HTA Austria
Austrian Institute for Health Technology Assessment GmbH

Lisocabtagene maraleucel (Breyanzi®)

for the treatment of adult patients with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy

General information

INN	®		ATC Code	Substance class	Type of indication[1]
Lisocabtagene maraleucel (Liso-Cel) [1]	Breyanzi® [1]	Bristol-Myers Squibb Pharma EEIG [1]	L01XL08 [1]	Antineoplastic agents [1]	Extension of indication [2]

Mechanism of action	Dosing & administration	Setting in Austria
Lisocabtagene maraleucel is an autologous, CD19-directed chimeric antigen receptor (CAR) T-cell therapy. It consists of patient-derived CD4+ and CD8+ T cells that are separately transduced with a replication-incompetent, self-inactivating lentiviral vector encoding a CAR containing a murine FMC63-derived single-chain variable fragment specific for CD19, coupled with 4-1BB (CD137) costimulatory and CD3ζ activation domains [2].	Lisocabtagene maraleucel is administered as a single intravenous (IV) infusion containing 100 × 10^6 CAR-positive viable T cells, consisting of equal numbers of CD8+ and CD4+ CAR+ T cells supplied separately in one to four vials. Before infusion, patients receive lymphodepleting chemotherapy with fludarabine (30 mg/m²/day) and cyclophosphamide (300 mg/m²/day) for three consecutive days. Premedication with acetaminophen (500–650 mg orally) and diphenhydramine (25–50 mg orally or intravenously) is given 30–60 minutes prior to infusion. The CAR T-cell infusion is performed 2–7 days after completion of lymphodepletion, with continuous monitoring of vital signs during and after infusion [2].	☒ Hospital ☐ Interface between hospital and outpatient sector ☐ Outpatient sector

Indication [2]	
Lisocabtagene maraleucel is indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy. Additionally, it is already approved in the European Union (EU) and the USA for the treatment of other malignancies in adult patients listed below.	
EMA approval status [1]	**FDA approval status [3, 4]**
☒ **Approved for this indication:** ✓ MAA submission: August 2024 ✓ CHMP opinion: January 2025 ✓ EC decision: March 2025 ☒ **Approved for other indications:** ✓ EC decision: January 2022 ○ Diffuse large B-cell lymphoma (DLBCL) ○ High-grade B-cell lymphoma (HGBCL) ○ Primary Mediastinal Large B Cell Lymphoma (PMBCL) ○ FL grade 3B (FL3B), who relapsed within 12 months from completion of, or are refractory to, first-line chemoimmunotherapy	☒ **Approved for this indication:** ✓ BLA: November 2023 ✓ Priority review: January 2024 ✓ Accelerated approval: May 2024 ☒ **Approved for other indications:** ✓ FDA approval: February 2021 ○ DLBCL ○ HGBCL ○ PMBCL ○ FL3B patients who relapsed within 12 months from completion of, or are refractory to, first-line chemoimmunotherapy ○ Refractory disease to first-line chemoimmunotherapy or relapse after first-

[1] New indication/extension to an existing indication/first-in-class.

○ Relapsed or refractory DLBCL, PMBCL and FL3B, after two or more lines of systemic therapy	line chemoimmunotherapy and are not eligible for hematopoietic stem cell transplantation due to comorbidities or age

Disease

Description	Prevalence & incidence	Mortality
FL is a heterogeneous B-cell malignancy and a form of non-Hodgkin lymphoma (NHL), originating from germinal centre B cells. It typically shows a nodular (follicular) growth pattern composed of centrocytes and centroblasts, resembling normal lymphoid follicles. In advanced stages, the nodular pattern may become less prominent. Classic FL (Grades 1–3A) is characterised by a predominance of centrocytes, whereas Grade 3B FL shows mainly centroblasts and behaves more aggressively (also referred to as follicular large B-cell lymphoma). Some cases may exhibit plasmacytoid or marginal zone differentiation. Most FL cases express B-cell surface antigens such as CD19, CD20, CD79a, CD21, and HLA-DR, and are frequently positive for CD10 (about 60%); CD23 expression is variable [2].	FL is one of the most common forms of NHL, accounting for approximately 35% of all NHL cases. The incidence of FL in the EU is approximately 2.2 cases per 100.000 persons per year [2]. The median age at diagnosis is 60—65 years, with a wide age range among patients [5]. Austria (2022) [5, 6]: ✓ The estimated prevalence of FL was 5,170 people, 53% of whom were male ✓ Approximately 200 new FL cases were diagnosed	Specific data on FL mortality are not available for Austria. In 2022, 630 people died from NHL (including FL), corresponding with a mortality rate of 6.7 per 100,000 persons. Over the past decades, mortality rates declined from 7.8 to 6.7 per 100,000 persons, while incidence remained stable [6].

Current treatment

The current treatment algorithms for relapsed or refractory FL are based on the European Society for Medical Oncology (ESMO) Living Guideline for FL [7], which is continuously updated to reflect emerging evidence. Current specific recommendations for the treatment of relapsed FL are provided in the Appendix below [5, 7]

Evidence [2, 8]

Trial name & NCT number	Trial characteristics	Population size (n)	Intervention (I)	Control (C)
TRANSCEND FL (FOL-001) NCT04245839 EudraCT Number: 2019-004081-18	Global, **ongoing**[2], phase 2, open-label, single-arm, multicohort, multicentre study	139	All participants received a single IV infusion of JCAR017 at a target dose of 100 × 10^6 CAR-positive viable T cells (CAR+ T cells), 2 to 7 days after completion of lymphodepleting chemotherapy. Each JCAR017 dose includes CD4+ CAR+ T cells and CD8+ CAR+ T cells.	No concurrent control group was included
Primary endpoint		**Follow-up, median**	**Treatment duration/ cycles**	
Overall response rate (ORR)		23.1 months	Each patient received one course of lymphodepletion (fludarabine + cyclophosphamide for 3 days) followed by a single CAR T-cell infusion. No repeated cycles were given.	
Main efficacy outcomes			**Main safety outcomes**	
3-year OS 88.2% (95% CI 80.1, 93.1) ORR by independent review committee (IRC): 97.1% (95% CI 91.7, 99.4) ORR per investigator assessment, 98.1% (95% CI 93.2, 99.8) Median PFS 36.1 months (95% CI 31.8, N.A.)			AEs of grade ≥3: prolonged cytopenia (22%), second primary malignancy (6.9%), infections (5.4%) Serious TEAEs: 23.8% Discontinuation due to AEs: 0.9% Deaths due to AEs: 2.9%	

[2] The trial is currently ongoing; the estimated study completion date is 09/2031.

Patient-reported outcomes (PROs)
PROs will be assessed in the ongoing clinical trial as secondary outcome measures by using the European Organisation for Research and Treatment of Cancer - Quality of Life C30 questionnaire (EORTC QLQ-C30) and the Functional Assessment of Cancer Therapy Lymphoma Subscale (FACT-LymS).
Limitations
✓ The evidence supporting the efficacy of this product comes from one ongoing, single, uncontrolled, open-label study. ✓ At the data cut-off in January 2024, analyses of long-term endpoints (e.g. OS, PFS) were not yet fully mature. ✓ External comparators (e.g. SCHOLAR-5 cohort) were used to contextualise efficacy but have inherent limitations due to non-randomised design and potential selection bias.

ESMO-MCBS version 1.1 (NCT04245839) [9]

Scale	Int.	Form	MG ST	MG	HR (95% CI)	Score calculation	PM	Toxicity	QoL	AJ	FM
Original	NC	3	-	ORR: 97%	-	ORR (PR+CR) ≥ 60%	3	-	QoL data pending	No adjustments	3

Risk of bias – study level (case series) (NCT04245839) [10]

Was the hypothesis/ aim/ objective of the study clearly stated?	Were the cases collected in more than one centre?	Were patients recruited consecutively?	Were the eligibility criteria (inclusion and exclusion criteria) for entry into the study clearly stated?	Did participants enter the study at a similar point in the disease?	Was the intervention clearly described?	Were additional interventions (co-interventions) clearly described?	Were relevant outcome measures established a priori?	Were outcome assessors blinded to the intervention that patients received?
yes	yes	yes	yes	no[3]	yes	partial[4]	yes	partial[5]
Were the relevant outcomes measured using appropriate objective/ subjective methods?	**Were the relevant outcomes measured before and after the intervention?**	**Were the statistical tests used to assess the relevant outcomes appropriate?**	**Was the length of follow-up reported?**	**Was the loss to follow-up reported?**	**Did the study provide estimates of random variability in the data analysis of relevant outcomes?**	**Were adverse events reported?**	**Were the conclusions of the study supported by results?**	**Were both competing interest and source of support for the study reported?**
yes	yes	yes	yes	partial[6]	yes	yes	partial	yes
Overall risk of bias: moderate								

Ongoing trials [11]

NCT number	Description	Estimated completion date
NCT05621096	Feasibility of Low Dose Radiation as Bridging Therapy for Lisocabtagene Maraleucel in Relapsed B-Cell Non-Hodgkin Lymphoma	09/2027 (active, not recruiting)
NCT04245839	Ongoing (see above under *Evidence)*	09/2031 (active, not recruiting)
NCT06313996	A Global Randomized Multicenter Phase 3 Trial to Compare the Efficacy and Safety of Lisocabtagene Maraleucel (JCAR017/BMS-986387) to Standard of Care in Adults With Relapsed or Refractory Follicular Lymphoma (TRANSFORM FL)	10/2031 (active, recruiting)

[3] The enrolled population showed substantial heterogeneity in disease stage (Ann Arbor staging).
[4] Additional interventions, such as bridging therapy, were not clearly described.
[5] Tumour response was evaluated by an IRC using predefined criteria.
[6] Censoring and disposition are reported; explicit loss to follow-up description is limited.

NCT06794268	Non-interventional Cohort Study of Patients Treated With Liso-cel (Lisocabtagene Maraleucel) for Relapsed/Refractory Follicular Lymphoma in the Postmarketing Setting	08/2044 (not yet recruiting)

Health Technology Assessments	
Institution	Report/ status
National Institute for Health and Care Excellence (NICE)	Lisocabtagene maraleucel for treating relapsed or refractory low-grade B-cell follicular lymphoma after 1 or more treatments [ID6564] (in development) [12].
Canada's Drug Agency – L´Agence des medicaments du Canada (CDA-AMC)	Lisocabtagene maraleucel – Reimbursement review (completed 2024); Recommended for reimbursement with conditions [13].
Institute for Quality and Efficiency in Health Care (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, IQWiG)	Lisocabtagene maraleucel (follicular lymphoma) – Benefit assessment according to §35a Social Code Book V (completed 2025); No proven benefit [14].
Institute for Quality and Efficiency in Health Care (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, IQWiG)	Lisocabtagene maraleucel (DLBCL, HGBCL, PMBCL and FL3B, each after one prior therapy) – Benefit assessment according to §35a Social Code Book V (completed 2023); Benefit proven only for certain patient group [15].

Costs

Costs per patient per		Costs for expected patient population per		Additional costs categories [16]
Cycle	Year	Cycle	Year	Diagnostics
Single IV infusion of lisocabtagene maraleucel: €227,500[7] [14]	€227,500	n/a No specific epidemiological data for relapsed or refractory FL cases are publicly available in Austria.		Histopathological diagnosis, laboratory tests, and imaging
				Monitoring
				Cytokine release syndrome, neurologic toxicities, T cell malignancies, hypogammaglobulinemia, serious infections, hypersensitivity reactions
				Additional medication
				Lymphodepleting chemotherapy, premedication

Other aspects and conclusions

- Lisocabtagene maraleucel represents an advanced, one-time, CD19-directed CAR T-cell therapy offering a potentially curative option for adult patients with relapsed or refractory FL after two or more prior systemic treatments.
- The pivotal TRANSCEND-FL (FOL-001) study demonstrated very high and durable response rates, with a 3-year OS of 88 % and manageable toxicity. However, the evidence is based on an ongoing, single, open-label, non-comparative Phase 2 trial, and long-term data on survival, relapse patterns, and real-world effectiveness remain limited.
- The administration of lisocabtagene maraleucel requires specialised CAR-T centres with certified infrastructure and rapid access to emergency management, which may pose organisational challenges.
- The FDA prescribing information includes a boxed warning for cytokine release syndrome and neurologic toxicities, indicating the potential for life-threatening or fatal adverse reactions [16].
- Several alternative treatments are already available for relapsed or refractory FL, including authorised CAR-T therapies, while bispecific antibodies such as mosunetuzumab (authorised) and investigational agents including epcoritamab and odronextamab continue to be evaluated in clinical studies [17, 18].

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[7] Price information: Based on the publicly available list price in Germany. No price information for Austria is available yet.

Abbreviations:

Abbreviations: AE…Adverse events, C.comparator, CAR.chimeric antigen receptor, CHMP.Committee for Medicinal Products for Human Use, CI.confidence interval, DLBCL….Diffuse large B-cell lymphoma, EMA…European Medicines Agency, EORTC QLQ-C30…European Organisation for Research and Treatment of Cancer - Quality of Life C30 questionnaire, ESMO-MCBS…European Society of Medical Oncology – Magnitude of Clinical Benefit Scale, EU…European Union, FACT-LymS…Functionality Assessment of Cancer Therapy Lymphoma Subscale, FDA…U.S. Food and Drug Administration, FL3B….Follicular lymphoma grade 3B, FM…final magnitude, HGBCL….High grade B cell lymphoma, I…intervention, ICC…investigator's choice of chemotherapy, INN…international non-proprietary name, IRC…independent review committee, IV….intravenous(ly), MAH…marketing authorisation holder, MG…median gain, n…number, n/a….not available, ORR…objective response rate, OS…overall survival, PFS….Progression-free survival, PM…preliminary magnitude, PMBCL….Primary Mediastinal Large B Cell Lymphoma, PRO….patient-reported outcome, RCT…randomised controlled trial, RoB…risk of bias, ST…standard treatment, TEAE….treatment emergent adverse effects

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Appendix: Treatment algorithm for relapsed or refractory follicular lymphoma (FL) based on the Onkopedia Guideline "Follikuläres Lymphom" (version 2025) [5].