular Lymphoma in the 5th Edition of the WHO-Classification of Haematolymphoid Neoplasms-Updated Classification and New Biological Data. *Cancers (Basel)*. 2023 Jan 27;15(3):785. doi: 10.3390/cancers15030785. PMID: 36765742; PMCID: PMC9913816. [https://pmc.ncbi.nlm.nih.gov/articles/PMC9913816/pdf/cancers-15-00785.pdf]

Clinical criteria

The Commentary noted that the clinical criteria have been amended to be consistent with LBCL criteria with respect to renal, cardiac and respiratory parameters; however consistency with LBCL criteria could not be independently verified during their evaluation.

The ADAR proposed an average net effective price for AXI for r/r FL of $redacted (compared with $redacted in the previous ADAR) per patient infused. The ADAR claimed this price was identical to the current price for funding AXI for r/r LBCL in the 2L setting and is noted by the department to also be the same for AXI for r/r DLBCL in the 3L setting.

The applicant has proposed a single upfront payment per patient successfully infused with AXI for r/r FL as follows:

1) $redacted per patient successfully infused with AXI for r/r FL;
2) limit of one successful CAR T infusion per lifetime funded for this indication through the National Health Reform Agreement Addendum 2020-2025; and
3) annual patient caps for patients treated with AXI for r/r FL that incorporates a single payment of $redacted for any patient treated in excess of the yearly cap.

The applicant, although having a preference for a single payment also proposes a pay for performance (PfP) option, if MSAC deems this as a preferred mechanism for funding, see Table 4 and Table 5 for a summary of the proposed structure and maximum amounts payable, respectively. To achieve an average effective net price of $redacted, the ADAR stated the proportion of patients who had achieved and maintained a complete response (CR) 12 months after infusion with AXI, has been derived from ZUMA-5 patient level data: at 12-months, redacted% of FL patients successfully infused with AXI in ZUMA-5 were in CR. This could not be independently verified during the evaluation. The ADAR states this methodology is aligned with the PfP for 2L LBCL and is noted by the department to also be the same with PfP for 3L DLBCL. The Commentary stated that the claim regarding whether the methodology is consistent with current PfP for LBCL could not be independently verified during the evaluation.

Table 4 Summary of the proposed pay for performance structure for AXI for r/r FL

	Payment per patient	Payable under the following condition	Comment
Where the number of patients in a year is less than or equal to the Cap			
Payment 1	$**redacted**	Upon successful infusion for the patient.	Payment amount and condition consistent with *3L DLBCL and 2L* LBCL.
Payment 2	(a) $**redacted**	Payable where the patient, when assessed between 11 and 13 months post successful infusion, is in complete metabolic response.	Adjusted to obtain the average price of $**redacted** based on a 12-month CR rate of **redacted**%. Methodology consistent with *3L DLBCL and 2L* LBCL.
	OR		
	(b) $**redacted**	The patient is lost to follow up between 11 and 13 months post successful infusion or the results of any and all assessments of complete metabolic response (CR) between 11 and 13 months post successful infusion are inconclusive or unable to be determined.	This payment is the difference between $**redacted** and Payment 1. Payment amount, methodology and condition consistent with *3L DLBCL and 2L* LBCL.
For each patient in excess of the Cap in a Year			
Payment 1	$**redacted**	Upon successful infusion for the patient.	Payment amount and arrangement consistent with *3L DLBCL and 2L* LBCL.

Source: Table 60, p92 of the re-application ADAR + in-line commentary
2L = second line; 3L = third line; CR = complete response; DLBCL= diffuse large B cell lymphoma; LBCL = large B cell lymphoma
Italics indicate changes made by the department

Table 5 Summary of maximum amounts payable by response to achieve weighted average net price

	Proportion of successfully infused patients	Amount
Maximum amount payable for patients not achieving CR (Payment 1 only)	**redacted**%	$**redacted**
Maximum amount payable for patients achieving CR (Payment 1 + Payment 2a)	**redacted**%	$**redacted**
Weighted average net price	-	$**redacted**

Source: Table 61, p92 of the re-application ADAR + in-line commentary
CR = complete response

7. Population

The proposed population of this re-application ADAR is adults with follicular lymphoma who are relapsed or refractory after two or more lines of systemic therapy and have disease requiring treatment. The population in the original ADAR (1771) was restricted to adult patients with Grade 1, Grade 2, or Grade 3a FL and r/r disease after two or more lines of therapy.

The proposed intervention would be available in the 3L setting and would be used in place of current technology. Compared to existing practice, this would result in reduced use of the comparator, standard of care (SOC), in the 3L setting. AXI would substitute SOC in Australia. However, of note, AXI is not expected to fully replace SOC for several reasons (e.g., failure of leukapheresis, preference, access).

8. Comparator

The comparator remained unchanged from the previous ADAR. The previous ADAR described that there is no uniformly recommended systemic treatment for patients with FL who are r/r after two or more lines of systemic therapy. Instead, treatments are chosen based on individual patient circumstances such as the mechanism of action and duration of response to prior treatments.

The ADAR's proposed comparator was standard of care (SOC), represented by a 'basket' of the following regimens, all currently funded on the Pharmaceutical Benefits Scheme (PBS):

- anti CD20 monotherapy
- anti CD20 therapy in combination with chemotherapy
- chemotherapy
- phosphoinositide 3-kinase-δ (PI3Kδ) inhibitor.

In the previous ADAR, the Evaluation Sub-Committee (ESC) considered that the proposed comparator, i.e. the SOC therapies in the SCHOLAR-5 cohort, was appropriate, and compares well to the current SOC in the Australian setting (p10, MSAC 1771 PSD, August 2024 MSAC meeting) noting there are no clear clinical guidelines or uniformly recommended 3L treatments for patients with r/r FL (p44, MSAC 1771 PSD, August 2024 MSAC meeting).

9. Summary of public consultation input

Consultation input was welcomed from:

1771.1 – Axicabtagene ciloleucel therapy for patients with relapsed or refractory follicular lymphoma (Gilead Sciences Pty Limited)	No. of Inputs Received
Organisations (8)	
I am providing input on behalf of a consumer group or organisation. Consumer organisations are not-for-profit organisations representing the interests of healthcare consumers, their families and carers.	4
I am providing input on behalf of a medical, health, or other (non-consumer) organisation. For example, input on behalf of a group of clinicians, research organisation, professional college, or from an organisation that produces a similar service or technology.	4
Health Professionals (5)	
I am a health professional or health academic working in the area.	5
Consumers (2)	
I have the health condition that this health service or technology is for.	1
I am a parent, partner or another person caring for someone from the above two groups.	1
Grand Total	**15**

The organisations that submitted input were:

- Australia and New Zealand Transplant & Cellular Therapies Ltd (ANZTCT)
- Barwon Health Department of Haematology (Barwon)
- The Leukemia Foundation (LF)
- Rare Cancers Australia (RCA)
- Australasian Leukemia & Lymphoma Group (ALLG)
- Lymphoma Australia (LA)
- National Immune Effector Cell Patient Prioritisation Committee (NIECPPC)
- Australasian Lymphoma Alliance (ALL).

Level of support for public funding

All organisations, health professionals, and consumers expressed support for the public funding of this application.

Comments on PICO

- Many health professionals described the proposed eligibility criteria as appropriate, agreed with the proposed approach, and stated the comparator accurately reflected Australian clinical practice.
- Barwon and RCA noted the proposed eligibility criteria as appropriate, with RCA noting that this intervention represents a promising treatment for individuals with relapsed or refractory follicular lymphoma (R/R FL).
- Barwon noted that CAR-T for FL would be administered only in State Government-approved chimeric antigen receptor T-cell (CAR-T) therapy infusion sites, of which there are only two in Victoria. RCA noted that the expansion of specialised centres gaining accreditation supports equitable access, and noted that through the logistical support provided by their organisation, logistics have not been an overwhelming barrier to receiving the therapy.
- Barwon and LA agreed the comparator accurately reflected Australian clinical practice, with ALLG noting no other specific therapies approved for the treatment of LF in the third line.
- Barwon and ALLG agreed with the outcomes set out in the PICO.
- Barwon and LA agreed with the proposed item descriptors, with Barwon describing them as ‘adequate’ and ‘comprehensive’.
- Barwon supported the proposed fee for the therapy, and LA noted comments as out of scope for their organisation.

Perceived Advantages

- Health professionals noted better revision and survival for patients as an advantage of this therapy.
- A parent of an individual with follicular lymphoma described the therapy as less invasive than other treatment options, and noted the high percentage of patients exhibiting no disease after five years.
- An individual with follicular lymphoma noted the therapy offers a potential for a cure or long-term remission, without the high mortality associated with stem cell transplant.
- Many organisations noted the current limited treatment options for FL patients who relapse early or are refractory to immunochemotherapy, noting the gap this therapy can potentially fill. NIECPPC noted there is currently no standard of care in the R/R FL setting, and particularly in third line and beyond.
- Many organisations referred to the ZUMA-5 clinical trial results, with ANZTCT describing the evidence supporting this therapy in R/R FL as strong, of high quality, and relevant to the Australian context given the national unmet need in this disease area. The organisation expressed a belief that with appropriate oversight, delivery, and registry participation, the proposed therapy represents a meaningful advance for patients with limited remaining options.
- LF noted that while the therapy is not free from adverse effects, the clinical trial has shown high rates of durable responses in patients who exhibit high-risk disease factors and are refractory to several lines of treatment. LF highlighted that for this cohort of patients, treatment with CAR-T cell therapy can often be a last resort if they are refractory to multiple chemoimmunotherapy regimens and not eligible for transplantation. LA also noted that whilst CAR-T has several toxicities that may need to be managed, clinical trial

data is showing side effects can be well managed and overall complete response (CR) rates and long-term remissions are 'impressive' for these patients.

- RCA highlighted that without government support, the cost of this therapy imposes a substantial financial burden on individuals and their families, placing potentially life-extending treatment out of reach. The organisation expressed a belief that a subsidised pathway would not only reduce financial stress but also offer renewed hope for patients who have exhausted standard options.
- RCA noted that as well as clinical effectiveness, patients have consistently reported enhanced quality of life after therapy, including reduced fatigue, diminished disease-related anxiety, and relief from the burdens of ongoing chemotherapy. RCA highlighted that for many, it has enabled a return to daily routines, work, and meaningful relationships, offering a renewed sense of stability and hope. ALA also noted the durability of response of this therapy reduces the need for successive lines of therapy, repeated hospitalisations, and supportive care requirements, particularly in a disease otherwise characterised by chronic relapsing management. The organisation highlighted that for many patients, the therapy represents a single definitive intervention that may obviate years of ongoing therapy, translating into meaningful downstream cost offsets.

Perceived Disadvantages

- Health professionals noted the current cost of the therapy as a disadvantage.
- A parent of an individual noted that while there will be adverse effects of the therapy, it is there understanding that this therapy is less problematic than a stem-cell transplant.
- An individual with follicular lymphoma noted that the current cost is the only disadvantage of the therapy, but noted that if it is curative, it will reduce costs in the long run.
- Many organisations noted the adverse events in response to this therapy in clinical trials, with LF stating it is important to note that the patient cohort reflected patients who were refractory to several lines of treatment and exhibiting high-risk disease features. NEICPPC and ALA stated that acute toxicities, such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) are lower in FL patients than in diffuse large B cell lymphoma. NEICPPC also noted that medium- and long-term risks, such as risk of infection and second cancers, can be managed and are likely not appreciably different than after serial treatments with 'less effective' therapies, such as dose-intense chemotherapy.
- Many organisations also highlighted the current inequity of access for patients in states without a CAR-T centre, as well as patients from rural, remote, and regional areas. LA also noted the responsibility of caregiving can be overwhelming for those providing support, potentially leading to a significant economic impact on families with the potential loss of dual incomes over an extended period.

Support for Implementation and Issues

- Barwon noted patient preference for CAR-T delivery at their local hospital, but noted they will continue to refer on to approved infusion sites until their facility is approved. ANZTCT advocated that any publicly funded CAR-T therapy be limited to delivery at qualified centres, ideally those that are accredited by or actively progressing towards Foundation for the Accreditation of Cellular Therapy standards. LA highlighted the need for an education process for clinicians from sites that have little knowledge of CAR-T and the referral process to ensure patient equity and centricity. The organisation also noted that follow up care should be available closer to home for the patient, with logistical

challenges of travel and the requirement for a dedicated caregiver sometimes resulting in a decision against pursuing CAR-T therapy.

- ANZTCT recommended that all patients treated with publicly funded CAR-T therapy be enrolled in long-term follow-up through the ANZTCT Registry, consistent with international data collection and clinical quality standards.
- RCA noted that while the logistics of accessing this therapy can be complex, Australia already has a functioning and expanding infrastructure capable of delivering it effectively. The organisation noted it has not identified any significant concerns, barriers, or disadvantages associated with the proposed health service.
- ALLG highlighted types of services it believes will be required pre- and post-CAR-T therapy, including:
    - Specific services in addition to specialist haematology care that are required before CAR-T cell infusion should include:
        - Established patient referral pathway and prioritisation algorithm, with a consistent national approach to access to support equitable and consistent approaches to care.
        - Multidisciplinary meeting (MDM) to discuss optimum treatment choice and appropriateness of CAR-T cell therapy.
        - CAR-T cell nurse to coordinate patient and family education about the process of CAR-T and the adverse events, as well as CAR-T cell therapy work up (infection screening venous access, leukapheresis, bridging therapy).
        - Social service support to facilitate local accommodation and support for patients from rural areas.
    - Services required post CAR-T cell infusion:
        - There needs to be adequate clinical services to manage the immediate complications of cytokine release syndrome (CRS), and immune effector cell associated neurological toxicity (ICANS) including experienced haematology service, 24-hr pharmacy dispensing, ICU, neurology, infectious disease, and radiology.
        - Allied health team including but not limited to physiotherapists, occupational therapists, dietician, and social workers.
        - 24-hour access emergency department with streamlined admission pathways and CRS/ICANS management procedures.
        - Hospital in the home service to facilitate ongoing patient monitoring and care for the immediate duration post discharge at home.
        - CAR-T cell nurse/coordinators to coordinate discharge planning and follow up procedures.
- LA noted the need to review the current data collection process, such as what data is being collected and who can access it, as well as consider adopting similar strategies demonstrated by overseas models of care in order to streamline the approach to the delivery of this therapy.

10. Characteristics of the evidence base

The re-application ADAR presented updated results from the ZUMA-5 study, a phase 2 single-arm multicentre, open-label study assessing the safety and efficacy of AXI with a median potential follow-up of 60 months, as opposed to a median follow-up of 48 months presented by the previous ADAR.

As ZUMA-5 was a single-arm study, clinical evidence presented by the previous ADAR on the comparative efficacy of AXI versus SOC was based on a comparison of patients enrolled in ZUMA-5 with an external control group of patients enrolled in an international, multicentre, retrospective cohort study, SCHOLAR-5. The previous ADAR considered it important to note that patients in the SCHOLAR-5 could be considered to be more frail compared to the patients in the ZUMA-5 study (pp10-11, MSAC 1771 PSD, August 2024 MSAC meeting).

The previous ADAR was based on a published comparison of ZUMA-5 and SCHOLAR-5 at 18 months (Ghione 2022[4]) with further analyses presented in the ADAR at 48 months. The re-application ADAR represented results of this propensity score matched analysis at 48 months but did not report updated results for SCHOLAR-5 at 60 months, nor provide an updated comparison of ZUMA-5 and SCHOLAR-5 at 60 months. The re-application ADAR stated that additional analysis of the SCHOLAR-5 cohort has not been undertaken and is not planned.

In the comparative analysis, select patient baseline characteristics (variables from the data that were prespecified to be of 'high' or 'medium' importance) were balanced between the ZUMA-5 and SCHOLAR-5 cohorts to account for the potential imbalance of confounders through the application of propensity score methods (via standardised mortality ratio (SMR) weighting). Like the Commentary to the previous ADAR, the Commentary noted that variables ranked as 'low' importance were unadjusted for as "the need to modify the propensity score from the initial implementation precluded the addition of low priority variables, as pre-specified in the statistical analysis plan" (p8 of the Appendix to Ghione 2022). For example, patients in ZUMA-5 tended to have better Eastern Cooperative Oncology Group (ECOG) performance status compared to patients in the SCHOLAR-5 cohort, which was unadjusted for (ECOG 0: primary analysis: 59% vs 33%; secondary analysis: 62% vs 33%); such differences may not be adequately accounted for in the analysis and may result in the comparison being biased in favour of AXI. Ultimately, this analysis was an unanchored comparison which, the Commentary considered, did not necessarily account for all observed (and unobserved) differences in the compared patient cohorts.

Like the Commentary to the previous ADAR, the Commentary considered that while the use of propensity weighting via SMRs improved the comparability between the ZUMA-5 and the SCHOLAR-5 cohorts, the use of SMRs was not justified by the ADAR and it was unclear how this was applied. It was also unclear whether the same propensity scoring methods that were applied in the primary (18 month) comparative analysis (Ghione 2022) were also used in the updated 48-month analysis.

Key features of the studies presented by the ADAR are detailed in Table 6.

[4] Ghione P et al. Comparative effectiveness of ZUMA-5 (axi-cel) vs SCHOLAR-5 external control in relapsed/refractory follicular lymphoma. *Blood.* 2022 Aug 25;140(8):851-860. doi: 10.1182/blood.2021014375. PMID: 35679476; PMCID: PMC9412012. [https://pmc.ncbi.nlm.nih.gov/articles/PMC9412012/]

Table 6 Key features of the included evidence

References	N	Design/duration	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
ZUMA-5	FL=127 Updated analysis (FAS)=127	Single arm, multicentre, Phase 2 study; 48-and 60-month follow-up analysis	High	Adult patients with indolent non-Hodgkin lymphoma (FL or MZL) and relapsed or refractory disease after two or more lines of therapy	Primary: ORR Key secondary: CRR, PFS, OS, TTNT, safety	Yes (60 months analysis data)
ZUMA-5 vs SCHOLAR-5 (Ghione 2022)	Updated analysis (FAS): 255 ZUMA-5=127 SCHOLAR-5=128	Patients enrolled in ZUMA-5 were compared with an external control group of patients enrolled in a multicentre, retrospective cohort study (SCHOLAR-5); 48-month follow-up analysis	High	Adult patients with follicular lymphoma and relapsed or refractory disease after two or more lines of therapy	ORR, CRR, PFS, OS, TTNT	Yes (to inform comparator arm)

Source: compiled during the evaluation
CRR = complete response rate; FAS = full analysis set; FL = follicular lymphoma; IAS = inferential analysis set; MZL = marginal zone lymphoma; ORR = overall/objective response rate; OS = overall survival; PFS = progression-free survival; TTNT = time to next treatment.

11. Comparative safety

The ADAR stated that the rate and nature of adverse events reported in patients with FL treated with AXI at the 60-month analysis of ZUMA-5 was consistent with that reported at the 48-month analysis. No new safety signals have emerged with extended follow-up of the ZUMA-5 study.

The Commentary considered that adverse events such as treatment-emergent secondary malignancies or other adverse events that may develop over time would be of interest with extended follow-up. It is noted that eight (5%) of the 146 patients with indolent non-Hodgkin lymphoma enrolled in ZUMA-5 experienced secondary malignancies at the 12-month analysis (Table 4, p17, MSAC 1771 PSD, August 2024 MSAC meeting). The proportion experiencing secondary malignancies was not reported at 48 months in the previous ADAR, nor at 60 months in the re-application ADAR.

The clinical claim remained unchanged from the previous ADAR, that is, the use of AXI results in inferior safety compared with SOC; however, the adverse event profile of AXI is manageable in clinical practice with increasing clinical experience in identifying adverse events and well established protocols for monitoring patients receiving CAR T therapies, including the management of cytokine release syndrome and neurotoxicity.

In its consideration of the previous ADAR and regarding comparative safety, MSAC noted that the ZUMA-5 study data (48-month follow-up) indicated that adverse events were similar to those seen following AXI treatment for other indications, and similar to other CAR T therapies. MSAC noted that in the ZUMA-5 study, 99% of patients experienced treatment emergent adverse events (TEAE) and out of those 86% of patients experienced a Grade 3 or higher TEAE, and 52% of patients experienced at least one serious TEAE. Furthermore, significant side effects such as cytokine release syndrome (78%), any neurological event (56%), cytopenia (73%), infection (56%), and hypogammaglobulinaemia (20%) were seen in patients treated with AXI (p5, MSAC 1771 PSD, August 2024 MSAC meeting). This remains relevant as no new adverse events were

reported at 60 months follow-up. MSAC concluded that the claim that AXI had inferior safety compared with SOC was likely reasonable, but noted that comparative safety of AXI versus SOC was based on naive comparisons of various clinical studies with a high risk of bias, and the limited and low-certainty data resulted in overall uncertainty (p5, MSAC 1771 PSD, August 2024 MSAC meeting).

The Commentary considered that although the re-application ADAR has appropriately provided safety data from ZUMA-5 with further follow-up, the evidence presented does not address the overall uncertainty of the comparative safety claim.

12. Comparative effectiveness

Overall/objective and complete response rates

The primary effectiveness outcome of the ZUMA-5 study was overall/objective response rate (ORR), defined as the incidence of CR or partial response (PR). In ZUMA-5, assessments of response were performed using fluorodeoxyglucose positron emission tomography with contrast-enhanced CT (PET-CT). The Commentary noted that comparatively, SCHOLAR-5 included some CT-based response assessment and some PET-alone-based response assessments, which may have introduced measurement bias.

The results for ORR and complete response (CR) in ZUMA-5 at 60 months and from the ZUMA-5 vs SCHOLAR-5: Updated 48-month comparative analysis is presented in Table 7.

Table 7 Results of overall/objective and complete response rates

	ZUMA-5	ZUMA-5 vs SCHOLAR-5: 48-month comparative analysis			
	60-month analysis of ZUMA-5 (N=127): FAS	ZUMA-5 (N=127)	Weighted SCHOLAR-5 (N=128)	Absolute difference (95% CI)	Odds ratio (95% CI)
Number of objective responders (CR+PR), n (%)	119 (94%) 95% CI (88%, 97%)	119 (94%)	69 (54%)	40% (30%, 49%), p <0.0001	12.7 (5.2, 30.6)
Number of complete responders (CR), n (%)	100 (79%) (95% CI 71%, 85%)	100 (79%)	45 (35%)	44% (32%, 54%), p <0.0001	6.9 (3.6, 13.2)

Source: Table 19, p32 and Table 22, p33 of the re-application ADAR + in-line commentary
CI = confidence interval; CR = complete response; N=total number of patients; n = number of patients with event; PR = partial response

The Commentary considered that although there has been no change in the ORR in ZUMA-5 with an additional 12 months of follow-up to 60 months, the re-application ADAR had not presented updated data for SCHOLAR-5. The commentary considered that this may be important as the ORR in SCHOLAR-5 increased from 50% at 12 months to 54% at 48 months (Table 8, p21, MSAC 1771 PSD, August 2024 MSAC meeting).

Progression-free survival

Progression free survival (PFS) was a secondary effectiveness outcome of ZUMA-5, defined as the time from the enrolment/leukapheresis date (analysis based on the full analysis set) to the date of disease progression or death due to any cause.

The results for PFS in ZUMA-5 at the 48- and 60-month analysis are presented in Table 8, with the Kaplan-Meier (KM) for PFS at 60 months presented in Figure 1.

Table 8 Progression-free survival in ZUMA-5

	48-month analysis of ZUMA-5 (N=127): FAS	60-month analysis of ZUMA-5 (N=127): FAS
Events, n (%)	57 (45%)	59 (46%)
Censored, n (%)	70 (55%)	68 (54%)
Censoring reason: response ongoing	61 (48%)	55 (43%)
Kaplan-Meier median, months (95% CI)	57.3 (30.9, NE)	57.3 (30.9, NE)
Progression free rate, % (95% CI)		
12 months	80% (72%, 86%)	80% (72%, 86%)
24 months	66% (57%, 74%)	66% (57%, 74%)
36 months	57% (43%, 62%)	57% (43%, 62%)
48 months	53% (43%, 62%)	54% (44%, 63%)
60 months	-	50% (40%, 59%)

Source: Table 24, p35 of the re-application ADAR + in-line commentary
CI = confidence interval; FAS = full analysis set; N=total number of patients; n = number of patients with event; NE = not estimable

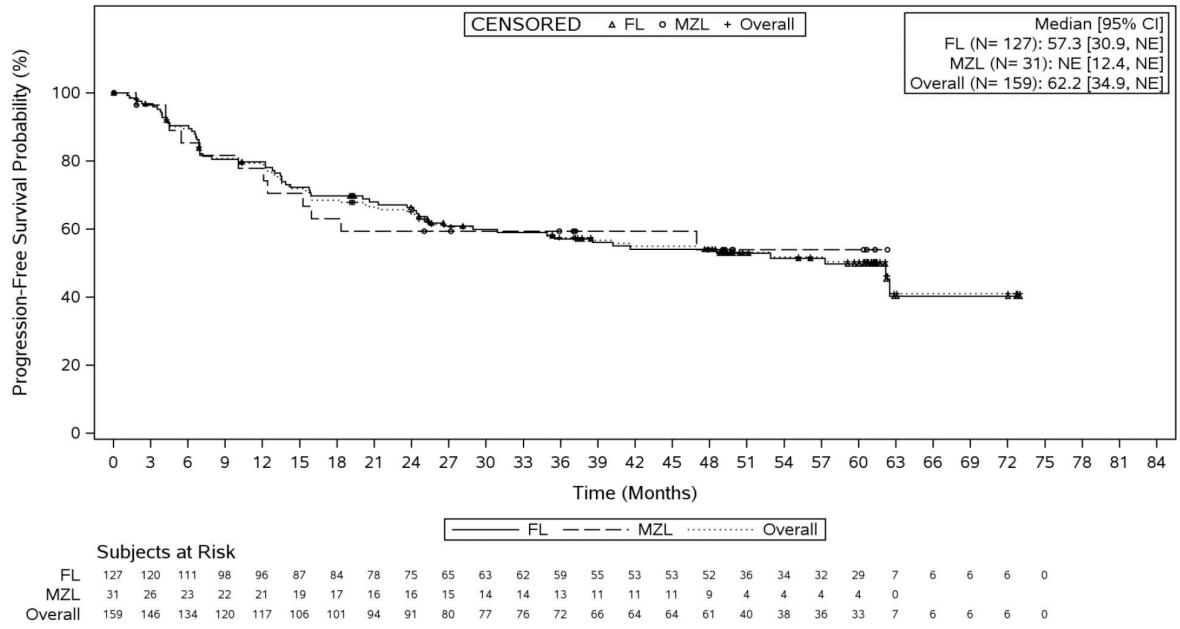

Figure 1 KM for PFS in ZUMA-5, updated to median 60 months follow-up

Source: Figure 2, p35 of the re-application ADAR + in-line commentary
CI =confidence interval; FL = follicular lymphoma; KM = Kaplan-Meier; MZL = marginal zone lymphoma; NE = not estimable

Progression events were reported in 2 of 127 (1.6%) patients enrolled in ZUMA-5 between the 48- and 60-month analysis. At the 60-month analysis 55/127 (43%) of patients that received AXI were assessed as having ongoing response to treatment and not assessed as experiencing disease progression or death. The Commentary considered that although there are a high proportion of patients remaining progression-free, there continues to be a decrease in the number of patients remaining progression-free which is not supportive of the assumption of 'cure' at 5 years as assumed in the economic evaluation.

It is also notable that the proportion of patients remaining progression-free at 48 months differed in the 48-month (53%) and 60-month (54%) analyses. Moreover, at 25.4292 months in the raw KM data for PFS, on which the respective economic models were based, the probability of being progression-free was 0.4636 in the previous ADAR compared with 0.4980 in the re-application ADAR.

The hazard ratio for PFS, estimated at the 48-month analysis between ZUMA-5 and SCHOLAR-5 was 0.27 (95% CI: 0.18, 0.40).

As no updated comparative data for PFS was presented by the re-application ADAR, per the Commentary on the previous ADAR, results presented by the ADAR suggested superiority of AXI over SOC in terms of ORR and PFS (p24, MSAC 1771 PSD, August 2024 MSAC meeting). However, the Commentary considered that the following points regarding the comparative efficacy of ZUMA-5 vs SCHOLAR-5 populations still exist and should be noted:

- Potential transitivity issues may exist between the cohorts used in the ADAR's comparative analysis, despite the application of propensity scoring.
- Even though the index date of treatment after July 2014 in SCHOLAR-5 cohort was chosen to reduce time-period bias due to the introduction of PI3Kδ inhibitors and because the Lugano criteria for disease assessment was formalised in 2014, Ghione 2022 (p854) acknowledged that "response assessment in subcohorts A and B included CT scans using older criteria". Therefore, this introduced measurement bias (unclear in what direction) given the ZUMA-5 cohort was assessed per the Lugano classification. It was unclear how many patients may have been affected.
- PFS censoring applied in ZUMA-5 (where patients who received any subsequent anti-cancer therapy (including SCT or retreatment with AXI) in the absence of prior documented progression were censored) may be biased in favour of ZUMA-5, while censoring rules for SCHOLAR-5 cohort were not provided by the ADAR and could not be located during the evaluation. Therefore, it was unclear how patients who 'progressed' were determined in SCHOLAR-5.
- Patients could be assessed as 'progressed' more quickly whilst receiving SOC in SCHOLAR-5 than compared to ZUMA-5, as clinicians may be more likely to push SOC patients to progress quicker in order to switch treatments when SOC was perceived as not working, particularly in a real-world setting.
- Bias may be introduced from the misalignment of the timing of assessments between the two studies, potentially overestimating time to progression in the study with less frequent disease assessments. Patients enrolled in ZUMA-5 were assessed at Week 4, then 3 monthly, and if a patient's disease had not progressed by Month 24, disease assessments were to continue to be performed per SOC, whereas the frequency of assessments in SCHOLAR-5 was not reported, though Ghione (2022) expected this to be less frequent in real-world practice.

Therefore, the Commentary considered results of this analysis should be considered highly uncertain.

Overall survival

Overall survival (OS) was a secondary effectiveness outcome of ZUMA-5, defined as the time from the enrolment/ leukapheresis date (analysis based on the full analysis set) to the date of death due to any cause.

The results for OS in ZUMA-5 at the 48- and 60-month analysis are presented in Table 9, with the KM for OS at 60 months presented in Figure 2.

Table 9 Overall survival in ZUMA-5

	48-month analysis of ZUMA-5 (N=127): FAS	60-month analysis of ZUMA-5 (N=127): FAS
Death from any cause, n (%)	38 (30%)	39 (31%)
Kaplan-Meier median, months (95% CI)	NE (62.2, NE)	NE (NE, NE)
Overall survival rate, % (95% CI)		
12 months	97% (92%, 99%)	97% (92%, 99%)
24 months	88% (81%, 93%)	88% (81%, 93%)
36 months	76% (67%, 83%)	76% (67%, 83%)
48 months	72% (64%, 79%)	73% (64%, 79%)
60 months	-	69% (60%, 76%)

Source: Table 26, p38 of the re-application ADAR + in-line commentary
CI= confidence interval; FAS = full analysis set; N=total number of patients; n = number of patients with event; NE = not estimable

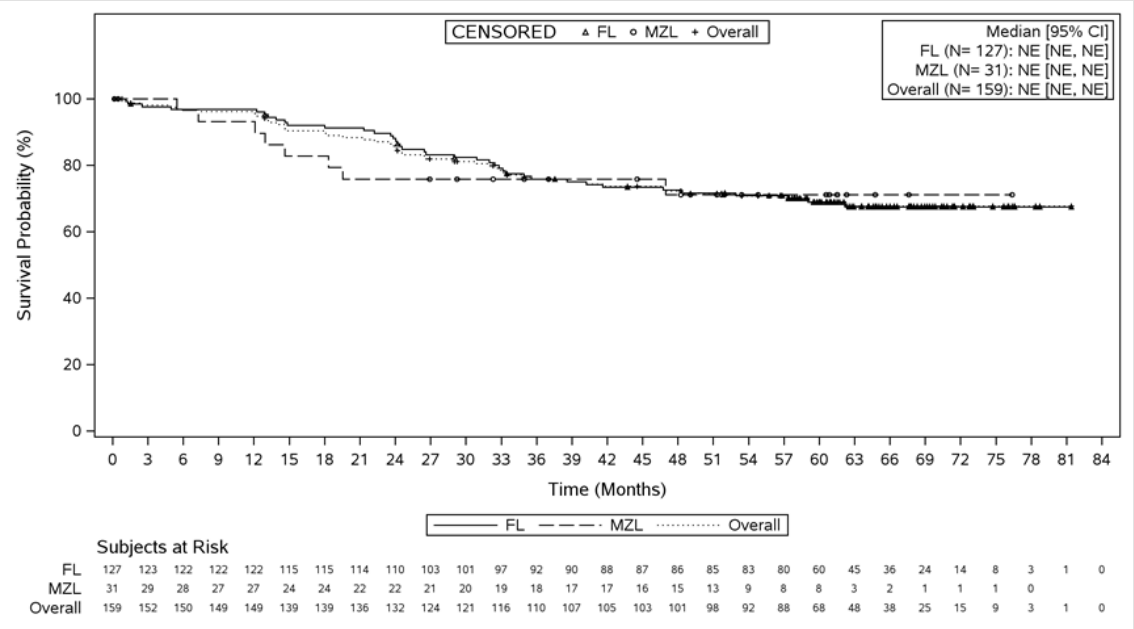

Figure 2 KM for OS in ZUMA-5, updated to median 60 months follow-up

Source: Figure 3, p38 of the re-application ADAR + in-line commentary
CI= confidence interval; FL = follicular lymphoma; KM = Kaplan-Meier; MZL = marginal zone lymphoma; NE = not estimable

Death from any cause was reported in 1 of 127 (0.8%) patients enrolled in ZUMA-5 between the 48- and 60-month analysis. It is also notable that the proportion alive at 48 months differs between the 48-month (72%) and the 60-month (73%) analyses. Moreover, at 69.3552 months in the raw KM data for OS, on which the respective economic models were based, the probability of being alive was 0.5962 in the previous ADAR compared with 0.6747 in the re-application ADAR (a difference of 0.079 (7.9%)) as presented below in Table 10. The commentary observed an increase in survival with extended follow-up of ZUMA-5.

Table 10 Reported proportion of patients remaining alive, KM data from ZUMA-5 in the re-application and previous ADARs

Timepoint (months)	Proportion in Overall Survival	
	Re-application ADAR	Previous ADAR
0.000 – 46.7515	1.00 decreasing to 0.7336	
46.7515	0.7252	0.7240
69.3552 (last timepoint for previous ADAR) and 69.3881 (closest timepoint for the re-application ADAR)	0.6747	0.5962
		0.00
81.3799	0.6747	-

Source: Commentary Table 2, p39 of the re-application ADAR + in-line commentary

Median OS had still not been reached at the 60-month analysis, with 69% of patients remaining alive at 60 months (5 years) after enrolment in ZUMA-5.

The hazard ratio for OS, estimated at the 48-month analysis between ZUMA-5 and SCHOLAR-5 was 0.58 (95% CI: 0.35, 0.96).

As no updated comparative data for OS was presented by the re-application ADAR, per the Commentary on the previous ADAR, the results presented by the ADAR suggested superiority of AXI compared to SOC (ZUMA-5 vs SCHOLAR-5) in terms of OS benefit. However, the Commentary noted there are concerns regarding the transitivity between the compared populations and bias. Overall, the Commentary considered magnitude of benefit is considered highly uncertain (p26, MSAC 1771 PSD, August 2024 MSAC meeting).

Clinical claim

The clinical claim made in the re-application ADAR remains unchanged from that made in the previous ADAR. That is, AXI represents a superior treatment than existing SOC for patients with r/r FL after two or more lines of therapy.

The claim of superiority for AXI is considered to be strongly supported by the ADAR based on:

- The long duration of follow-up of the ZUMA-5 study (median 60 months).
- The intra-trial consistency of results reported across multiple efficacy outcomes and follow-up times for ZUMA-5.
- The magnitude of the improvement in treatment response (ORR and CR), PFS and OS reported in the ZUMA-5 vs SCHOLAR-5 comparison.

In its consideration of the previous ADAR, MSAC acknowledged the clinical need for new therapies for this patient population, and considered that AXI appeared to offer clinical benefit, particularly in progression free survival. However, MSAC noted that due to the low certainty of evidence, the magnitude of benefit was highly uncertain. The Commentary considered that although the re-application ADAR has appropriately provided effectiveness data from ZUMA-5 with further follow-up and has demonstrated that the benefit appears to be sustained, the evidence presented does not address the overall uncertainty of the comparative effectiveness claim in terms of magnitude of benefit.

13. Economic evaluation

Based on the claim of superior efficacy and inferior safety, the ADAR presented a cost-utility analysis examining the cost-effectiveness of AXI versus SOC for the treatment of patients with r/r FL after two or more lines of systemic therapy. The analysis is based on extrapolation of outcomes from ZUMA-5 and data from the propensity weighted SCHOLAR-5 analysis.

Though the curves incorporated into the model appeared consistent with the KM curves presented in Figure 1 and Figure 2, the Commentary could not fully verify these curves due to the non-transparent nature of the analysis.

The ADAR modelled cure using a piecewise approach, assuming a cure point at 5 years, at which OS in 40% of patients in the AXI arm was assumed to match general population mortality with a SMR applied to model excess mortality (with the remainder of the population following the parametric extrapolation of survival).

This extrapolation was based on an unanchored propensity weighted comparison of ZUMA-5 (updated 60-month median potential follow-up) and SCHOLAR-5.

Table 11 presents an overview of the model structure and key parameters.

Table 11 Summary of the economic evaluation

Component	Description
Perspective	Health care system perspective
Population	Adult patients with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy
Prior testing	Not applicable
Comparator	Standard of care (including cyclophosphamide, fludarabine, bendamustine, obinutuzumab, rituximab, doxorubicin, vincristine, bortezomib, idelalisib, prednisolone)
Type(s) of analysis	Cost-utility analysis
Outcomes	Life years gained, quality-adjusted life years
Time horizon	30 years in the model base case vs 5 years (60 months) in the ZUMA-5 study
Computational method	Partitioned survival analysis
Generation of the base case	Modelled. The economic model applies outcomes from the modelled comparison of ZUMA-5 vs SCHOLAR-5 presented in Figure 1 and Figure 2. (Based on the unanchored propensity weighted comparison of ZUMA-5 and SCHOLAR-5)
Health states	Progression free survival Progressed disease Dead
Cycle length	1 month - Half cycle correction was applied for costs (except for those assumed to occur at the start of the model) and outcomes.
Transition probabilities	Extrapolated survival data (PFS and OS) for AXI and standard of care derived from the comparison of ZUMA-5 vs SCHOLAR-5 and background (all-cause) mortality used to transition patients between health states. (In addition to extrapolation, cure was assumed for all progression free AXI patients at 5 years, after which point a SMR of 1.09 was applied).
Discount rate	5% for both costs and outcomes
Software	Microsoft Excel

Source: Table 30, p43 of the re-application ADAR + in-line commentary
AXI = axicabtagene ciloleucel; OS = overall survival; PFS = progression free survival; SMR = standardised mortality ratio

The fundamental approach taken in the economic evaluation presented in the re-application ADAR was consistent with that taken by the previous ADAR, with the following notable updates:

- The incorporation of longer-term follow-up data from ZUMA-5 study (at 60-month analysis, as opposed to the 48-month analysis previously presented); and
- A reduced price for AXI ($**redacted**, reduced from $**redacted**).

No adjustments were made by the re-application ADAR to patient characteristics (based on ZUMA-5) or utility values (Papaioannou 2012[5]). The Commentary to the previous ADAR noted that these utilities reflected newly diagnosed FL patients and not necessarily those who are r/r after 2 or more lines of therapy. For indicative purposes, utility values from Cher 2020[6] in r/r diffuse large B cell lymphoma (DLBCL) were tested as they may better approximate utility for a refractory setting in haematological malignancy. Overall, however, the Commentary considered that the model was not substantially sensitive to choice of utility. Minor changes were made to cost inputs in the revised economic model, which also had a minimal impact on the resultant ICER.

From the KM data from ZUMA-5, OS for AXI was modelled up to 5 years using a log-logistic extrapolation and PFS was extrapolated using a generalised gamma extrapolation. After 5 years, cure was assumed by the model for 40% of those progression free at 5 years with a survival matched general population mortality and a SMR of 1.09 (based on Maurer 2014[7]).

From the propensity weighted SCHOLAR-5 curve, OS for standard of care was modelled up to the end of the time horizon (30 years) using a Weibull curve and PFS was modelled by a Gompertz curve (exponential in the previous model). No cure was assumed for standard of care.

Figure 3 and Figure 4 presents the survival curves considered in the economic evaluation.

[5] Papaioannou D et al. Rituximab for the first-line treatment of stage III-IV follicular lymphoma (review of Technology Appraisal No. 110): a systematic review and economic evaluation. *Health Technol Assess*. 2012;16(37):1-253, iii-iv. doi: 10.3310/hta16370. PMID: 23021127. [https://www.journalslibrary.nihr.ac.uk/hta/HTA16370]

[6] Cher BP et al. Cost utility analysis of tisagenlecleucel vs salvage chemotherapy in the treatment of relapsed/refractory diffuse large B-cell lymphoma from Singapore's healthcare system perspective. *J Med Econ*. 2020 Nov;23(11):1321-1329. doi: 10.1080/13696998.2020.1808981. Epub 2020 Aug 25. PMID: 32780608. [https://www.tandfonline.com/doi/10.1080/13696998.2020.1808981?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed#abstract]

[7] Maurer MJ et al. Event-free survival at 24 months is a robust end point for disease-related outcome in diffuse large B-cell lymphoma treated with immunochemotherapy. *J Clin Oncol*. 2014 Apr 1;32(10):1066-73. doi: 10.1200/JCO.2013.51.5866. Epub 2014 Feb 18. PMID: 24550425; PMCID: PMC3965261. [https://pmc.ncbi.nlm.nih.gov/articles/PMC3965261/]

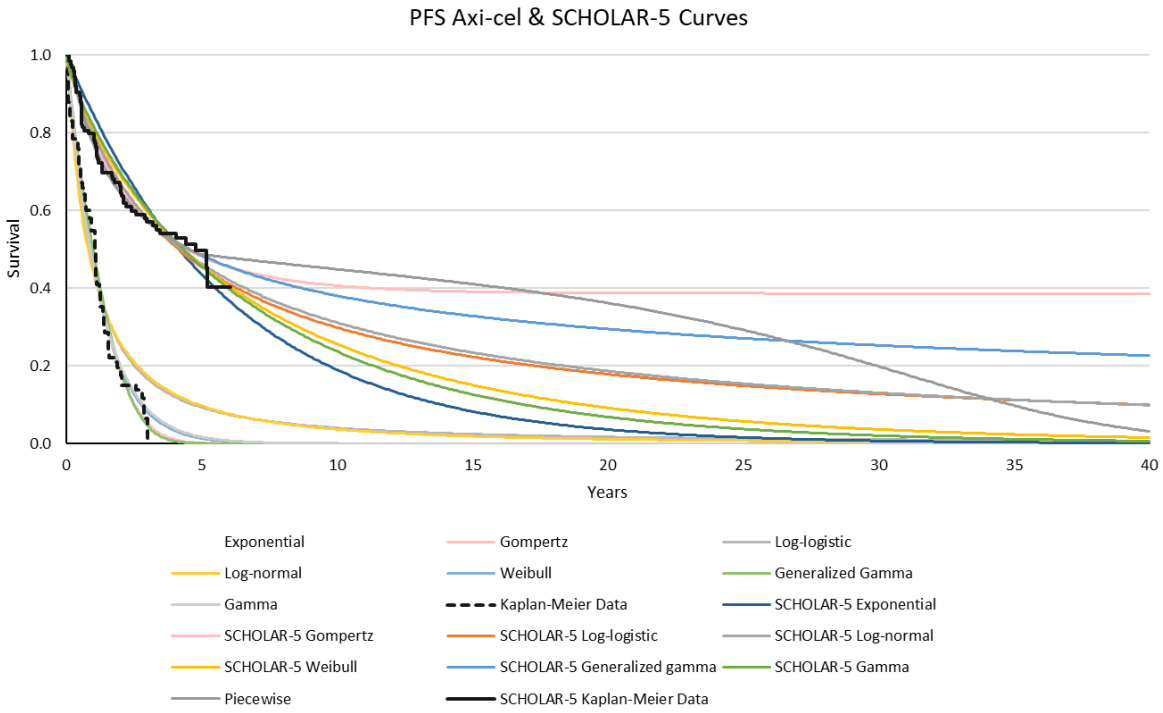

Figure 3 Parametric extrapolations of PFS for AXI and SOC

Source: Sheet "display_SurvCurves" from the economic model "Axi-cel Follicular Lymphoma Resubmission_Section 3 Workbook"
AXI/axi-cel = axicabtagene ciloleucel; PFS = progression-free survival; SOC = standard of care

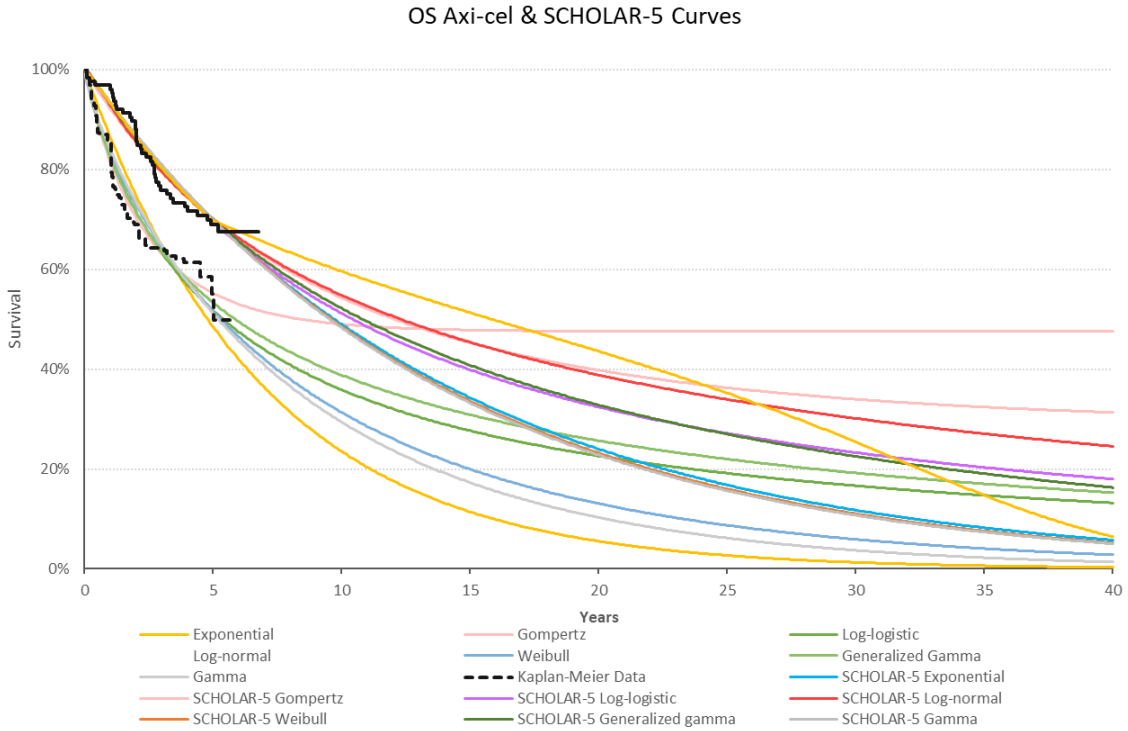

Figure 4 Parametric extrapolations of OS for AXI and SOC

Source: Sheet "display_SurvCurves" from the economic model "Axi-cel Follicular Lymphoma Resubmission_Section 3 Workbook"
AXI/axi-cel = axicabtagene ciloleucel; OS = overall survival; SOC = standard of care

The following should be noted regarding the SOC arm of the economic model:

- For PFS: The Commentary to the previous ADAR noted that all the extrapolations appeared to underestimate long term PFS in SCHOLAR-5, and this may indicate that long term survival (beyond the SCHOLAR-5 data) is substantially underestimated, favouring AXI. Overall, however, SOC PFS was not a driver of the model, with the choice of extrapolation having minimal impact on the ICER.
- While the re-application ADAR stated that SOC arm remained unchanged, a different PFS curve (Gompertz, as opposed to exponential) was used in the model presented in the re-application ADAR. Therefore, base case results for the SOC arm of the model differed from the previous model.
- For OS: The Commentary to the previous ADAR noted that it appeared there was little basis to conclude that the Weibull's extrapolation was a more accurate modelling of long-term survival than the log-logistic, log-normal and generalised gamma models. Selecting any of these in the revised model increased the ICER by 14 to 22%.

The economic model did not model KM survival data directly at any point. The Commentary considered that given concerns regarding the fit of the curves to the KM data, it would have been useful to include data from model initiation until data becomes less reliable.

Cure assumption

The economic model presented by the previous ADAR applied a 40% cure rate after 5 years of PFS in patients treated with AXI. However, for the previous ADAR MSAC agreed with ESC that this "was not well supported by the evidence presented in the ADAR. MSAC reiterated that, given that r/r FL is an indolent disease, the duration of follow-up in the clinical study was insufficient to justify the modelled cure assumption. MSAC agreed with ESC that there was a need to consider a longer period of remission for FL (at least 10 years, given that some patients relapse at 10 years) before assuming that a patient with r/r FL may be cured" (p5, MSAC 1771 PSD, August 2024 MSAC meeting).

The re-application ADAR maintained that the application of a cure assumption for AXI was reasonable based on the totality of evidence available:

- FL is not considered to be a slowly progressing/indolent disease in patients r/r to at least 2 prior lines of therapy (the modelled population).
- Updated analysis of ZUMA-5 (with 60 months of follow-up) demonstrated sustained durations of PFS and avoidance of new anti-cancer therapy 5 years after being treated with AXI.
- A long-term study (Puckrin 2023[8]) reported that autologous stem cell transplant (ASCT) may result in a functional cure in a cohort of patients with r/r FL.

The ADAR claimed that data captured in the Lymphoma and Related Disease Registry (LaRDR) showed that FL is not indolent in nature at more advanced stages of disease, with additional lines of therapy, the PFS period becomes significantly shortened. For patients receiving third line therapy (who would be eligible for AXI; n=13), median PFS was only 13.1 months. However, the Commentary considered this was likely a function of bias; the LaRDR report (p15) acknowledged

[8] Puckrin R et al. Long-term follow-up demonstrates curative potential of autologous stem cell transplantation for relapsed follicular lymphoma. *Br J Haematol*. 2023 Apr;201(2):319-325. doi: 10.1111/bjh.18640. Epub 2023 Jan 10. PMID: 36625160. [https://onlinelibrary.wiley.com/doi/10.1111/bjh.18640]

that “due to the long natural history of the disease, and the relatively limited follow-up on these patients, patients who had commenced later lines of therapy were biased towards those with poor prognosis, with poorer ECOG performance status, more advanced Ann Arbor stage and poorer FLIPI [Follicular Lymphoma International Prognostic Index] risk”. Further, given very few patients commenced third line therapy (n=13), “those that did are not expected to be representative” (LaRDR 2024; p15) and therefore this data may not be meaningful. The Commentary considered that while an inverse relationship between length of overall survival and line of therapy have been observed (i.e. shorter survival at later lines of therapy), the studies (LaRDR; Ghione 2022) presented by the ADAR did not explicitly comment on FL becoming increasingly aggressive.

The ADAR provided outcomes from an updated analysis of ZUMA-5 with 60 months of follow-up. Notably, 1 patient had their PFS event attributed to disease progression between the 36-month and 48-month analysis of ZUMA-5 and 1 additional patient had their PFS event attributed to disease progression between the 48-month and 60-month analysis of ZUMA-5. The ADAR claimed that the incorporation of the long-term clinical benefits of AXI into the economic evaluation was supported by the evidence reported from the 60 months analysis of ZUMA-5 where 54% of patients remained alive and progression-free. The Commentary considered that while updated data suggests the maintenance of response in patients treated with AXI up to 60 months (5 years), long-term evidence (at least ten years) was not provided by the ADAR. For the previous ADAR, at the August 2024 MSAC meeting, “MSAC agreed with ESC that there was a need to consider a longer period of remission for FL (at least 10 years, given that some patients relapse at 10 years) before assuming that a patient with r/r FL may be cured” (p5, MSAC 1771 PSD, August 2024 MSAC meeting); this was not addressed by the re-application ADAR. The Commentary noted that even though new data was presented by the re-application ADAR, this data may be too immature and insufficient to support the curative assumption applied in the economic model.

Lastly, the ADAR claimed the clinical plausibility of the curative potential of treatments for r/r FL was demonstrated by the long-term outcomes of patients treated with ASCT (Puckrin 2023). For the 162 patients with relapsed FL, “ASCT was found to achieve high rates of durable remissions with a plateau emerging on the TTP [time-to-progression] curve suggesting that more than 50% of transplanted patients may be functionally cured of their lymphoma” (pp322-323). However, the Commentary noted that this may not be representative of the 34% (n=52) of patients that received ASCT at third line or later (same place in therapy as AXI), particularly as the study (p323) found that compared to patients treated at third or later relapse, “patients undergoing ASCT at first or second relapse experienced superior outcomes”. The TTP curve was not reported for patients that received ASCT at third line or later and therefore this was unclear. Further, the Commentary noted that treatment with ASCT differs from that of CAR T-cell therapy; in this context, the clinical plausibility of applying a cure assumption based on this evidence may not be reasonable. Puckrin (2023; p323) commented that although promising, the long-term outcomes of CAR T-cell therapy and potential for cure are not yet known.

The ADAR presented the results of an economic evaluation with the application of the cure assumption of 40% applied to all progression free patients treated with AXI from 5 years, after which point a SMR of 1.09 was applied to adjust for excess mortality (unchanged from previous ADAR) as the base case (the remainder of the population followed the parametric extrapolation of survival). While the re-application ADAR did not mention a SMR, the economic model assumed that ‘cured’ patients would revert to the general population mortality with a SMR of 1.09 (based on Maurer 2014) in the base case, even though ESC considered this for the previous ADAR “highly optimistic” (p47, MSAC 1771 PSD, August 2024 MSAC meeting). In the absence of a clear SMR value for FL, alternative SMR values were tested by the previous Commentary (2.7 and 3.7 from a retrospective study in FL after auto- haematopoietic stem cell transplantation (HSCT)

using patient data from national transplant registry in Japan). The Commentary noted these had a considerable impact on the ICER (19% and 31% respectively), however, ESC considered these alternate values "may be overly conservative" (p47, MSAC 1771 PSD, August 2024 MSAC meeting). "ESC considered the appropriate SMR value was somewhere between the ADAR's base case and the Commentary sensitivity analyses" (p47, MSAC 1771I PSD, August 2024 MSAC meeting). Therefore, alternative SMR values of 1.895 (mean of 1.09 and 2.7) and 2.50 (mean of 1.09, 2.7 and 3.7) were tested during the evaluation, which increased the ICER by 9% and 15%, respectively.

Overall, the Commentary considered that no compelling new evidence was presented by the re-application ADAR to reasonably support a cure assumption. The evidence (LaRDR; Puckrin 2023) provided were of low quality or not directly relevant to the proposed treatment or requested population. Moreover, despite updated data from the ZUMA-5 study (60-month analysis), the re-application ADAR did not address the recommendation from the previous ADAR the "need to consider a longer period of remission for FL (at least 10 years, given that some patients relapse at 10 years) before assuming that a patient with r/r FL may be cured" (p5, MSAC 1771 PSD, August 2024 MSAC meeting).

While a modelling approach incorporating a cure rate in some patients was adopted in previous economic evaluations of CAR T therapies assessed by MSAC (MSAC 1519.1, MSAC 1587), MSAC had consistently expressed concern regarding the uncertainty of modelling cure and had not explicitly accepted the ICERs as cost-effective (p5, MSAC 1771 PSD, August 2024 MSAC meeting). The Commentary noted that overall, MSAC's previous consideration and basis of support for CAR T therapy for other indications does not create a precedent and does not support the modelling approach used by the ADAR (p31, MSAC 1771 PSD, August 2024 MSAC meeting).

The Commentary further noted that FL is currently considered incurable (Tonino & Kersten 2024[9]). Consequently, assumptions of long-term cure based on 5-year median survival results may have been optimistic, and would favour AXI (p33, MSAC 1771 PSD, August 2024 MSAC meeting). Given the uncertainty regarding the cure assumption and SMR, which created significant uncertainty in the model, ESC previously considered that cure assumption should be removed from the base case model and instead focus on the PFS gains (p47, MSAC 1771 PSD, August 2024 MSAC meeting). This would also remove the uncertainty regarding the SMR applied in the base case (p47, MSAC 1771 PSD, August 2024 MSAC meeting). However, the Commentary noted this was not addressed by the re-application ADAR (in the base case) and only performed as part of sensitivity analyses. The model presented in the re-application ADAR was found to be sensitive to the application of a cure assumption; the removal of the cure assumption led to an increase of the resultant ICER by 30%.

The Commentary considered that assuming a cure at 5 years was not strongly supported by the evidence, and is thus primarily speculative. Given the uncertainty regarding the cure assumption and SMR, which created significant uncertainty in the model, ESC considered for the previous ADAR that cure assumption should be removed from the base case model and instead focus on the PFS gains (p4, MSAC 1771 PSD, August 2024 MSAC meeting). Consequently, the ADAR's univariate sensitivity analysis with the removal of the cure assumption may be viewed as reasonable estimation.

[9] Tonino SH et al. The quest for a cure in follicular lymphoma. *Blood 2024.* 143(6):475–476. doi: https://doi.org/10.1182/blood.2023022796

Results

Table 12 presents the results of the economic evaluation.

Table 12 Results of the economic evaluation

	AXI	SOC	Increment	ICER
Previous ADAR				
Cost	$**redacted**	$82,227	$**redacted**	-
Life-years	8.92	5.98	2.94	$**redacted**/LY
Quality-adjusted life years	6.80	4.07	2.72	$**redacted**/QALY
Re-application ADAR (base case)				
Cost	$**redacted**	$79,663	$**redacted**	-
Life-years	9.64	5.98	3.66	$**redacted**/LY
Quality-adjusted life years	7.32	4.03	3.29	$**redacted**/QALY
Re-application ADAR (removal of cure assumption)				
Cost	$**redacted**	$79,663	$**redacted**	-
Life-years	8.68	5.98	2.70	$**redacted**/LY
Quality-adjusted life years	6.61	4.03	2.58	$**redacted**/QALY

Source: Table 40, p65 and Table 42, p70 of the re-application ADAR + in-line commentary
ADAR= applicant-developed assessment report; AXI = axicabtagene ciloleucel; ICER = incremental cost-effectiveness ratio; LY = life year; QALY = quality-adjusted life year; SOC = standard of care

Uncertainty analysis

Key drivers of the model that are presented in Table 13.

Table 13 Key drivers of the model

Description	Method/Value	Impact Base case: $redacted/QALY gained
Cure assumption	40% of AXI patients in PFS state at 5 years will be cured, remainder will continue to follow parametrically extrapolated OS and PFS	High, favours AXI. The Commentary considered removing the cure assumption increased the ICER to $**redacted**/QALY gained (alternate base case).
SOC OS extrapolation	Weibull	High, uncertain. The Commentary considered selecting an exponential extrapolation decreased the ICER to $**redacted**/QALY gained. Selecting a lognormal extrapolation increased the ICER to $**redacted**/QALY gained.
AXI OS extrapolation	Based on KM estimates from ZUMA-5 at 60-month analysis; log-logistic	Moderate, favours AXI. The Commentary considered selecting an exponential extrapolation based on KM estimates from the ZUMA-5 study at 48-month analysis (as presented in the previous ADAR) increased the ICER to $**redacted**/QALY gained.
SMR	1.09	Moderate, favours AXI. The Commentary considered increasing the SMR to 1.895 increases the ICER to $**redacted**/QALY gained. Increasing the SMR to 2.50 increases the ICER to $**redacted**/QALY gained.

Source: constructed during the evaluation.
AXI = axicabtagene ciloleucel; ICER = incremental cost-effectiveness ratio; KM= Kaplan Meier; OS = overall survival; PFS = progression free survival; QALY = quality adjusted life-year; SMR = standardised mortality ratio; SOC = standard of care

The commentary noted possible uncertainty due to a discrepancy in OS between the raw KM data for OS in ZUMA-5 between the re-application and original application, where a difference of 0.079 (7.9%) was observed at about 69 months presented in Table 10. The commentary tested using the 48-month OS data for AXI in the re-application model and noted that the ICER increased to $redacted/QALY (16% increase from the base case) as presented within Table 14 below.

The results of key sensitivity analysis are presented in Table 14.

Table 14 Sensitivity analyses

Analyses	Incr cost	Incr QALY	ICER	% change
Base case	**$redacted**	**3.29**	**$redacted /QALY**	**-**
Discount rate of 3.5% (5% in base case)	$**redacted**	3.89	$**redacted** /QALY	-15%
Time horizon of 20 years (30 years base case)	$**redacted**	2.66	$**redacted**/QALY	23%
Utilities from Cher 2020 (Papaioannou 2012 in base case)	$**redacted**	2.97	$**redacted** /QALY	11%
40% cure fraction at 10 years (40% cure fraction at 5 years in base case)	$**redacted**	2.85	$**redacted** /QALY	17%
No cure (40% cure fraction at 5 years in base case)	$**redacted**	2.58	$**redacted** /QALY	30%
SMR (1.09 in base case) [a]				
1.895	$**redacted**	3.03	$**redacted**/QALY	9%
2.50	$**redacted**	2.85	$**redacted**/QALY	15%
SOC OS extrapolation (Weibull in base case)				
Gompertz	$**redacted**	1.90	$**redacted**/QALY	69%
Lognormal	$**redacted**	2.63	$**redacted**/QALY	24%
Exponential	$**redacted**	3.76	$**redacted**/QALY	-12%
AXI OS extrapolation (Log-logistic in base case)				
Gompertz	$**redacted**	3.44	$**redacted**/QALY	-4%
Weibull	$**redacted**	3.07	$**redacted**/QALY	7%
KM estimates from ZUMA-5 at 48-month analysis (at 60-month analysis in base case) [b]	$**redacted**	2.82	$**redacted**/QALY	16%

Source= Table 42, p70 of the re-application ADAR + in-line commentary and analyses conducted during the evaluation
AXI = axicabtagene ciloleucel; ICER = incremental cost-effectiveness ratio; Incr = incremental; KM = Kaplan Meier; OS = overall survival; QALY = quality adjusted life year; SMR = standardised mortality ratio; SOC = standard of care
a SMR was adjusted during the evaluation in Sheet "calcs_SurvSelections" AO35:1018 and CF35:1018.
b Changes made to "calcs_SurvSelections AQ34:AQ1018.

The results of key sensitivity analysis for the ICER with no cure assumed are presented in Table 15. The Commentary considered removing the explicit cure assumption, and relying on parametric plateaus to estimate the cure rate led to higher and wider range of ICERs across PFS and OS extrapolations.

Table 15 Sensitivity analyses for alternate estimate with no cure assumed

Analyses	Incr cost	Incr QALY	ICER	% change
Base case	**$redacted**	**2.58**	**$redacted/QALY**	**-**
Discount rate of 3.5% (5% in base case)	$**redacted**	2.98	$**redacted**/QALY	-13%
Time horizon of 20 years (30 years base case)	$**redacted**	2.14	$**redacted**/QALY	20%
Utilities from Cher 2020 (Papaioannou 2012 in base case)	$**redacted**	2.36	$**redacted**/QALY	9%
SOC OS extrapolation (Weibull in base case)				
Gompertz	$**redacted**	1.19	$**redacted**/QALY	112%
Lognormal	$**redacted**	1.92	$**redacted**/QALY	33%
Exponential	$**redacted**	3.05	$**redacted**/QALY	-15%
AXI OS extrapolation (Log-logistic in base case)				
Gompertz	$**redacted**	2.88	$**redacted**/QALY	-10%
Weibull	$**redacted**	2.16	$**redacted**/QALY	19%
KM estimates from ZUMA-5 at 48-month analysis (at 60-month analysis in base case) [a]	$**redacted**	2.73	$**redacted**/QALY	-5%

Source: constructed during the evaluation
AXI = axicabtagene ciloleucel; ICER = incremental cost-effectiveness ratio; Incr = incremental; KM = Kaplan Meier; OS = overall survival; QALY = quality adjusted life year; SOC = standard of care
[a] = Changes made to "calcs_SurvSelections AQ34:AQ1018.

The base case analysis reported an ICER of $**redacted**/QALY. However, the Commentary noted that largely due to the speculative nature of cure assumptions in third line or later FL, the ICER should be considered highly uncertain, and carries a high risk of being underestimated. The Commentary presented an estimate with no cure assumption resulting in an ICER of $**redacted**/QALY, which was calculated with the removal of the cure assumption (as advised from ESC (p4, MSAC 1771 PSD, August 2024 MSAC meeting).

The Commentary considered that, overall, the model was sensitive to the assumptions made regarding long term survival for either treatment. This included the cure assumption, OS parametric extrapolation choice for SOC, and the SMR for cured patients. The impact of varying any of these assumptions on the ICER suggests how uncertain the long-term benefit of AXI would be over a 30-year time horizon. Given the lack of consensus on the possibility of cure in r/r FL, the Commentary considered the re-application ADAR's cure assumptions likely favour AXI and likely underestimate the ICER.

The Commentary further noted that the benefit was estimated based on the clinical comparison of ZUMA-5 and the propensity weighted SCHOLAR-5 results. This analysis was an unanchored comparison which, the Commentary considered, did not necessarily account for all observed (and unobserved) differences in the compared patient cohorts. This was highly uncertain, and the model did not include functionality to test this uncertainty. This was also noted in the Commentary to the previous ADAR.

Additional sensitivity analysis by the department considered by MSAC is presented below in Table 16.

Table 16 Results of economic evaluation and additional sensitivity analysis using hospital cost estimates from jurisdictions of $redacted, $redacted & $redacted (calculated by the department)

	AXI	SOC	Increment	ICER
Resubmission ADAR (base case)				
Total Costs	**$redacted** ($redacted)	$79,663	**$redacted**	-
Life-years	9.64	5.98	3.66	**$redacted**/LY
Quality-adjusted life years	7.32	4.03	3.29	**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(lowest)				**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted** (2nd lowest)				**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(average)				**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(highest)				**$redacted**/QALY
AXI Price when ICER set to $redacted/QALY (base case with cure assumption)				
Total Costs	**$redacted** ($redacted)	$79,663	**$redacted**	**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(lowest)	**$redacted**			**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(2nd lowest)	**$redacted**			**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(average)	**$redacted**			**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(highest)	**$redacted**			**$redacted**/QALY
Resubmission ADAR (removal of cure assumption)				
Cost	**$redacted** ($redacted)	$79,663	**$redacted**	-
Life-years	8.68	5.98	2.7	**$redacted**/LY
Quality-adjusted life years	6.61	4.03	2.58	**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(lowest)				**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(2nd lowest)				**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(average)				**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(highest)				**$redacted**/QALY

AXI Price when ICER set to $redacted/QALY & no cure assumption				
Total Costs	**$redacted** ($AXI price = **$redacted**)	$79,663	**$redacted**	**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(lowest)	**$redacted**			**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(2nd lowest)	**$redacted**			**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(average)	**$redacted**			**$redacted**/QALY
Total PFS cost = AXI cost + Jurisdiction admin costs **$redacted**(highest)	**$redacted**			**$redacted**/QALY

Source: Table 11, p25 of the 1771.1 Executive Summary
ADAR= applicant-developed assessment report; AXI = axicabtagene ciloleucel; ICER = incremental cost-effectiveness ratio; LY = life year; QALY = quality-adjusted life year; SOC = standard of care
Green text = calculations by the department

14. Financial/budgetary impacts

The financial implications to the NHRA resulting from the proposed listing of AXI are summarised in Table 17, along with estimates derived in the previous ADAR.

Table 17 Net financial implications of AXI to the NHRA

Parameter	Year 2026	Year 2027	Year 2028	Year 2029	Year 2030	Year 2031
Estimated use and cost of AXI						
Number of people eligible for AXI	**redacted**	**redacted**	**redacted**	**redacted**	**redacted**	**redacted**
Number of people who receive AXI	**redacted**	**redacted**	**redacted**	**redacted**	**redacted**	**redacted**
Cost to the NHRA	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Cost to the NHRA (previous ADAR)	**$redacted**	**$redacted**	**$redacted**	**$redacted**	Not in scope	Not in scope
Change in use and cost of other health technologies						
Estimated hospital costs for apheresis	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Estimated hospital costs for AXI administration	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Estimated hospital costs for treating adverse events Grade ≥3	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Estimated hospital cost offsets for substituted treatment	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Estimated hospital cost offsets for treating adverse events Grade ≥3	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Overall net hospital costs	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**

Parameter	Year 2026	Year 2027	Year 2028	Year 2029	Year 2030	Year 2031
Estimated bridging treatment costs	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted
Estimated conditioning chemotherapy costs	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted
Estimated PBS cost for treatment of cytokine release syndrome and neurotoxicity	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted
Estimated PBS cost offsets: SOC	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted
Overall net PBS costs	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted
Overall net PBS costs (previous ADAR)	$redacted	$redacted	$redacted	$redacted	Not in scope	Not in scope
Cost of bridging therapy administration	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted
Cost of conditioning chemotherapy administration	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted
Estimated MBS cost offsets: SOC	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted
Overall net MBS costs	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted
Overall net MBS costs (previous ADAR)	$redacted	$redacted	$redacted	$redacted	Not in scope	Not in scope
Overall net cost to government	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Overall net cost to government (previous ADAR)	$redacted	$redacted	$redacted	$redacted	Not in scope	Not in scope

Source: Table 45, p78, Table 46, p79, Table 47, p80, Table 48, p81, Table 50, p82 of the resubmission ADAR + in-line commentary
ADAR= applicant-developed assessment report; AXI = axicabtagene ciloleucel; MBS = Medicare Benefits Schedule; NHRA = National Health Reform Agreement; PBS = Pharmaceutical Benefits Scheme; SOC = standard of care

The re-application ADAR made no changes to the estimated number of patients who were eligible and would be treated with AXI compared with those derived for the previous ADAR. Acting on advice, the re-application ADAR triangulated the number of PBS items processed for the initial treatment PBS restrictions of idelalisib (PBS codes 11165P and 11171Y) for the last full calendar year with data available (2023). Patients must be refractory to at least 2 prior therapies in order to meeting the eligibility criteria to access idelalisib through these PBS restrictions, that is, treatment is restricted to a third line and later setting. The Commentary noted that PBS items 11165P and 11171Y are for the treatment of 'refractory follicular B-cell non-Hodgkin's lymphoma'. While FL is represented under this restriction, so are diffuse large B cell, mantle cell, marginal zone and Burkitt lymphomas. Thus, the Commentary considered while the estimated numbers corroborated with the re-application ADAR's epidemiological approach to estimation, estimates derived from idelalisib scripts are a likely to overestimate the FL population.

Compared with the previous ADAR, differences in the estimates were noted by the Commentary and can be explained by:

- Cost to the NHRA: lower in the re-application ADAR directly due to the reduced price of AXI.
- No change in the estimated hospital costs (after correction of an error identified in the previous ADAR).

- A reduction in PBS cost-offsets: primarily as a result of removal of all use of obinutuzumab combinations, which were the most expensive SOC treatment regimens.
- Increased MBS cost-offsets: unit cost per administration has increased from $118.90 to $123.05, and as the re-application ADAR has removed all use of obinutuzumab combinations, those patients are now assumed to be treated with rituximab + bortezomib which is associated with 20 administrations, compared with between 10 and 18 administrations for various obinutuzumab combinations.

MSAC considered the financial impact was highly uncertain due to uncertainty in the estimated utilisation, adjunctive hospital costs being underestimated and potential cost-savings being overestimated (p6, MSAC 1771 PSD, August 2024 MSAC meeting). Given the estimation of the number of patients and the hospital costs remained unchanged in the re-application ADAR, the Commentary considered uncertainty remains.

Additional sensitivity analysis of financial implications by the department is presented below in Table 18.

Table 18 Sensitivity analyses for alternate estimate of net financial implications of AXI to the NHRA using jurisdiction hospital cost estimates of $redacted and $redacted per patient as hospital costs and using AXI price alternatives from economic evaluation sensitivity analysis (calculated by the department)

Parameter	Year 2026	Year 2027	Year 2028	Year 2029	Year 2030	Year 2031
Estimated use and cost of AXI						
Number of people eligible for AXI	**redacted**	**redacted**	**redacted**	**redacted**	**redacted**	**redacted**
Number of people who receive AXI	**redacted**	**redacted**	**redacted**	**redacted**	**redacted**	**redacted**
Original financial implications from the resubmission						
Overall NHRA Addendum costs	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Overall net hospital costs	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Overall net PBS costs	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Overall net MBS costs	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Overall net cost to government	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Financial implications using AXI hospital cost of $redacted per patient						
Re-calculated Overall net hospital costs	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Re-calculated Overall net cost to government	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Financial implications using AXI hospital cost of $redacted per patient						
Re-calculated Overall net hospital costs	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Recalculated Overall net cost to government	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Financial implications using AXI price of $redacted (value from $redacted ICER with cure assumption analysis) + AXI hospital cost of $redacted per patient						

Parameter	Year 2026	Year 2027	Year 2028	Year 2029	Year 2030	Year 2031
Re-calculated Overall NHRA Addendum costs	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted
Re-calculated Overall net cost to government	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**

Source: Table 45, p78, Table 51, p82 of the resubmission ADAR + in-line commentary
ADAR= applicant-developed assessment report; AXI = axicabtagene ciloleucel; ICER = incremental cost-effectiveness ratio; MBS = Medicare Benefits Schedule; NHRA = National Health Reform Agreement; PBS = Pharmaceutical Benefits Scheme; Green text = calculations by the department

15. Other relevant information

The re-application ADAR requests that MSAC considers including funding AXI for patients with r/r marginal zone lymphoma (MZL) on the basis that:

- MZL are a subtype of non-Hodgkin lymphoma (NHL), representing less than 10% of NHLs (compared with 20-30% for FL).
- Clinicians have indicated this is a population with unmet need and given the low incidence and heterogeneity in presentation, large scale trials are challenging.
- No standard treatment for MZL due to its heterogeneity, however treatment regimens for MZL in the relapsed or refractory setting are similar to those employed for FL.
- The ZUMA-5 study included 31 patients with MZL and appear to have similar safety and effectiveness outcomes to the FL population, see Table 19 and Table 20 below.
- While FDA approval was initially sought for both FL and MZL, the FDA requested to remove the MZL indication due to lack of data and agreed to an accelerated approval for the indication of 'adult patients with r/r FL after two or more lines of systemic therapy' based on ZUMA-5. As such, when Gilead subsequently sought to register AXI on the ARTG for r/r FL, MZL was not included in the requested indication to the TGA.

Table 19 Summary of adverse events by preferred term: Safety Analysis Set

	60-month analysis of ZUMA-5, Follicular lymphoma (N=124)	60-month analysis of ZUMA-5, Marginal Zone Lymphoma (N=28)
Any TEAE	123 (99%)	28 (100%)
Worst Grade 5	10 (8%)	3 (11%)
Worst Grade ≥ 3	107 (86%)	27 (96%)
Any Serious TEAE	65 (52%)	19 (68%)
Worst Grade 5	10 (8%)	3 (11%)
Worst Grade ≥ 3	52 (42%)	16(57%)
Any AXI Related TEAE	118 (95%)	28 (100%)
Worst Grade 5	2 (2%)	0 (0%)
Worst Grade ≥ 3	72 (58%)	20 (71%)
Any Serious AXI Related TEAE	41 (33%)	14 (50%)
Worst Grade 5	2 (2%)	0 (0%)
Worst Grade ≥ 3	29 (23%)	10 (36%)

Source Table 57, p88 of the resubmission ADAR + in-line commentary
N = total number of patients; TEAE = treatment-emergent adverse event;
Note: Adverse events for the Safety Analysis Set, comprised of all patients treated with any dose of AXI

Table 20 Summary of efficacy from ZUMA-5

	60-month analysis of ZUMA-5, Follicular lymphoma (N=127)	60-month analysis of ZUMA-5, Marginal Zone Lymphoma (N=31)
Response rates		
Objective responders (CR+PR), n (%)	119 (94%) 95% CI (88%, 97%)	24 (77%) 95% CI (59%, 90%)
Complete responders, n (%)	100 (79%) 95% CI (71%, 85%)	20 (65%) 95% CI (45%, 81%)
Progression free survival		
Kaplan-Meier median, months (95% CI)	57.3 (30.9, NE)	NE (12.4, NE)
PFS rate: 48 months	54% (44%, 63%)	54% (33%, 71%)
PFS rate: 60 months	50% (40%, 59%)	54% (33%, 71%)
Overall survival		
Kaplan-Meier median, months (95% CI)	NE (NE, NE)	NE (NE, NE)
OS rate: 48 months	73% (64%, 79%)	71% (50%, 85%)
OS rate: 60 months	69% (60%, 76%)	71% (50%, 85%)

Source: Table 58, p88 of the resubmission ADAR + in-line commentary

CI = confidence interval; N = total number of patients; n = number of patients with event; NE = not estimable; OS = overall survival; PFS = progression-free survival Note: Effectiveness outcomes reported for the Full Analysis Set, comprised of all enrolled (leukapheresed) patients

The Commentary noted that the 2020-25 NHRA Addendum defines HSTs [highly specialised therapies] as: **TGA approved medicines and biologicals** delivered in public hospitals where the therapy and its conditions of use are recommended by MSAC or PBAC; and the average annual treatment cost at the commencement of funding exceeds $200,000 per patient (including ancillary services) as determined by the MSAC or PBAC with input from the IHACPA; and where the therapy is not otherwise funded through a Australian Government program or the costs of the therapy would be appropriately funded through a component of an existing pricing classification. AXI is not TGA-approved for MZL. Additionally, no formal assessment of the safety, effectiveness or cost-effectiveness of AXI for the treatment of MZL has been provided. The re-application ADAR also did not provide any estimation of the number of MZL patients likely to be treated with AXI, other than stating the number would be low and that these patients be incorporated into the risk share proposed (i.e., no increase in patient caps) under the same pricing conditions as patients treated for r/r FL.

16. Key issues from ESC to MSAC

Main issues for MSAC consideration

Clinical issues:

- Updated follow-up effectiveness data for AXI from the single arm ZUMA-5 study, extending from 48 to 60 months, were included in the re-application. However, 60-month comparative effectiveness data from ZUMA-5 vs SCHOLAR-5 were only provided in the pre-ESC response and could not be verified or evaluated by the assessment group or fully considered by ESC. ESC noted that some of the data in the pre-ESC response showed identical figures for 48 months and 60 months, and requested that these numbers are verified by the applicant. Subsequently, the assessment group produced an Addendum which included evaluation of the additional data. Of note, as detailed in the Addendum, it is difficult to verify whether the SCHOLAR-5 data has been updated since the 48-month analysis as the comparison presented by the applicant could be interpreted as 60-month ZUMA-5 data versus 48-month SCHOLAR-5 data.
- The magnitude of differences in safety and effectiveness between the intervention and the comparator remained uncertain.
- MSAC's concerns in the original application regarding the proposed clinical and treatment criteria have only been partially addressed in the re-application. The re-application made new changes to the indication and treatment criteria including removal of follicular lymphoma (FL) grading which ESC considered would need to be scrutinised. MSAC had previously noted that it is broadly accepted that grade 3B FL is managed as diffuse large B-cell lymphoma (MSAC 1676)[10]. The indication supported by the Joint Chairs Group was for Grade 1, 2, or 3A FL, and did not include Grade 3B FL.
- ESC advised against the inclusion of marginal zone lymphoma (MZL) in the patient population, as MZL is not a TGA-approved therapeutic indication for AXI.

Economic issues:

- Key economic issues identified by MSAC had not been fully addressed in the re-application – in particular, the cure assumption remains in the base case of the economic model and the modelled time horizon remains at 30 years. Removing the cure assumption increased the ICER from $**redacted** per quality-adjusted life year (QALY) gained to $**redacted** per QALY gained (30% increase).
- The ICER was sensitive to the choice of extrapolation function used and ESC considered that determining the extrapolation function that best fits the observed data is highly uncertain due to the immature follow-up data presented and also the error identified by the commentary in the economic model worksheet.

Financial issues:

- ESC considered that the revised price for AXI remains high and unjustified.
- The financial impacts in the re-application remain high and highly uncertain as uncertainty in estimated utilisation and ancillary hospital costs remain.

[10] https://www.msac.gov.au/sites/default/files/documents/1676%2520Final%2520PSD%2520-%2520July%25202021_redacted.pdf

Other relevant information:

- ESC noted the proposed risk-sharing arrangement and payment structures. ESC noted that the single payment on successful infusion structure preferred by the applicant was not supported by the jurisdictions. ESC considered that a pay for performance (PfP) structure with 2-stage payment was preferred and that this should be based on clinical outcomes. Given the more indolent nature of FL, MSAC may wish to consider whether the timepoint for a second payment should be tied to an outcome more than 12 months after successful infusion. This timepoint should be based on the available data with the aim to mitigate the risks associated with uncertainty in outcomes and treatment success.
- ESC noted the submissions from jurisdictions and some proposals about the use of annual patient caps for the risk sharing arrangement and requested that the department seek further information from jurisdictions regarding the full costs of therapy.
- Funding of AXI for r/r FL may create capacity challenges as the number of patients receiving CAR-T therapies would increase staffing and resource requirements.

ESC discussion

ESC noted that this reapplication from Gilead Sciences Pty Limited sought public funding under the National Health Reform Agreement (NHRA) as a Highly Specialised Therapy (HST) for axicabtagene ciloleucel (AXI, also known as Yescarta®, a chimeric antigen receptor T-cell [CAR-T] therapy) for patients with relapsed or refractory (r/r) follicular lymphoma (FL) after two or more lines of systemic therapy. MSAC had previously considered this application at its August 2024 meeting and had not supported public funding at that time, due to uncertainty about the magnitude and duration of benefits, and therefore uncertainty about likely cost-effectiveness. ESC noted this re-application was supported by the inclusion of longer-term follow-up data (increased from 48 months to 60 months), an updated analysis from the single arm ZUMA-5 study, amendments to the patient eligibility criteria, a price reduction for the therapy, and a proposed single upfront payment per patient successfully infused with AXI or an alternative risk-share arrangement (RSA) payment structure incorporating a pay-for-performance (PfP). ESC noted the re-application claimed that the longer-term follow-up data supported and maintained the same outcomes as the original submission being the clinical claim of superior effectiveness and inferior safety of AXI compared with standard of care (SOC).

ESC noted and welcomed the public consultation feedback from one consumer, 3 health professionals and 2 organisations. Feedback was supportive of the application, noting the clinical need for this population of patients and evidence of improved outcomes. ESC noted one health professional considered the proposed criteria were reasonable and delivery of AXI by CAR T-cell centres only to be appropriate. The input also highlighted that defining standard of care in the comparator arm is challenging partly due to international standards of care differing from those in Australian clinical practice. ESC noted that input from Australia and New Zealand Transplant and Cellular Therapies (ANZTCT) stated FL is an incurable and progressive condition with a high risk of mortality. ESC noted that ANZTCT highlighted that potential current treatments such as allogeneic stem cell transplantation often lead to patients having chronic infections which necessitates complex long-term specialist care. Therefore, new therapies for r/r FL are urgently needed and if publicly funded, CAR-T therapy such as AXI would address this area of high unmet need. ANZTCT further emphasised that AXI treatment should be delivered at specialist and qualified centres for treatment. ESC noted the regional healthcare provider organisation would support administration of CAR-T therapies to be limited to approved CAR-T infusion sites but would also support implementation that allowed administration at local healthcare centres to improve access for regional patients.

ESC noted submissions from New South Wales, Victoria, Queensland, South Australia and Western Australia as joint funders of HSTs via the NHRA. Jurisdictions considered that the full costs of delivering AXI had not been captured in the application. ESC noted that the jurisdictions were supportive of a pay-for-performance arrangement with 2 payments based on meaningful

clinical outcomes; one jurisdiction suggested that the use of a meaningful clinical endpoint where timing of the second payment could be made after 24 months rather than 12 months. ESC further noted that some jurisdictions supported the use of annual caps to share the burden of risk between government and the applicant which would support sustainability. Some jurisdictions also advised that funding of AXI for FL would increase the number of patients treated with CAR-Ts, which will require additional staff and resources to deliver. ESC noted that the jurisdictions emphasised the need to review all CAR-T therapies with respect to costs and benefits. ESC requested that the department seek further information from jurisdictions regarding the full costs of therapy.

ESC noted that the re-application requested public funding of AXI for r/r marginal zone lymphoma (MZL) in addition to r/r FL; however, jurisdictions did not support this, noting AXI is not approved by the Therapeutic Goods Administration (TGA) for use in r/r MZL[11]. Given that TGA approval is one of the eligibility criteria for funding of a HST under the NHRA, ESC agreed that this patient group was outside the scope of the NHRA HST provisions and advised against further consideration by MSAC. ESC noted that the indication supported by the Joint Chairs Group was for Grade 1, 2 and 3A FL, and did not include r/r MZL.

ESC noted that the clinical claim was superior effectiveness and inferior safety of AXI compared with standard of care (SOC) which is represented by a 'basket' of PBS-funded treatments. The re-application included updated 60-month follow-up data but retained the same comparative analysis based on 48-month data and the SCHOLAR-5 comparison study as in the original application. The applicant's pre-ESC response presented an updated assessment of comparative effectiveness of AXI with SOC incorporating 60 months follow-up data that had become available after the re-application was lodged in February 2025. ESC noted the summary statistics of SCHOLAR-5 presented for overall survival (OS) and progression free survival (PFS) were identical for 48 months and 60 months, and therefore requested that these be verified by the applicant. ESC further noted the data provided were not evaluated by the assessment group, and requested evaluation be undertaken before the re-application is considered by MSAC.

ESC noted the updated Kaplan–Meier (KM) analysis from ZUMA-5 in the applicant developed assessment report (ADAR) demonstrated a gradual decline in PFS over time, with a flattening of the curve observed in the later follow-up period. ESC noted that whilst this trend may suggest a sustained treatment effect in a proportion of patients, there remains considerable uncertainty regarding the median PFS. Additionally, ESC noted that censoring both before and after the 5-year mark introduces further complexity. ESC noted the inclusion or exclusion of these data points impacts the reliability of the PFS estimates, contributing to uncertainty regarding the durability of response.

Overall, ESC considered AXI likely has superior effectiveness compared with SOC, but this also has uncertain magnitude due to several factors, including differences in baseline characteristics of the study populations between the ZUMA-5 and the SCHOLAR-5 studies, high risk of bias in both studies, limitations of the propensity score method used, inconsistencies in the timing and type of PFS assessments across treatment arms, and differences in the censoring approaches applied in each study.

Regarding safety, ESC noted that whilst updated safety from 60 months follow-up from the ZUMA-5 study were presented in the re-application ADAR, no additional comparative safety data with SOC were presented. ESC noted for the additional safety data provided in the ADAR, the number of adverse events recorded was identical at 48 months and 60 months and therefore considered

[11] https://www.ebs.tga.gov.au/servlet/xmlmillr6?dbid=ebs/PublicHTML/pdfStore.nsf&docid=400895&agid=%28PrintDetailsPublic%29&actionid=1

that these numbers should be verified. Furthermore, ESC noted FL is a more indolent, slow-growing disease associated with a high incidence of serious adverse events (SAEs). As such, ESC considered the availability of long-term safety data is essential to adequately assess the risk profile. ESC noted the ADAR did not present any new information regarding longer term safety concerns, particularly the risk of secondary malignancies, which further contributes to the overall uncertainty. ESC concluded that AXI likely has inferior safety compared with SOC, but the magnitude of this difference is uncertain due to the nature of the comparison, population and methods of analysis.

ESC noted the applicant's changes to the proposed indication in the re-application. The applicant had removed references to Grade 1, Grade 2 or Grade 3A FL based on clinical advice and in an effort to future-proof the indication considering evolving World Health Organization (WHO) classifications of lymphoma. ESC noted there are two alternate lymphoma classifications in widespread use – the WHO and the International Consensus Classification (ICC). ESC advised that the WHO system is most widely used in Australia. ESC noted these lymphoma classifications evolve over time. Currently the ICC system recommends grading follicular lymphoma as Grade 1, Grade 2, Grade 3A or Grade 3B. Currently the WHO system considers grading optional and uses the term 'Classic Follicular Lymphoma' to cover the entities considered as Grade 1, Grade 2 or Grade 3A under the ICC system; and the term 'Follicular Large B-Cell Lymphoma' to cover the entity known as Grade 3B follicular lymphoma under the ICC system. ESC noted AXI would only be appropriate for Classic Follicular Lymphoma under the WHO system, or Grade1, Grade 2 or Grade 3A follicular lymphoma under the ICC system. The treatment would not be appropriate for 'Follicular Large B-cell Lymphoma' under the WHO system or Grade 3B follicular lymphoma under the ICC system. Therefore, ESC considered it appropriate to use the term 'classic follicular lymphoma' in the indication to align with the WHO terminology provided it is clearly stated that follicular large B cell lymphoma under the WHO system (which is considered Grade 3B FL under the ICC system) is excluded from the indication, as it is a distinct clinical entity. ESC recalled that MSAC had previously noted that it is broadly accepted that grade 3B FL is managed as diffuse large B-cell lymphoma (MSAC 1676). It was noted that the indication supported by the Joint Chairs Group was for Grade 1, 2 and 3A FL, and did not include Grade 3B FL.

ESC noted that the indication in the re-application was changed from 'symptomatic disease and/or high tumour burden' to 'have disease requiring treatment'; however, this did not match the clinical management algorithm. ESC also noted that the applicant had not addressed MSAC's proposed wording regarding the use of alkylating agents. MSAC had recommended that patients should have received prior treatment with an anti-CD20 + alkylating agent unless the alkylating agent is contraindicated (rather than the anti-CD20 agent being contraindicated).

ESC noted that the applicant did not wish to adopt MSAC's proposed wording in the treatment criteria regarding exclusion of patients with central nervous system (CNS) lymphoma. ESC noted that MSAC's proposed wording reflected the inclusion criteria of the ZUMA-5 study. ESC advised that it agreed with MSAC's earlier advice and that it would be appropriate to exclude patients with CNS lymphoma. ESC noted that the applicant had revised the clinical criteria regarding renal, cardiac and respiratory parameters in line with MSAC's advice.

The economic evaluation included changes to cost inputs that reduced the base case incremental cost effectiveness ratio (ICER) from $redacted per quality-adjusted life year (QALY) gained in the original application to $redacted per QALY gained in the re-application. However, ESC noted that key issues with the economic evaluation identified previously by MSAC are unaddressed in the re-application, in particular, the assumption that 40% of patients remain progression-free and achieve a functional cure beyond 5 years remains in the base case of the economic evaluation. In the sensitivity analyses, removal of the cure assumption increases the ICER by 30% (from $redacted per QALY gained to $redacted per QALY gained). ESC considered applying a cure assumption was not well justified for the proposed population because FL is more slowly progressing than other lymphomas previously considered by MSAC. ESC emphasised

that MSAC's previous support for other CAR-T therapies does not mean MSAC has accepted claimed cure assumptions.

ESC noted that the assessment group had identified an inconsistency in the base-case results in the re-application –QALYs gained from SOC were specified as 4.03 in the re-application, but this should have been 4.07 in line with the original submission. ESC also considered that the QALY increment for AXI between the original submission and the re-application appeared unexpectedly large, considering that only 12 months of additional data were now included. ESC advised that the reduction in the base-case ICER ($redacted per QALY gained in the re-application, compared with $redacted per QALY gained in the original submission) was largely attributable to this increased incremental QALY estimate and not the relatively small price reduction proposed for AXI.

ESC noted MSAC's concern that the parametric extrapolation of the SOC arm underestimated PFS and favoured AXI. Regarding the extrapolation used in the SOC arm, ESC noted disagreement between the assessment group and the applicant regarding the extrapolation that was used in the model. The assessment group identified in the commentary that the re-application stated that exponential extrapolation was used, while the actual method applied was Gompertz. ESC noted the pre-ESC response restated an exponential extrapolation was used. The assessment group subsequently provided a rebuttal identifying labelling errors within the model worksheet and confirming Gompertz extrapolation was used, which resulted in the SOC appearing to perform worse than it actually did for PFS. ESC noted the ICER was highly sensitive to the choice of extrapolation function used for both OS and PFS, and ESC considered that the extrapolation function that would best fit the observed data was highly uncertain. ESC also maintained that the model time horizon of 30 years was not well justified, even with the 5 years of observed data now available from ZUMA-5. ESC noted that reducing the time horizon to 20 years in sensitivity analyses increased the ICER by 23%.

Overall, ESC agreed with the commentary that lack of reliable evidence underpinning the economic model combined with high risk of bias in the clinical estimates, flows into the economic model resulting in an overall economic evaluation that is highly uncertain.

ESC noted the applicant's revised net effective price for AXI of $redacted per successfully infused patient in the re-application, compared with $redacted in the original submission – a reduction of 9%. ESC considered that the revised price remained high and unjustified. ESC noted the applicant's proposed payment structure, with preference for a single payment on successful infusion, or an alternative PfP structure with redacted% of the total on successful infusion and redacted% of the total on demonstration of complete response by fluorodeoxyglucose (FDG) positron emission tomography with computed tomography (PET-CT) at 12 months. ESC noted a single payment on successful infusion was not supported by the jurisdictions. ESC advised that a 2-stage payment was preferred and that this should be based on clinical outcomes. ESC considered that, given the more indolent nature of FL, the timepoint for a second payment should be longer than 12 months after successful infusion. This timepoint should be based on the available data with the aim of mitigating the risks associated with uncertainty in outcomes and treatment success. ESC noted the submission proposed a 3-year risk share agreement with annual national patient caps consistent with current AXI funding for Large B-Cell Lymphoma (LBCL) and Diffuse Large B-Cell Lymphoma (DLBCL). ESC considered the uncertainty in estimated utilisation in FL remains, with one jurisdiction (Queensland) stating based on unpublished data from the Queensland Cancer Alliance patient numbers in Queensland alone could be close to redacted patients per year, in contrast to the estimate of ~redacted patients per annum in Australia presented in the re-application. ESC noted currently funded use of AXI shares patient caps with other CAR-T therapies. ESC noted the financial impacts in the re-application and considered that these remained high and highly uncertain.

Furthermore, ESC noted CAR-T cell therapy prices are likely to drop substantially within the next 5 years due to streamlining and automating processes in manufacturing[12]. ESC noted researchers in Australia are locally manufacturing CAR-T therapies in clinical trials, with over 150 trials underway in Australia and more than 3,500 globally, now exploring combinations with gene therapy.

17. Applicant comments on MSAC's Public Summary Document

Gilead Sciences welcomes MSAC's decision to support public funding of YESCARTA® (axicabtagene ciloleucel) for the treatment of patients with relapsed or refractory follicular lymphoma. Gilead Sciences would like to sincerely thank those who contributed through the consumer input process, and the broader clinical and patient communities for their continued support. Gilead Sciences is committed to working constructively with the Commonwealth and State and Territory governments to identify a path forward that enables timely access to this important treatment.

18. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: visit the MSAC website

[12] https://www.sciencedirect.com/science/article/abs/pii/S0167779923001270