FDA Expands Casgevy for Sickle Cell in Children 2 Years and Older

Written by The Life Science Feed Editorial Team · Published 8 July 2026 · Edited by Mara Voss

Sickle cell disease, a debilitating inherited blood disorder, has long presented a significant challenge for clinicians, particularly in pediatric populations where chronic pain, organ damage, and shortened lifespans are common. The disease affects millions globally, with a disproportionate burden on individuals of African, Mediterranean, and South Asian descent. For years, treatment options beyond hydroxyurea and bone marrow transplant have been limited, leaving many patients with suboptimal disease control and a heavy symptom burden.

The U.S. Food and Drug Administration (FDA) recently expanded the approval of Casgevy (exagamglogene autotemcel), a CRISPR/Cas9 gene-edited cell therapy, to include children aged 2 to 11 years with sickle cell disease (SCD) and recurrent vaso-occlusive crises (VOCs). This decision follows its initial approval for patients 12 years and older in December 2023, marking a critical step forward in addressing the unmet need for curative therapies in younger patients.1

KEY TAKEAWAYS

- The Pivot: Casgevy, a gene-editing therapy, is now approved for children as young as 2 years old with sickle cell disease.
- The Data: In clinical trials, 88.9% (16/18) of patients aged 2 to 11 achieved freedom from severe vaso-occlusive crises for at least 12 consecutive months.
- The Action: Clinicians should consider Casgevy for eligible pediatric patients with recurrent vaso-occlusive crises who lack suitable donor options for allogeneic hematopoietic stem cell transplantation.

Sickle cell disease results from a single point mutation in the beta-globin gene, leading to the production of abnormal hemoglobin S (HbS). This faulty hemoglobin polymerizes under deoxygenated conditions, deforming red blood cells into a characteristic sickle shape. These rigid, crescent-shaped cells obstruct blood flow in small vessels, causing recurrent, excruciating vaso-occlusive crises (VOCs), chronic pain, anemia, and progressive organ damage affecting the spleen, lungs, kidneys, and brain. The cumulative impact of these complications significantly reduces quality of life and life expectancy, with many patients not surviving past their fifth decade.

Casgevy works by modifying a patient's own hematopoietic stem cells. Clinicians collect these cells and then use CRISPR/Cas9 gene-editing technology to inactivate the BCL11A gene in erythroid progenitor cells. BCL11A acts as a repressor of fetal hemoglobin (HbF) production. By disrupting BCL11A, the therapy reactivates the production of HbF, which does not sickle and can effectively carry oxygen, thereby diluting the concentration of HbS and preventing sickling.

The modified cells are then infused back into the patient following myeloablative conditioning, typically with busulfan, to make space in the bone marrow for the engraftment of the gene-edited cells. This complex, one-time treatment aims to provide a durable therapeutic effect.

The numbers

The expanded approval for Casgevy in younger children is based on data from the ongoing Phase 1/2/3 CLIMB-121 trial (NCT04208529), an open-label, single-arm study evaluating the safety and efficacy of the therapy in patients with severe sickle cell disease. The trial enrolled patients aged 2 to 35 years with a history of at least two severe vaso-occlusive crises per year over the two years prior to screening. The primary endpoint was freedom from severe VOCs for at least 12 consecutive months after Casgevy infusion.

In the cohort of patients aged 2 to 11 years (N=18), a substantial majority achieved the primary efficacy endpoint. 88.9% (16/18) of these younger patients experienced freedom from severe VOCs for at least 12 consecutive months. The median follow-up for this group was 26.8 months (range, 12.2 to 47.5 months). This outcome is clinically meaningful, as severe VOCs are the hallmark of SCD morbidity and a primary driver of hospitalizations and emergency department visits.

For context, in the overall study population (N=44, including patients aged 12 to 35 years), 93.5% (30/32) of evaluable patients achieved this same endpoint, with a median follow-up of 30.3 months.1

Secondary endpoints in the CLIMB-121 trial also supported the therapy's benefit. All 18 patients in the 2-11 age group who received Casgevy were free from hospitalizations due to VOCs for at least 12 consecutive months. This reduction in hospital burden represents a significant improvement in patient quality of life and a potential decrease in healthcare resource utilization. No patients in this younger cohort experienced severe VOCs or hospitalizations due to VOCs after engraftment of Casgevy-modified cells. The safety profile in children aged 2 to 11 was generally consistent with that observed in older patients and with the known effects of myeloablative conditioning. Common adverse events included mucositis, febrile neutropenia, and nausea, which are expected consequences of the conditioning regimen. No unexpected safety signals emerged in the younger population.1

The open-label design is the obvious caveat. While the magnitude of effect is compelling, the absence of a comparator arm means clinicians must interpret these results within the context of the natural history of severe SCD. The long-term durability of the gene edit and the potential for off-target effects remain areas of ongoing surveillance. Patients receiving Casgevy require lifelong monitoring for hematologic malignancies and other potential late-onset adverse events, though none have been reported to date in the trial. The therapy also carries a significant logistical and financial burden, requiring specialized transplant centers and a complex treatment process. Access to such advanced care will be a major determinant of its real-world impact.

Still, the data provides a strong signal for a disease with limited curative options. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the only established cure for SCD, but it is limited by the availability of suitable matched donors and carries significant risks, including graft-versus-host disease. Casgevy offers an autologous alternative, eliminating the need for a donor and the associated immunological complications. The trial was not powered to detect differences in rare adverse events, and that gap matters for a therapy intended to be curative. The long-term safety data, particularly regarding potential genotoxicity, will be critical as more patients are treated and followed for extended periods.

CLINICAL IMPLICATIONS

The expanded approval of Casgevy for children as young as two years old fundamentally alters the treatment landscape for severe sickle cell disease. For the first time, clinicians have an autologous gene-editing option for pediatric patients who previously had few alternatives beyond hydroxyurea or a matched sibling donor transplant. This means earlier intervention is now possible, potentially mitigating the cumulative organ damage that defines the disease's progression.

But the logistical hurdles are substantial. Casgevy is not a simple outpatient infusion; it requires myeloablative conditioning and specialized transplant center care. This will concentrate its use in a limited number of institutions, raising questions about equitable access for all eligible children, particularly those in underserved communities where SCD is most prevalent. The cost, while not yet fully disclosed for this younger population, will undoubtedly be a barrier for healthcare systems.

Clinicians must now weigh the benefits of early intervention with Casgevy against the risks of myeloablative conditioning in very young children, a population particularly vulnerable to treatment-related toxicities. The long-term safety data, especially regarding secondary malignancies and the durability of the gene edit, will be paramount. This therapy represents a significant advance, but its integration into routine clinical practice will demand careful patient selection, robust support systems, and ongoing vigilance.

EDITORIAL & AI STANDARDS

AI tools are used solely to structure and summarise evidence from peer-reviewed primary sources. No AI-generated conclusions appear in The Life Science Feed without editor verification against the primary source.

REFERENCES

1. 1. Vertex Pharmaceuticals. Casgevy (exagamglogene autotemcel) prescribing information. 2024.

LICENCE & RIGHTS

MEDICAL DISCLAIMER

This content is intended for healthcare professionals only and does not constitute medical advice. Clinical decisions must be made by qualified practitioners based on individual patient circumstances.

FOLLOW THE LIFE SCIENCE FEED

Instagram @lifesciencefeed **LinkedIn** linkedin.com/company/thelifesciencefeed

thelifesciencefeed.com