Exagamglogene autotemcel (sickle cell disease with recurrent vaso-occlusive crises; ≥ 12 years; no HLA-matched related stem cell donor available)

Resolution of: 3 July 2025 /18 September 2025 Valid until: unlimited
Entry into force on: 3 July 2025/18 September 2025
Federal Gazette, BAnz AT 06 08 2025 B2/ 17 10 2025 B7

Therapeutic indication (according to the marketing authorisation of 9 February 2024):

Casgevy is indicated for the treatment of severe sickle cell disease (SCD) in patients 12 years of age and older with recurrent vaso-occlusive crises (VOCs) for whom haematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen (HLA)-matched related HSC donor is not available.

Therapeutic indication of the resolution (resolution of 3 July 2025):

See therapeutic indication according to marketing authorisation.

1. Extent of the additional benefit and significance of the evidence

Exagamglogene autotemcel is approved as a medicinal product for the treatment of rare diseases in accordance with Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional medical benefit is considered to be proven through the grant of the marketing authorisation.

The G-BA determines the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5 Section 12, paragraph 1, number 1, sentence 2 of its Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5 Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

Patients 12 years of age and older with severe sickle cell disease and recurrent vaso-occlusive crises for whom haematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen (HLA)-identical related stem cell donor is not available

Extent of the additional benefit and significance of the evidence of exagamglogene autotemcel:

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification

Study results according to endpoints:[1]

Patients 12 years of age and older with severe sickle cell disease and recurrent vaso-occlusive crises for whom haematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen (HLA)-identical related stem cell donor is not available

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		

CLIMB-SCD-121: single-arm, open-label, multicentre phase I/II/III study and

CTX001-131: extension study; 5th data cut-off: 2 January 2025, ITT population

Mortality

Endpoint	Exagamglogene autotemcel	
	N[a]	*Patients with event n (%)*
Deaths	58	1 (1.7)
Transplantation-related deaths	58	1 (1.7)

Morbidity

Endpoint	Exagamglogene autotemcel	
	N	*Patients with event n (%)*
Freedom from severe vaso-occlusive crises for 12 months (VF12)[b, c]	63	43 (68.3)
Annualised rate of severe VOC	-	n.d.
Pain NRS-11 – improvement by ≥ 15% at month 24[c]		

[1] Data from the dossier evaluation of the G-BA (published on 15. April 2025), and from the amendment to the dossier assessment from 13 June 2025, unless otherwise indicated.

Endpoint	Exagamglogene autotemcel	
	N	*Patients with event n (%)*
(≥ 18 to ≤ 35 years)	50	13 (26.0)
(≥ 12 to < 18 years) [d]	13	1 (7.7)
EQ-5D-VAS – improvement by ≥ 15% at month 24[c]		
(≥ 18 to ≤ 35 years)	50	13 (26.0)
(≥ 12 to < 18 years) [d]	13	4 (30.8)
ASCQ-Me SCD-MHC – improvement by ≥ 15% at month 24 [c]		
(≥ 18 to ≤ 35 years)	50	7 (14.0)

Health-related quality of life

Endpoint	Exagamglogene autotemcel	
	N	*Patients with event n (%)*
ASCQ-Me – improvement by ≥ 15% at month 24, (≥ 18 to ≤ 35 years) [c]		
Impairment due to pain crises – frequency	50	28 (56.0)
Impairment due to pain crises – severity	50	7 (14.0)
Emotional burden	50	11 (22.0)
Impairment due to pain	50	11 (22.0)
Impairment of social life	50	16 (32.0)
Impairment due to stiffness	50	11 (22.0)
Sleep impairment	50	10 (20.0)
PedsQL – improvement by ≥ 15% at month 24, (≥ 12 to < 18 years) [c]		
Total score	13	6 (46.2)
Physical health	13	7 (53.8)
Psychosocial health	13	6 (46.2)
PedsQL-SCD – improvement by ≥ 15% at month 24, (≥ 12 to < 18 years) [c]		
Total score	13	6 (46.2)
Communication I	13	5 (38.5)
Communication II	13	4 (30.8)
Emotions	13	5 (38.5)
Pain and injury	13	8 (61.5)

Endpoint	**Exagamglogene autotemcel**	
	N	*Patients with event n (%)*
Pain effect	13	6 (46.2)
Pain management and control	13	5 (38.5)
Treatment	13	7 (53.8)
Care I	13	7 (53.8)
Care II	13	5 (38.5)
FACT-BMT at month 24, (≥ 18 to ≤ 35 years) [c] *(presented additionally)*		
FACT-G – total score	50	12 (24.0)
FACT-BMT – total score	50	8 (16.0)
Bone marrow transplantation subscale	50	8 (16.0)

Side effects

Endpoint MedDRA system organ classes/ AEs of special interest	**Exagamglogene autotemcel**	
	N[a]	Patients with event n (%)[e]
Total adverse events (presented additionally)	58	58 (100.0)
Serious adverse events (SAE)	58	38 (65.5)
Severe adverse events (CTCAE grade 3 or 4)	58	53 (91.4)
Therapy discontinuation due to adverse events	58	0
Severe adverse events according to MedDRA system organ class (with an incidence ≥ 10%)		
Blood and lymphatic system disorders	58	**38 (65.5)**
Febrile neutropenia	58	25 (43.1)
Anaemia	58	14 (24.1)
Thrombocytopenia	58	12 (20.7)
Neutropenia	58	11 (19.0)
Gastrointestinal disorders	58	**32 (55.2)**
Stomatitis	58	25 (43.1)
Abdominal pain	58	7 (12.1)
Nausea	58	7 (12.1)
Investigations	58	**27 (46.6)**
Thrombocytopenia	58	21 (36.2)
Neutropenia	58	17 (29.3)
Leukopenia	58	6 (10.3)

Endpoint MedDRA system organ classes/ AEs of special interest	**Exagamglogene autotemcel**	
	N[a]	Patients with event n (%)[e]
Metabolism and nutrition disorders	58	**27 (46.6)**
Loss of appetite	58	19 (32.8)
Iron overload	58	6 (10.3)
General disorders and administration site conditions	58	**24 (41.4)**
Mucositis	58	15 (25.9)
Infections and infestations	58	**20 (34.5)**
Injury, poisoning and procedural complications	58	**13 (22.4)**
Musculoskeletal and connective tissue disorders	58	**13 (22.4)**
Back pain	58	7 (12.1)
Hepatobiliary disorders	58	**12 (20.7)**
Cholelithiasis	58	7 (12.1)
Nervous system disorders	58	**12 (20.7)**
Respiratory, thoracic and mediastinal disorders	58	**11 (19.0)**
Vascular disorders	58	**8 (13.8)**
Skin and subcutaneous tissue disorders	58	**6 (10.3)**
SAEs according to MedDRA system organ class (with an incidence ≥ 10%)		
Infections and infestations	58	**22 (37.9)**
General disorders and administration site conditions	58	**11 (19.0)**
Gastrointestinal disorders	58	**9 (15.5)**
Hepatobiliary disorders	58	**8 (13.8)**
Cholelithiasis	58	6 (10.3)
Musculoskeletal and connective tissue disorders	58	**8 (13.8)**
Back pain	58	6 (10.3)
Respiratory, thoracic and mediastinal disorders	58	**8 (13.8)**
Nervous system disorders	58	**6 (10.3)**
Injury, poisoning and procedural complications	58	**7 (12.1)**

a. Safety population. AE from enrolment in the study to month 24.
b. Primary endpoint of the SCD-121
c. Subjects who discontinued the study before receiving exagamglogene autotemcel are considered non-responders.
d. The presentation takes place up to a point in time with sufficiently high return rates (70%) in the enrolled set (ITT population).
e. Enrolment until month 24

Endpoint MedDRA system organ classes/ AEs of special interest	**Exagamglogene autotemcel**	
	N[a]	Patients with event n (%)[e]
Abbreviations used: CTCAE = Common Terminology Criteria for Adverse Events; n.d.: = no data available; N = number of patients evaluated; n = number of patients with (at least one) event		

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

Patients 12 years of age and older with severe sickle cell disease and recurrent vaso-occlusive crises for whom haematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen (HLA)-identical related stem cell donor is not available

Approx. 130 to 330 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 Casgevy (active ingredient: exagamglogene autotemcel) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 25 March 2025):

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

Treatment with exagamglogene autotemcel should only be initiated and monitored by specialists who are experienced in the treatment of patients with sickle cell disease. Exagamglogene autotemcel must be used in a qualified treatment facility.

The quality assurance measures according to the ATMP Quality Assurance Guideline apply to the use of ATMP exagamglogene autotemcel in the therapeutic indication of sickle cell disease. Further details are regulated in Annex VI "Exagamglogene autotemcel in β-thalassemia and sickle cell disease" of the ATMP Quality Assurance Guideline.

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients (including patient identification card).

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material and a patient identification card. The training material for health professionals who prescribe, use or supervise the use of exagamglogene autotemcel includes information on the important identified risk of delayed platelet engraftment and the important potential risks of neutrophil engraftment failure and oncogenesis associated with genome editing and how to minimise these risks. It also contains instructions on how to provide the patient identification card and the guideline for patients.

The guideline for patients is intended to explain the risks and benefits of exagamglogene autotemcel treatment, the limited data on long-term effects, the signs of low platelet or leucocyte counts and blood cancers, as well as the need to report symptoms immediately to the treating doctor and to always carry the patient identification card with them.

This medicinal product received a conditional marketing authorisation. This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

4. Treatment costs

Annual treatment costs:

Patients 12 years of age and older with severe sickle cell disease and recurrent vaso-occlusive crises for whom haematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen (HLA)-identical related stem cell donor is not available

Designation of the therapy	Treatment costs/ patient[2]
Medicinal product to be assessed:	
Exagamglogene autotemcel	€ 2,200,000
Additionally required SHI services:	€ 2,448.92 - € 3,661.58

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 June 2025)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Busulfan	Surcharge for the production of a parenteral preparation containing cytostatic agents	€ 100	4	4	€ 400

5. Designation of 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:

[2] Exagamglogene autotemcel is used once only.

Patients 12 years of age and older with severe sickle cell disease and recurrent vaso-occlusive crises for whom haematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen (HLA)-identical related stem cell donor is not available

– 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.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

6. Percentage of study participants at study centres within the scope of SGB V in accordance with Section 35a, paragraph 3, sentence 5 SGB V

The medicinal product Casgevy is a medicinal product placed on the market from 1 January 2025.

The percentage of study participants in the clinical studies of the medicinal product conducted or commissioned by the pharmaceutical company in the therapeutic indication to be assessed who participated at study sites within the scope of SGB V (German Social Security Code) is ≥ 5% of the total number of study participants.

The clinical studies of the medicinal product in the therapeutic indication to be assessed were therefore conducted to a relevant extent within the scope of SGB V.