Zorginstituut Nederland

> Return address PO Box 320, 1110 AH Diemen

Minister of Medical Care and Sports
PO Box 20350
2500 EJ THE HAGUE

National Health Care Institute
Care I
Oncology

Willem Dudokhof 1
1112 ZA Diemen
PO Box 320
1110 AH Diemen
www.zorginstituutnederland.nl
info@zinl.nl

T +31 (0)20 797 85 55

Contact
Ms J.E. de Boer
T +31 (0)6 215833 54

2021007175

Our reference
2021007175

Date 26 July 2021
Subject Advice on the reassessment of axicabtagene ciloleucel (Yescarta®)

Dear Ms van Ark,

On 1 May 2020, after successful price negotiations with the supplier, you authorised axicabtagene ciloleucel (Yescarta®) in the basic health insurance package for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and primary mediastinal B-cell lymphoma (PMBCL) after two or more lines of systemic therapy. The financial arrangement runs until 1 December 2021. You have agreed with the supplier that the National Health Care Institute will be given the opportunity to carry out a reassessment of the medicine.

The National Health Care Institute has now carried out the said reassessment and we are informing you of the outcome by means of this letter.

Background
In the package advice of 7 March 2019, the National Health Care Institute concluded that axicabtagene ciloleucel (hereinafter "axi-cel") meets the statutory criterion of 'established medical science and medical practice' for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and primary mediastinal B-cell lymphoma (PMBCL), after two or more lines of systemic therapy. The median overall survival in the ZUMA-1 trial was 17.4 months, based on an intention-to-treat analysis (95% confidence interval 11.6 months to (not reached)), and the overall survival gain over salvage chemotherapy (+SCT) was estimated at 11.1 months.

As estimates of the number of patients vary, the National Health Care Institute had calculated two scenarios for the budget impact, the 'low-impact' and 'high-impact' scenarios. In the third year after admission, the additional cost of treatment is estimated at €29.3 million in the low-impact scenario and €43.9 million in the high-impact scenario. It was also noted that the budget impact may increase significantly in the future because of the registered indications expanding.

National Health Care Institute
Care I
Oncology

Date
26 July 2021

Our reference
2021007175

The National Health Care Institute deemed the manufacturer's pharmacoeconomic model to be insufficient in terms of methodological quality and therefore had no confidence in the incremental cost-effectiveness ratio (ICER) presented of €61,967/QALY. Given that sufficient data on long-term survival was not available, no reliable cost-effectiveness estimate could be made. However, the Institute deemed it more than likely that the actual ICER of axi-cel will exceed the relevant reference value that applies to this serious disease, namely €80,000/QALY. For that reason, we advised you against including axicabtagene ciloleucel in the health care package at that time unless a price reduction could be agreed.

The outcomes of the reassessment

Data has now been published on overall survival in the ZUMA-1 trial after a median follow-up duration of 39 months, reporting a median overall survival of 25.8 months based on a modified intention-to-treat (mITT) analysis. For a median follow-up duration of 51 months, the median survival based on the mITT analysis was also 25.8 months. Data for the intention-to-treat analysis was not reported. At the initial assessment, after a median follow-up duration of 15.1 months, the median overall survival had not been reached (mITT OS: not reached; 95% confidence interval 12.8 months to (not reached)). After 12 months, 60.4% of the patients were still alive (95% confidence interval 50.2% to 69.2%). In the newly published data, about 60% of the patients were still alive after 12 months. The 24-month survival rate was estimated at the time to be around 50% and the survival curve still shows this. The difference in overall survival gain therefore remains clinically relevant and axi-cel still meets the statutory criterion of 'established medical science and medical practice' for the indications mentioned.

Including axi-cel (Yescarta®) for the above-mentioned indication will involve additional costs of €44.9 million in the third year. This assumes there will be 129 patients using axi-cel in year 3. There is uncertainty about various aspects, such as patient numbers, the distribution of patients over different treatment lines and market penetration (because of the potential for competition in the years to come, etc.). There is a considerable likelihood of the actual budget impact of this therapy exceeding €44.9 million in the future given the anticipated expansion of the indications. The 2019 assessment estimated the budget impact, depending on the scenario, at €29.3 to €44 million. This assumed that 90-135 patients would be eligible for treatment.

The National Health Care Institute deems the new pharmacoeconomic analysis to be sufficient in terms of methodological quality. It shows a gain of 5.29 QALYs for axi-cel versus standard therapy and the incremental costs work out as €440,120. The new ICER reported by the marketing authorisation holder is €83,184/QALY. The probabilistic sensitivity analysis shows that the probability of axi-cel being cost-effective at a reference value of €80,000/QALY is about 51%. As there is now less uncertainty about the effects on overall survival, the National Health Care Institute believes that an ICER range no longer needs to be used and that point estimation can be used instead.

Conclusion
Axi-cel meets established medical science and medical practice after a median follow-up period of 51 months. The budget impact after 3 years is estimated at approximately €44.9 million in the third year. There is a considerable likelihood of the actual budget impact of this therapy exceeding €44.9 million in the future given the anticipated expansion of the indications. Assuming an ICER of €83,184/QALY, the price of axi-cel would have to be reduced by at least 5% for it to go below the reference value of €80,000/QALY.

Yours sincerely,

Sjaak Wijma
Chair of the Executive Board

National Health Care Institute
Care I
Oncology

Date
26 July 2021

Our reference
2021007175