

Axicabtagene ciloleucel (reassessment of an orphan drug after exceeding the EUR 30 million turnover limit: diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma, after at least 2 prior therapies)

Resolution of: 21 December 2023/6 June 2024 valid until: unlimited
Entry into force on: 21 December 2023/6 June 2024
Federal Gazette, BAnz AT 01 02 2024 B6/ BAnz AT 05 07 2024 B3

Therapeutic indication (according to the marketing authorisation of 23 August 2018):

Yescarta is indicated for the treatment of adult patients with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and primary mediastinal large B-cell lymphoma (PMBCL), after two or more lines of systemic therapy.

Therapeutic indication of the resolution (resolution of 21 December 2023):

See therapeutic indication according to marketing authorisation.

1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

Adults with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and primary mediastinal large B-cell lymphoma (PMBCL), after two or more lines of systemic therapy, who are eligible for CAR-T cell therapy or stem cell transplantation

Appropriate comparator therapy:

- Tisagenlecleucel (only for subjects with DLBCL)
- or
- Lisocabtagene maraleucel

Extent and probability of the additional benefit of axicabtagene ciloleucel compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:¹

Adults with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and primary mediastinal large B-cell lymphoma (PMBCL), after two or more lines of systemic therapy, who are eligible for CAR-T cell therapy or stem cell transplantation

No adequate data are available to allow an assessment of the additional benefit.

¹Data from the dossier evaluation of the Institute for Quality and Efficiency in Health Care (IQWiG) (A23-65) unless otherwise indicated.

Summary of results for relevant clinical endpoints

| Endpoint category | Direction of effect/ risk of bias | Summary |
|--|-----------------------------------|-------------------------------|
| Mortality | n.a. | There are no assessable data. |
| Morbidity | n.a. | There are no assessable data. |
| Health-related quality of life | n.a. | There are no assessable data. |
| Side effects | n.a. | There are no assessable data. |
| Explanations: ↑: statistically significant and relevant positive effect with low/unclear reliability of data ↓: statistically significant and relevant negative effect with low/unclear reliability of data ↑↑: statistically significant and relevant positive effect with high reliability of data ↓↓: statistically significant and relevant negative effect with high reliability of data ↔: no statistically significant or relevant difference ∅: No data available. n.a.: not assessable | | |

2. Number of patients or demarcation of patient groups eligible for treatment

Adults with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and primary mediastinal large B-cell lymphoma (PMBCL), after two or more lines of systemic therapy, who are eligible for CAR-T cell therapy or stem cell transplantation

Approx. 680 to 1,200 patients

3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Yescarta (active ingredient: axicabtagene ciloleucel) at the following publicly accessible link (last access: 4 October 2023):

https://www.ema.europa.eu/en/documents/product-information/yescarta-epar-product-information_en.pdf

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material and a patient emergency card. Training material for all healthcare professionals who will prescribe, dispense, and administer axicabtagene ciloleucel includes instructions for identifying, treating, and monitoring cytokine release syndrome and neurological side effects. It also includes instructions on the cell thawing process, availability of 1 dose of tocilizumab at the point of treatment, provision of relevant information to patients, and full and appropriate reporting of side effects.

The patient training programme should explain the risks of cytokine release syndrome and serious neurologic side effects, the need to report symptoms immediately to the treating

physician, to remain close to the treatment facility for at least 4 weeks after infusion of axicabtagene ciloleucel and to carry the patient emergency card at all times.

Axicabtagene ciloleucel must be used in a qualified treatment facility. For the infusion of axicabtagene ciloleucel in the present therapeutic indication, the quality assurance measures for the use of CAR-T cells in B-cell neoplasms apply (ATMP Quality Assurance Guideline, Annex 1).

4. Treatment costs

Annual treatment costs:

The costs for the first year of treatment are shown for the cost representation in the resolution.

Adults with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and primary mediastinal large B-cell lymphoma (PMBCL), after two or more lines of systemic therapy, who are eligible for CAR-T cell therapy or stem cell transplantation

| Designation of the therapy | Annual treatment costs/ patient |
|--|---------------------------------|
| Medicinal product to be assessed: | |
| Axicabtagene ciloleucel | € 272,000.00 |
| <i>Additionally required SHI costs</i> | <i>€ 741.89</i> |
| Appropriate comparator therapy: | |
| <i>CAR-T cell therapies</i> | |
| Tisagenlecleucel | € 239,000.00 |
| <i>Additionally required SHI costs</i> | <i>€ 390.26</i> |
| Lisocabtagene maraleucel | € 345,000.00 |
| <i>Additionally required SHI costs</i> | <i>€ 724.61</i> |

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 December 2023.

Other SHI services:

| Designation of the therapy | Type of service | Costs/ unit | Number/ cycle | Number/ patient/ year | Costs/ patient/ year |
|---|--|-------------|---------------|-----------------------|----------------------|
| Medicinal product to be assessed | | | | | |
| <i>Axicabtagene ciloleucel: Lymphocyte depletion</i> | | | | | |
| Cyclophosphamide | Surcharge for production of a parenteral solution containing cytostatic agents | € 100 | 3 | 3.0 | € 300 |
| Fludarabine | Surcharge for production of a parenteral solution containing cytostatic agents | € 100 | 3 | 3.0 | € 300 |
| Appropriate comparator therapy | | | | | |
| <i>Tisagenlecleucel: Lymphocyte depletion</i> | | | | | |
| Cyclophosphamide | Surcharge for production of a parenteral solution containing cytostatic agents | € 100 | 3 | 3.0 | € 300 |
| Fludarabine | Surcharge for production of a parenteral solution containing cytostatic agents | € 100 | 3 | 3.0 | € 300 |
| <i>Lisocabtagene maraleucel: Lymphocyte depletion</i> | | | | | |
| Cyclophosphamide | Surcharge for production of a parenteral solution containing cytostatic agents | € 100 | 3 | 3.0 | € 300 |
| Fludarabine | Surcharge for production of a parenteral solution | € 100 | 3 | 3.0 | € 300 |

| | | | | | |
|--|---------------------------------|--|--|--|--|
| | containing cytostatic agents | | | | |
|--|---------------------------------|--|--|--|--|

5. Medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

Adults with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and primary mediastinal large B-cell lymphoma (PMBCL), after two or more lines of systemic therapy, who are eligible for CAR-T cell therapy or stem cell transplantation

- No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.