

- Title** Axicabtagene ciloleucel for adults with relapsed and refractory large B-cell lymphoma
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- Reference** Axicabtagene ciloleucel for adults with relapsed or refractory large B-cell lymphoma. CADTH Optimal Use Project Number: CT0002-000. Ottawa (ON): CADTH. Available from:  
<https://www.cadth.ca/axicabtagene-ciloleucel-adults-relapsed-or-refractory-large-b-cell-lymphoma>.  
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## Aim

The objective of this Health Technology Assessment (HTA) is to inform decisions on how to optimally structure the provision of axicabtagene ciloleucel for adults with eligible types of relapsed or refractory large B-cell lymphoma. The focus is to evaluate the clinical effectiveness and safety, cost-effectiveness, budget impact of axicabtagene ciloleucel implementation on public funding, ethical issues relating to the provision of axicabtagene ciloleucel, as well as patients' and caregivers' perspectives and preferences.

## Conclusions and results

The HTA found that most patients who were treated with axicabtagene ciloleucel in the pivotal trial achieved either a complete or partial response within six months or 24 months after infusion. The overall survival at 24 months was 50.5% of treated patients. Axicabtagene ciloleucel has the potential to exert severe adverse events, and in the pivotal trial all patients experienced at least one adverse event, and more than half of the patients experienced a serious adverse event. However, long-term and direct comparative data were not available, and it is uncertain how well the therapy performs in the real world. At a willingness-to-pay threshold of \$50,000 or \$100,000 per quality-adjusted life-year (QALY) the probability that axicabtagene ciloleucel was the most likely cost-effective intervention was 0%. Price reductions of 60% and 83% would be required to achieve an incremental cost-utility ratio of \$100,000 and \$50,000 per QALY, respectively. The results of the implementation analysis indicated that there is a need to adequately manage potential toxicities and adverse events and collect data to address uncertainties in long-term safety and effectiveness. More consideration is needed about the manufacturers' role in the oversight of treatment facilities, the challenges in supporting patients and their caregivers who need to travel for treatment, and the development of eligibility criteria for real-world patient selection that anticipates potential clinician and patient challenges that may arise when applied. The ethics review highlighted the importance of informed choice and consent in treatment decision-making, given the uncertainty about safety and efficacy. It also called for the recognition of the barriers to accessing treatment, the high cost of treatment from both the patient and societal perspectives, the need for clear and transparent eligibility criteria, and questions about who owns genetically modified T cells.

## Recommendations

Based on the evidence from the review, the Health Technology Expert Review Panel (HTERP) recommended the provision of axicabtagene ciloleucel in Canada for adult patients with r/r large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma, on the condition that there is a substantial reduction in price.

Regarding implementation of this therapy, HTERP recommends:

- the creation of interprovincial agreements to ensure equitable access to eligible patients in all jurisdictions, including consideration of financial and logistical support for required travel and short-term relocation
- the development of clear and transparent eligibility criteria that are acceptable to patients' and clinicians' needs, based on the approved indications
- the collection of standardized outcomes data in a pan-Canadian registry of patients, which uses a defined set of outcomes and definitions to generate additional real-world evidence, for consideration in future reassessments of longer-term effectiveness, safety, and cost-effectiveness.

## Methods

The HTA was based on a systematic review of relevant literature identified through comprehensive searches of multiple databases and grey literature. The searches were performed by an information specialist using a peer-reviewed search strategy. The methodology for the review was guided by the criteria outlined in the checklist described in AMSTAR II and other relevant reporting guidelines such as the PRISMA statement and the PRISMA harms, and the report followed the CADTH standards for Optimal Use reviews. The clinical review also involved an assessment of the manufacturer-submitted pivotal trial. Economic assessments involved a reanalysis of the manufacturer-submitted economic evaluation and budget impact analysis. The implementation analysis considered input from patient groups and clinicians, published literature relating to the implementation of axicabtagene ciloleucel, and a synthesis of qualitative literature on patients' and caregivers' perspectives. The ethics analysis consisted of a review of published literature and an analysis on ethical issues relating to the provision of axicabtagene ciloleucel.

**Further research/reviews required**

The primary gaps in the evidence were the absence of data that directly compared axicabtagene ciloleucel with other treatments used in relapsed or refractory large B-cell lymphoma, as well as long-term data on the clinical effectiveness and safety. Additional real-world evidence is needed to demonstrate the effectiveness of axicabtagene ciloleucel outside of a controlled clinical trial. More long-term follow-up and comparator data will be required to fully understand the benefit-risk profile of axicabtagene ciloleucel and its place in therapy for adults with relapsed or refractory large B-cell lymphoma.

**Written by**

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