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2026004541

National Health Care Institute
Research, Development and Medicinal Products
Medicinal Products Team

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Our reference
2026004541

Date: 25 February 2026
Re: Lock procedure medicinal product exagamglogene autotemcel (Casgevy®) for sickle cell disease

Dear Ms Hermans,

The National Health Care Institute advises you on the assessment of exagamglogene autotemcel (exa-cel; Casgevy®) for the treatment of certain patients with severe sickle cell disease. This advice was prompted by the placement of exa-cel in the lock procedure for expensive medicinal products. The National Health Care Institute advises you not to include exa-cel for the registered indication in the basic health insurance package, unless the net price is reduced by at least 24% after successful price negotiations.

Sickle cell disease is a hereditary red blood cell disorder. This produces an abnormal form of haemoglobin, which is present in the red blood cells. This changes the shape of the red blood cells, which is why they are called sickle cells. These sickle cells are quick to clot and can clog blood vessels. This can cause a lot of pain and is called a vaso-occlusive crisis. Other symptoms include chronic anaemia, fatigue, organ damage and infections. In the Netherlands, there are approximately 2000 patients with sickle cell disease. Some of them have a severe form of sickle cell disease. The average life expectancy of patients with severe sickle cell disease is less than 50 years. In the Netherlands, these patients are currently being treated with hydroxycarbamide, blood transfusions and symptomatic treatment of vaso-occlusive crises. Allogeneic stem cell transplants are also used when an appropriate donor is available.

Exa-cel is an innovative, single-use treatment of a person's own stem cells, called an autologous stem cell transplant, using CRISPR/Cas9 technology to genetically modify the stem cells.

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

Exa-cel is also indicated for certain patients with transfusion-dependent β-thalassaemia. A reimbursement advice on this subject was issued by the National

Health Care Institute in July 2025[1]. Price negotiations are still ongoing.

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Claim by the marketing authorisation holder (MAH)
In the treatment of patients with severe sickle cell disease with recurrent vaso-occlusive crises for whom a suitable donor is not available or for whom the risks of allogeneic stem cell transplantation are considered too high, exa-cel has a therapeutic added value compared to standard treatment.

The claim made by the marketing authorisation holder is therefore broader than the registered indication, as the claim also covers patients for whom a donor is available but for whom the risks of an allogeneic stem cell transplant are considered too high.

Reimbursement advice
The National Health Care Institute advises you not to include exa-cel for the registered indication in the basic health insurance package, unless the price is reduced by at least 24% after successful price negotiations. The National Health Care Institute has established that exa-cel meets the legal criterion of 'established medical science and medical practice' for the registered indication and that it offers an added value compared to standard treatment with, among others, hydroxycarbamide, blood transfusions and symptomatic treatment of vaso-occlusive crises. Based on the available data, the cost-effectiveness is, however, considered unfavourable.

The price negotiations should be negotiated at a discount of more than 24%, due to the very high macro costs if all patients are treated with exa-cel. Due to uncertainty about the continued effect of exa-cel, a reassessment by the National Health Care Institute could be requested prior to a re-negotiation of the price if more long-term data become available.

The National Health Care Institute advises you to align the negotiations for the sickle cell disease indication with the ongoing price negotiation for the β-thalassemia indication, so that treatment can be made available at the same time for both patient groups if the price negotiations are successfully concluded.

We explain the preparation of this reimbursement advice below.

General
At your request, the National Health Care Institute assesses whether care should be part of the standard health insurance package from the perspective of the basic health insurance package paid from joint premiums.

[1] Advice - reimburse maralixibat (Livmarli®) for the treatment of rare and severe liver disease | National Health Care Institute

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The National Health Care Institute assesses on the basis of the four reimbursement criteria[2]: effectiveness[3], cost-effectiveness[4], necessity[5] and feasibility[6]. The Scientific Advisory Board (WAR) advises the National Health Care Institute on the (scientific) support and the conclusion of the assessment. If there are risks regarding the accessibility and affordability, the assessment of the reimbursement criterion of effectiveness (established medical science and medical practice) will be placed in the wider social context of the four reimbursement criteria. The Insured Package Advisory Committee (hereinafter also "ACP") advises the Executive Board of the National Health Care Institute in this regard. This social weighting results in the reimbursement advice. Stakeholders are consulted during the process.

Comprehensive weighting of reimbursement criteria

Effectiveness

Established medical science and medical practice

The single-arm CLIMB-SCD-121 study investigated exa-cel in patients with severe sickle cell disease who had ≥2 vaso-occlusive crises per year, and for whom no suitable donor for stem cell transplantation was available. The study showed that 71% of the patients that had started the treatment course were completely free from severe recurrent vaso-occlusive crises for at least 12 months and that 73% had not been hospitalised for at least 12 months due to these crises. For the patients actually receiving exa-cel, this was 96% and 100%, respectively. It is not yet known whether the effects on the prevention of vaso-occlusive crises persist for life. It also improved the quality of life of patients. The treatment course of exa-cel lasts several months and is intensive, but is comparable to that of autologous stem cell transplantation.

Patients for whom the risks of stem cell transplantation are too high, but for whom a donor is available, were not included in the clinical study. This group, therefore, is not included in the registered indication. The National Health Care Institute has been in contact with the physicians' associations about this during the evaluation. According to the physicians' associations, exa-cel should only be considered in cases where no suitable donor is available.

The National Health Care Institute, advised by the Scientific Advisory Board (WAR), concluded that exa-cel has added value for the registered indication compared to standard treatment including hydroxycarbamide, blood transfusions and symptomatic treatment of vaso-occlusive crises.

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[2] Real-world package management 4 (2023). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.

[3] Assessment of the established medical science and medical practice (2023). National Health Care Institute. Via www.zorginstituutnederland.nl.

[4] Healthcare cost-effectiveness report (2024) National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.

[5] Necessity is related to both the medical need due to the severity of a disease for the patient (burden of disease) and the need to insure something. See the report on real-world package management 4 (2023).

[6] The reimbursement criterion of feasibility deals with whether it is feasible or sustainable to include a specific type of care in the basic health insurance package. It is therefore mainly a test of a number of implementation aspects
such as the healthcare organisation, support, ethical and legal aspects, budget impact and so on. See the report on real-world package management 4 (2023).

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Cost-effectiveness
The cost-effectiveness analysis by the marketing authorisation holder is of sufficient quality and can be used for decision-making. The cost-effectiveness estimate is higher than the reference value considered relevant for this condition; therefore, exa-cel is not considered a cost-effective intervention. The ICER is €112,068/QALY. With a reference value of €80,000, the price of exa-cel would have to be reduced by at least 24% to be cost-effective. There is also uncertainty in the cost-effectiveness analyses about the long-term impact of exa-cel. Scenario analyses show that if the effectiveness of exa-cel decreases over time, this would severely impact the ICER.

Feasibility
Currently, due to limited hospital capacity, it is not possible to treat all patients eligible for exa-cel immediately. Only a few patients with sickle cell disease are expected to be treated with exa-cel annually. The fact that exa-cel can therefore also be used in transfusion-dependent β-thalassaemia also plays a role. The limited capacity will have to be distributed between patients with transfusion-dependent β-thalassaemia and those with sickle cell disease. Capacity may be increased over a number of years.

Budget impact analysis
The National Health Care Institute estimates that due to capacity constraints, 7 patients will be treated with exa-cel for the above indication in year 3 after inclusion in the package. The total single-use cost of exa-cel comes to €1.9 million per patient. This results in macro costs of €13.5 million in the third year. Due to the relatively limited medication costs of standard treatment, the budget impact of exa-cel is also €13.5 million. Costs of blood transfusions are not included as these do not include medication costs. The costs of blood transfusions are relatively limited (around €10,000 per patient per year). If all 85 patients with sickle cell disease are treated with exa-cel, the macro costs are €164 million.

Social appraisal
The social appraisal shows that it is important that exa-cel for the treatment of sickle cell disease becomes available in the short term, but only at a socially acceptable price. Because of the high cost of exa-cel, price negotiations must take place. If the price negotiations are successfully concluded, exa-cel should be available simultaneously for the two different indications, so that a choice can be made based on medical arguments which patients should be treated first. In addition, arrangements for appropriateness of exa-cel should be made determining the role of centres of expertise and the establishment of a national, multidisciplinary indication commission.

Appropriateness
The National Health Care Institute acknowledges the importance of establishing arrangements for the appropriateness of exa-cel. The National Health Care Institute is already in contact with the physicians' association, patient association and health care insurers on this matter following the reimbursement advice of exa-cel for transfusion-dependent β-thalassemia. The use of exa-cel for sickle cell disease will be included.

Should you need any further information, please do not hesitate to contact us.

Yours sincerely,

M.J. Janssen
Chairperson of the Executive Board

Annexes:
- -Pharmacotherapeutic report
- -Budget impact analysis
- -Pharmaco-economic report

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