Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a (SGB V)
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)

of 21 December 2023

At its session on 21 December 2023, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. Annex XII is amended as follows:

1. **The information on Axicabtagene ciloleucel in the version of the resolution of 3 November 2022 (Federal Gazette AT 23.12.2022 B9) is repealed.**
2. **Annex XII shall be amended in alphabetical order to include the active ingredient Axicabtagene ciloleucel as follows:**

Axicabtagene ciloleucel

Resolution of: 21 December 2023
Entry into force on: 21 December 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

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.

[1] Data 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
Additionally required SHI costs	*€ 741.89*
Appropriate comparator therapy:	
CAR-T cell therapies	
Tisagenlecleucel	€ 239,000.00
Additionally required SHI costs	*€ 390.26*
Lisocabtagene maraleucel	€ 345,000.00
Additionally required SHI costs	*€ 724.61*

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					
Axicabtagene ciloleucel: Lymphocyte depletion					
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					
Tisagenlecleucel: Lymphocyte depletion					
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
Lisocabtagene maraleucel: Lymphocyte depletion					
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.

II. Entry into force

1. **The resolution will enter into force on the day of its publication on the website of the G-BA on 21 December 2023.**

2. **The period of validity of the resolution is limited to 1 July 2024.**

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 21 December 2023

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken