MILLIMAN WHITE PAPER

Optimizing case management to improve outcomes for Medicaid enrollees with sickle cell disease

An adaptive approach in a transformative era of healthcare

Shelley Perino, RN, MPH
Rachel Ferguson, MHA, CAPM
Jim Davidson, PharmD, MBA

When it comes to improving clinical outcomes for individuals with sickle cell disease, there are many considerations, including access to specialized services, continuity of care, patient education, and psychosocial support.

Innovative cell and gene therapies (CGT) such as Casgevy® (exagamglogene autotemcel) and Lyfgenia™ (lovotibeglogene autotemcel) offer the promise of life-changing treatment for individuals living with sickle cell disease (SCD). For the first time since bone marrow transplantation (BMT) was used to treat SCD, patients have a therapeutic option that not only offers a durable treatment, but one that does not require a donor or the long-term use of immunosuppressive agents.[1]

Despite their therapeutic potential, widespread adoption of CGTs will hinge on overcoming significant challenges, including accurately identifying medically eligible patients and ensuring they have appropriate access to care. Characteristics of CGTs that affect patients' access to care include the therapy's multimillion-dollar cost, manufacturing capacity constraints for customized biologics, and the limited number of facilities equipped to administer the treatment. Furthermore, not all individuals with a sickle cell diagnosis will meet the stringent eligibility criteria, and even those who qualify may face significant obstacles to accessing treatment.

This Milliman white paper reviews the basics of SCD, the role of health equity in approaching care and services, and the impact of newly approved disease-modifying gene therapies. The discussion addresses three core business questions:

1. How can managed care plans optimize treatment plans for individuals living with SCD?
2. How can technology enhance care coordination and minimize avoidable costs?
3. How can strategies to incorporate the *CMS Sickle Cell Disease Action Plan*[2] and *CMS Health Equity Framework*[3] into Medicaid managed care impact acute care utilization?

A primer on sickle cell disease

SCD is an inherited disorder resulting from a defect in the production of hemoglobin (Hgb), a protein found on the surface of erythrocytes, or red blood cells (RBCs). The Hgb protein carries oxygen to tissues, helps remove carbon dioxide waste, and plays a critical role in maintaining the body's acid-base balance. In SCD, a genetic miscode replaces one hemoglobin-building amino acid with another, forming hemoglobin S (HbS). Instead of maintaining the normally biconcave or disc-shaped RBC, the altered hemoglobin protein combines to form long polymers that act like adhesive fibers that pull the RBC into a crescent or sickle shape. This distortion shortens the lifespan of the RBC, makes it less flexible and more prone to rupture, and significantly reduces its ability to transport oxygen. Instead of easily flowing through blood vessels, sickle-shaped RBCs impede normal blood circulation, impair oxygen delivery to tissues and organs, instigate inflammatory processes, and cause blood clots. The end result is a vaso-occlusive crisis (VOC), which can lead to intense pain, tissue damage, and potentially life-threatening complications.

1. Kanter J, Liem RI, Bernaudin F, Bolaños-Meade J, Fitzhugh CD, Hankins JS, Murad MH, Panepinto JA, Rondelli D, Shenoy S, Wagner J, Walters MC, Woolford T, Meerpohl JJ, Tisdale J. American Society of Hematology 2021 guidelines for sickle cell disease: stem cell transplantation. Blood Adv. 2021 Sep 28;5(18):3668-3689. doi: 10.1182/bloodadvances.2021004394C. PMID: 34581773; PMCID: PMC8945587.
2. Centers for Medicare and Medicaid Services. (September 2023). CMS Sickle Cell Disease Action Plan. Retrieved February 24, 2025, from https://www.cms.gov/files/document/sickle-cell-disease-action-plan.pdf.
3. Centers for Medicare and Medicaid Services. (April 2022). CMS Framework for Health Equity 2022–2032. Retrieved February 24, 2025, from https://www.cms.gov/files/document/cms-framework-health-equity.pdf.

Infants and young children with SCD experience frequent infections, chronic anemia, and acute dactylitis, a painful condition causing unpredictable swelling in the fingers and toes. SCD can delay growth and puberty. Approximately 10% of children with SCD will have a clot in the brain that causes an ischemic stroke. Before 20 years of age, as many as 40% of children with SCD will experience a "silent" stroke that, while not overtly apparent, has the potential to damage cognitive development.[4] Infants and children with SCD are also vulnerable to SCD complications in the spleen. A highly vascular organ, the spleen produces and stores specialized infection-fighting cells, filters pathogens, and removes aged RBCs from the blood. In SCD, impaired splenic circulation can disrupt these vital functions. While some children with SCD live with chronic enlargement of the spleen, others will experience acute splenic sequestration, in which multiple clots trap blood in the spleen and trigger life-threatening circulatory collapse.

Adults with SCD live with chronic anemia, fatigue, and VOCs that can cause hospitalizations for the management of leg ulcers, deep vein thrombosis, and pulmonary embolism. Repeated assaults from VOCs and inflammation can damage the retina, increase the risk of gallstones and bile duct blockage, and instigate severe damage to the kidneys, lungs, and heart.[5] Additionally, respiratory infections can trigger acute chest syndrome (ACS), a life-threatening condition in which multiple clots impede blood circulation in the lungs and dangerously impair blood oxygenation.

A PRIMER ON SICKLE CELL DISEASE

MISCODED HEMOGLOBIN DISTORTS RBCS

- RBCs take on the shape of a crescent moon or sickle.
- "Sickled" cells are less able to carry oxygen, are less flexible, and are prone to adhering to blood vessel walls.

VASO-OCCLUSIVE CRISIS (VOC)

- In VOCs, distorted RBCs can occlude blood flow and trigger a potentially life-threatening medical emergency.
- In addition to pain control, treatment may include laboratory evaluations, supplemental oxygen, fluid management, and blood transfusion.

CONSEQUENCES OF SCD

- The lifespan for an individual with SCD is typically 20–25 years shorter than the average lifespan.
- Pediatric populations suffer from infection, anemia, painful VOCs in the fingers and toes, and potentially life-threatening stroke and splenic sequestration.
- Adults can experience anemia, VOCs, deep vein thrombosis, pulmonary embolism, and damage to the retina, kidneys, lungs, and heart.

MANAGEMENT AND TREATMENT

- Management of sickle cell disease involves routine monitoring by a multidisciplinary team to address pain episodes, organ health, and complications like infections or anemia.
- Treatment often includes hydroxyurea to reduce complications, blood transfusions to prevent stroke, and newer targeted therapies.

SCD AND HEALTH EQUITY

- Patients frequently encounter racial bias and inequities in pain management, resulting in inconsistent and suboptimal treatment outcomes.
- Many individuals with sickle cell disease experience financial and social hardships that exacerbate health disparities and limit access to necessary resources and support.

The risk of pregnancy-related morbidity and mortality increases for pregnant people with SCD, who are best served by obstetrical providers with expertise in SCD and high-risk pregnancies. SCD in pregnancy can increase the risks of hypertension and eclampsia, ACS, anemia, and infection. Pregnant people with SCD face an increased risk of preterm labor or delivering a preterm infant, have a higher prevalence of anemia, and may suffer from more frequent and debilitating VOCs.[6]

4. American Stroke Association. (2024). Sickle Cell Disease and Pediatric Stroke Risk. Retrieved February 24, 2025, from https://www.stroke.org/en/about-stroke/stroke-in-children/sickle-cell-disease.

5. Liem, R. I., Lanzkron, S., Coates, T. D., DeCastro, L., Desai, A. A., Ataga, K. I., Cohen, R. T., et al. (2019). American Society of Hematology 2019 guidelines for sickle cell disease: Cardiopulmonary and kidney disease. Blood Advances, 3(23), 3867–3897. Retrieved February 24, 2025, from https://doi.org/10.1182/bloodadvances.2019000916.

6. National Heart, Lung, and Blood Institute. (2025). Pregnancy, reproduction, and sickle cell disease. Retrieved February 24, 2025, from https://www.nhlbi.nih.gov/health/sickle-cell-disease/pregnancy.

Medicaid, health equity, and SCD

As over 90% of individuals with an SCD diagnosis are Black or African-American, the impact of institutional and interpersonal racism on treatment modalities, access to specialists, and respectful, person-centered care cannot be underestimated.[7] Despite the recent innovations in CGTs, a significant body of literature and peer-reviewed studies evidence persistent bias in research funding for SCD. Compared to other genetic disorders such as cystic fibrosis or hemophilia that largely impact white individuals, SCD research has suffered from decades of underinvestment.[8,9]

VOCs are unpredictable, can escalate quickly, and frequently require urgent medical attention in the emergency department (ED). In the midst of a VOC, individuals with SCD may face stigmatization, be inappropriately labeled as high utilizers or "frequent flyers," and face discrimination. Patients presenting with pain but whose laboratory findings are inconsistent with a VOC may face the threat of being characterized as "drug seeking" and may be discharged early, increasing the risk of a recurrence.[10] These stigmatizations can lead to delays in treatment and ineffective pain management or become barriers to receiving evidence-based care from well-trained providers.

Outside the acute care setting, individuals with SCD often encounter significant barriers to accessing essential care. Medicaid network limitations compound the challenge, further restricting access to specialists in hematology, immunology, nephrology, and other critical fields. A two-state study of Medicaid enrollees conducted between 2016 and 2018 revealed striking gaps in care: 13%–25% of pediatric enrollees with SCD had no encounters with a hematologist, while the percentage of adults without hematologist encounters rose to 34%–56%.[11]

The CMS cell gene therapy access model

In August 2024, the Centers for Medicare and Medicaid Services (CMS) announced a Notice of Funding Opportunity (NOFO) aimed at addressing the significant cost issues associated with CGTs and facilitating care for the estimated 42,000 Medicaid beneficiaries living with SCD.[12,13] The Cell and Gene Therapy Access Model introduced an outcomes-based payment approach, offering states an innovative risk-sharing framework to expand access to life-altering therapies. Key components of the NOFO included requirements for network adequacy to ensure access for both managed care and fee-for-service (FFS) populations, as well as provisions for transportation, data submission, and reporting.

States that apply for the competitive award may also use the funding for optional model elements, such as raising awareness of CGTs, accelerating access to specialty care and behavioral health services, and addressing health-related social needs. Whether state Medicaid agencies and managed care organizations (MCOs) independently navigate the complexities of CGT access or apply for the CMS CGT Access Model, it is critical for states and MCOs to ensure that Medicaid enrollees with SCD have effective access to supportive non-CGT therapies. While these therapies are not as durable as CGT, they reduce the frequency and severity of SCD complications, improve quality of life, and establish a pathway for eligible consumers to access CGT. Ultimately, supportive SCD therapies serve as a bridge to preserve health and function and ensure that CGT remains a viable treatment option.

This funding opportunity application has been extended through March 14, 2025.

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7. Centers for Disease Control and Prevention. (2024). Data and statistics on sickle cell disease. Retrieved February 24, 2025, from https://www.cdc.gov/sickle-cell/data/index.html.

8. Power-Hays, A., & McGann, P. T. (2020). When actions speak louder than words: Racism and sickle cell disease. New England Journal of Medicine, 383(20), 1902–1903. Retrieved February 24, 2025, from https://doi.org/10.1056/NEJMp2022125.

9. Farooq, F., Mogayzel, P. J., Lanzkron, S., Haywood, C., & Strouse, J. J. (2020). Comparison of US federal and foundation funding of research for sickle cell disease and cystic fibrosis and factors associated with research productivity. JAMA Network Open, 3(3), e201737. Retrieved February 24, 2025, from https://doi.org/10.1001/jamanetworkopen.2020.1737.

10. Childerhose, J. E., Cronin, R. M., Klatt, M. D., & Schamess, A. (2023). Treating chronic pain in sickle cell disease: The need for a biopsychosocial model. New England Journal of Medicine, 388(15), 1349–1351. Retrieved February 24, 2025, from https://doi.org/10.1056/NEJMp2301143.

11. Horiuchi, S. S., Zhou, M., Snyder, A., & Paulukonis, S. T. (2022). Hematologist encounters among Medicaid patients who have sickle cell disease. Blood Advances, 6(17), 5128–5131. Retrieved February 24, 2025, from https://doi.org/10.1182/bloodadvances.2022007622.

12. The Cell and Gene Therapy (CGT) Access Model application is available at https://www.cms.gov/priorities/innovation/innovation-models/cgt. CMS is accepting state applications through March 14, 2025.

13. Desai, P., Naber, J., Bhatt, P., & Engel, T. (April 25, 2024). CMS Cell and Gene Therapy Access Model: Exploring the benefits, limitations, and considerations for expansion [Milliman white paper]. Retrieved February 24, 2025, from https://www.milliman.com/-/media/milliman/pdfs/2024-articles/4-25-24_cms-cell-and-gene-therapy-access-model.ashx.

SCD treatment, uptake, and barriers to care

The treatment approach for SCD focuses on managing anemia, preventing infections, addressing pain, and reducing the frequency and duration of VOCs. While treatment options have historically been limited, the introduction of two CGTs expands the available therapies. Two cellular-based gene therapies are now approved for SCD. Lyfgenia is a one-time gene therapy in which a patient's blood-forming stem cells are collected, genetically modified in a laboratory, and reintroduced to produce a form of healthy, non-sickling hemoglobin. In clinical trials, 88% of recipients who were evaluated achieved "complete resolution" of VOCs within 18 months of completing treatment with Lyfgenia.[14,15] Casgevy capitalizes on the non-sickling features of fetal hemoglobin (HbF) and edits out a portion of the genome that typically inhibits HbF production. With the HbF gene reactivated, specialized RBC-producing cells in the bone marrow start producing an increased volume of HbF, mitigating the effects of abnormal hemoglobin.[16]

Outside the newly approved CGTs, disease-modifying options to achieve treatment goals remain limited. To decrease the incidence of VOCs, one therapeutic mainstay is to stimulate the production of HbF in the circulating blood of individuals with SCD. Normally present in a developing fetus, HbF has a heightened preference for oxygen uptake compared to other hemoglobin, and because it is missing the faulty gene present in HbS, it does not sickle.[17] After birth and during infancy, HbF is largely replaced by adult hemoglobin (HbA), but remains present in very low levels in children and adults.

Hydroxyurea (HU) stimulates the production of HbF to decrease the incidence of VOC. Used off-label since the 1980s, the U.S. Food and Drug Administration (FDA) formally approved HU's SCD indication in 1998 for adults, and in 2017 for children.[18] While not a cure, daily use of oral HU has demonstrated efficacy in decreasing the incidence of VOCs, stroke, and ACS. Although generally well tolerated, HU may cause gastrointestinal upset, mouth ulcers, and fatigue, and may increase the risk of infection in some individuals. Whether from lack of awareness, concerns about adverse effects, or lack of prescription, the uptake of HU is limited. The Centers for Disease Control and Prevention (CDC) reports that less than 50% of children and youth under age 16 use HU.[19] Broadly, HU utilization patterns are similar in adults, with estimates of daily use ranging from 22% to 48%.[20]

In addition to HU, individuals with SCD may also receive blood transfusions to increase the number of healthy RBCs in circulation. While useful at improving tissue oxygenation, frequent blood transfusions can result in dangerously high levels of iron. Iron is an oxidizing element that, at higher than normal levels, can cause damage to the joints, heart, and liver. Iron overload must be countered with chelating agents to bring iron levels closer to normal. Frequent transfusions can also interfere with quality of life, pose a risk of infection and immune reactions, and may increase the risk of stroke.

Another therapeutic approach focuses on preserving the health of existing RBCs by minimizing oxidative damage associated with SCD. Approved by the FDA in 2017, L-glutamine, an amino acid essential for protein formation, has been shown to significantly reduce the frequency of sickle cell crises, hospitalizations due to sickle cell–related pain, and the incidence of ACS.[21]

14. Lyfgenia. LYFGENIA™ is a one-time transformational gene therapy with the potential to decrease or stop VOEs. Retrieved February 24, 2025, from https://www.lyfgeniahcp.com/clinical-trials.

15. U.S. Food and Drug Administration. (December 8, 2023). FDA approves first gene therapies to treat patients with sickle cell disease [Press release]. Retrieved February 24, 2025, from https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease.

16. Casgevy. The role of fetal hemoglobin in SCD: In patients with SCD, disease pathology arises as fetal hemoglobin (HbF) shifts to adult hemoglobin (HbA).https://www.casgevyhcp.com/sickle-cell-disease/role-fetal-hemoglobin.

17. Kaufman, D. P., Khattar, J., & Lappin, S. L. (March 20, 2023). Physiology, fetal hemoglobin. In Stat Pearls [Internet]. Stat Pearls Publishing. Available from https://www.ncbi.nlm.nih.gov/books/NBK500011/.

18. Ibid.

19. Centers for Disease Control and Prevention. (2024). Data and statistics on sickle cell disease. Retrieved February 24, 2025, from https://www.cdc.gov/sickle-cell/data/index.html.

20. Anderson, D., Syed, S., Ang, P., Agwu, C., Lien, K., Hines, J., & Baker, N. A. (2022). Understanding hydroxyurea utilization in sickle cell disease: Exploring patient and provider attitudes and beliefs. Blood, 140(Supplement 1), 7879–7880. Retrieved February 24, 2025, from https://doi.org/10.1182/blood-2022-167817.

21. U.S. Food and Drug Administration. (August 18, 2017). FDA approved L-glutamine powder for the treatment of sickle cell disease. Retrieved February 24, 2025, from https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approved-l-glutamine-powder-treatment-sickle-cell-disease.

The FDA granted Oxbryta® (voxelotor) an accelerated approval for the treatment of SCD in adults in 2019 and in patients ages 4–11 in 2021. The FDA accelerated approval process is used for earlier approval of drugs that treat serious conditions and may be granted based on the drug's surrogate clinical endpoints that may predict clinical benefit. The FDA requires post-marketing studies to verify the actual clinical benefit. Oxbryta was thought to inhibit RBC sickling, improve RBC deformability, and reduce whole-blood viscosity. In post-marketing clinical trials of Oxbryta, the manufacturer reported a higher rate of VOC in patients with SCD receiving Oxbryta compared to placebo. Because of this, Oxbryta was voluntarily withdrawn from the U.S. market in September 2024.[22,23]

A second drug, Adakveo® (crizanlizumab-tmca), uses monoclonal antibody infusions to reduce VOCs in patients ages 16 and older by specifically inhibiting selectin, a substance that contributes to cells sticking together and leads to VOCs.[24,25] Although approved in the U.S. since 2019, Adakveo was withdrawn by the European Medicines Agency in 2023 due to limited efficacy.[26]

Hematopoietic stem cell, or BMT, has been an option for eligible individuals with SCD for more than 20 years. Typically used in children without significant end-organ damage but with severe disease including multiple VOCs and history of stroke, BMT replaces HbS cells with donor stem cells that do not produce HbS. While generally successful at reducing VOCs and the end-organ damage associated with SCD, BMT is a complex, multistep treatment. In addition to the necessity of having a matched donor, BMT requires treatment at a qualified hospital. Procedural risks include adverse impacts on fertility and the risk of graft-versus-host disease, or rejection, a potentially life-threatening event. BMT is performed infrequently in the SDC population. Barriers to care include access to specialized providers, insurance authorization processes, concerns about adverse events, and the availability of a matching donor.

An estimated 29% of adults with SCD experience daily chronic pain, with another 50% experiencing pain at least 50% of the time. The chronic and acute pain of SCD may be managed using nonsteroidal anti-inflammatory drugs (NSAIDs) or narcotic analgesics such as oxycodone or morphine.[27] Pain triggered by tissue hypoxia resulting from VOCs may be poorly managed, minimized, or dismissed by providers. Patients who seek help in acute care settings may experience early discharge with suboptimal pain control or incomplete resolution of the VOC.

Service uptake for SCD-related preventive measures, including infection prevention and stroke screening, remains variable. Evidence-based guidelines recommend prophylactic immunization to reduce infection risk. Among children with SCD under the age of 2, 59% of those eligible received pneumococcal vaccination. Stroke screening rates are lower, with 37% of children ages 2–16 undergoing transcranial Doppler (TCD) ultrasound, a tool used for identifying stroke risk and prior events. Although life expectancy for individuals with SCD has improved in the last decades, it remains 20–25 years lower than that of the overall U.S. population.[28,29,30] Compared to those without SCD, people living with SCD experience the need for increased emergency care to

22. Pfizer. (September 25, 2024). Pfizer voluntarily withdraws all lots of sickle cell disease treatment OXBRYTA® (voxelotor) from worldwide markets [Press release]. Retrieved February 24, 2025, from https://www.pfizer.com/news/press-release/press-release-detail/pfizer-voluntarily-withdraws-all-lots-sickle-cell-disease.

23. U.S. Food and Drug Administration. (September 26, 2024). FDA is alerting patients and health care professionals about the voluntary withdrawal of Oxbryta from the market due to safety concerns. Retrieved February 24, 2025, from https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerting-patients-and-health-care-professionals-about-voluntary-withdrawal-oxbryta-market-due.

24. U.S. Food and Drug Administration. (November 15, 2019). FDA approves first targeted therapy to treat patients with painful complication of sickle cell disease [Press release]. Retrieved February 24, 2025, from https://www.fda.gov/news-events/press-announcements/fda-approves-first-targeted-therapy-treat-patients-painful-complication-sickle-cell-disease.

25. Novartis. (November 15, 2019). New Novartis medicine Adakveo® (crizanlizumab-tmca) approved by FDA to reduce frequency of pain crises in individuals living with sickle cell disease. Retrieved February 24, 2025, from https://www.novartis.com/us-en/news/media-releases/new-novartis-medicine-adakveo-crizanlizumab-tmca-approved-fda-reduce-frequency-pain-crises-individuals-living-sickle-cell-disease.

26. European Medicines Agency. (May 26, 2023). Revocation of authorisation for sickle cell disease medicine Adakveo. Retrieved February 24, 2025, from https://www.ema.europa.eu/en/news/revocation-authorisation-sickle-cell-disease-medicine-adakveo.

27. Brandow, A. M., Carroll, C. P., Creary, S., Edwards-Elliott, R., Glassberg, J., Hurley, R. W., Kultar, A., et al. (2020). American Society of Hematology 2020 guidelines for sickle cell disease: Management of acute and chronic pain. Blood Advances, 4(12), 2656–2701. Retrieved February 24, 2025, from https://doi.org/10.1182/bloodadvances.2020001851.

28. Centers for Disease Control and Prevention. (May 15, 2024). Complications of sickle cell disease. Retrieved February 24, 2025, from https://www.cdc.gov/sickle-cell/complications/index.html.

29. Lubeck, D., Agodoa, I., Bhakta, N., Danese, M., Pappu, K., Howard, R., Gleeson, et al. (2019). Estimated life expectancy and income of patients with sickle cell disease compared with those without sickle cell disease. JAMA Network Open, 2(11), e1915374. Retrieved February 24, 2025, from https://doi.org/10.1001/jamanetworkopen.2019.15374.

30. Centers for Medicare and Medicaid Services. CMS Sickle Cell Disease Action Plan , op cit.

manage VOCs and the severe pain that occurs with the crisis.[31] Acute care utilization among individuals with SCD varies based on age and comorbidities. Approximately 19% of individuals with SCD will have at least one ED visit annually, 36% will have two to five visits, and 23% will have six or more. Among people with SCD ages 0 to 20, 32% of ED visits result in an inpatient hospital stay.[32]

Hospital admissions are more frequent among individuals with SCD compared to those without. A national study of Medicaid claims found that almost half (49%) of individuals with SCD experienced at least one inpatient stay, in contrast to Medicaid recipients without SCD.[33] Similarly, individuals with SCD averaged nine hospital days during the year compared to only one for individuals without SCD. The same study identified that in the Medicaid SCD population, hospitalization frequency varies. While 21% of beneficiaries experienced only one admission, another 21% had two to five admissions, and 7% experienced six or more. Despite the high rate of acute care utilization, individuals with SCD also actively engage in outpatient care, with 99.5% attending at least one ambulatory visit annually, with a median of 14 visits per year.[34]

Inadequate care for SCD often worsens the prevalence of anxiety, depression, and functional limitations. As state agencies evaluate the CMS Cell and Gene Therapy Access Model or other types of SCD care management (CM) initiatives, they should prioritize immediate actions to enhance outcomes, optimize utilization, and improve the quality of life for enrollees with SCD. This includes ensuring better access to existing therapies, specialized care, and support services. Individuals with end-organ damage from repeated VOCs face significantly greater losses in productivity, spending twice as much time seeking healthcare compared to those without SCD. This burden may severely limit their ability to focus on education, employment, and career development, further compounding their challenges.[35]

Figure 1 summarizes the diverse treatment options available for managing SCD, highlighting their benefits and limitations to support informed decision making and improved outcomes for individuals living with SCD.

FIGURE 1: TREATMENT OPTIONS FOR SCD

TREATMENT OPTIONS FOR SCD

TREATMENT OPTION	DESCRIPTION	BENEFITS	LIMITATIONS/RISKS
CELL AND GENE THERAPY (CGT)	Includes Lyfgenia and Casgevy, which modify or reactivate hemoglobin to prevent sickling of RBCs.	Durable therapy with significant reduction in VOCs.	High cost, complex manufacturing, limited availability, and eligibility criteria.
HYDROXYUREA (HU)	Stimulates HbF production to reduce VOCs and complications.	Reduces VOCs, stroke risk, and ACS.	Side effects include gastrointestinal upset and increased infection risk; uptake remains below 50% in many populations.
BLOOD TRANSFUSIONS	Increases healthy RBCs to improve oxygenation.	Improves tissue oxygenation and reduces stroke risk.	Risks include iron overload, infection, immune reactions, and quality-of-life impacts due to frequent procedures.

31. Desai, R. J., Mahesri, M., Levin, R., Globe, D., McKerracher, K., Mutebi, A., Bohn, R., et al. (2019). Clinical outcomes and healthcare utilization in patients with sickle cell disease: A nationwide cohort study of Medicaid beneficiaries. Blood, 134(Supplement 1), 3459. Retrieved February 24, 2025, from https://doi.org/10.1182/blood-2019-130373.

32. Attell, B. K., Barrett, P. M., Pace, B. S., McLemore, M. L., McGee, B. T., Oshe, R., DiGirolamo, A. M., et al. (2024). Characteristics of emergency department visits made by individuals with sickle cell disease in the U.S., 1999–2020. AJPM Focus, 3(1), 100158. Retrieved February 24, 2025, from https://doi.org/10.1016/j.focus.2023.100158.

33. Wilson-Frederick, S., Hulihan, M., Mangum, A., Khan, T., Geibel, M., Malsberger, R., Verghese, S., et al. (2021). Medicaid and CHIP sickle cell disease report,
T-MSIS Analytic Files (TAF) 2017. Centers for Medicare and Medicaid Services. Retrieved February 24, 2025, from https://www.medicaid.gov/medicaid/quality-of-care/downloads/scd-rpt-jan-2021.pdf.

34. Centers for Medicare and Medicaid Services. (2020). At a glance: Medicaid and CHIP beneficiaries with sickle cell disease (SCD), T-MSIS Analytic Files (TAF) 2017. Retrieved February 24, 2025, from https://www.medicaid.gov/medicaid/quality-of-care/downloads/sickle-cell-disease-infographic.pdf.

35. Campbell, A., Cong, Z., Agodoa, I., Song, X., Martinez, D. J., Black, D., Lew, C. R., et al.. (2020). The economic burden of end-organ damage among Medicaid patients with sickle cell disease in the United States: A population-based longitudinal claims study. Journal of Managed Care and Specialty Pharmacy, 26(9), 1121–1129. Retrieved February 24, 2025, from https://doi.org10.18553/jmcp.2020.20009.

TREATMENT OPTIONS FOR SCD			
TREATMENT OPTION	**DESCRIPTION**	**BENEFITS**	**LIMITATIONS/RISKS**
L-GLUTAMINE	Reduces oxidative damage to RBCs, decreasing the frequency of sickle cell crises.	Reduces crises, hospitalizations, and ACS.	Limited data on long-term efficacy; may not address all complications.
ADAKVEO (CRIZANLIZUMAB)	Monoclonal antibody therapy to reduce VOCs in patients ages 16 and up.	Reduces VOC frequency.	Withdrawn in Europe due to limited efficacy; requires regular infusions.
HEMATOPOIETIC STEM CELL TRANSPLANT (BMT)	Replaces faulty stem cells with donor cells to eliminate HbS production.	Can significantly reduce VOCs and associated organ damage.	Requires matched donor and specialized facilities; risks include rejection and long-term adverse effects like infertility.
PAIN MANAGEMENT	Includes NSAIDs and opioids like oxycodone or morphine to address acute and chronic pain from VOCs.	Reduces pain and improves quality of life during crises.	Risk of undertreatment, provider biases, and potential for opioid misuse or dependency.
PREVENTIVE CARE	Includes immunizations to prevent infections and transcranial Doppler (TCD) screenings for early stroke detection.	Prevents infections and reduces stroke risk.	Suboptimal uptake; only 59% of eligible children receive pneumococcal vaccination; TCD screening uptake at 37%.
SUPPORTIVE CARE SERVICES	Focuses on addressing social determinants, mental health needs, and education for improved care outcomes.	Improves quality of life and reduces functional limitations.	Gaps in access and insufficient integration with CM programs.

Optimize care management to drive access and improve quality of care

Traditionally, public payers and MCOs rely on CM programs to address access challenges, population health priorities, and specialized disease management for their beneficiaries. We have observed that while these programs are now standard across the Medicaid landscape, they sometimes become routine processes rather than the impactful, outcomes-driven services they are designed to be. With the introduction of CGT and the increasing focus on individuals living with SCD, payers should consider reassessing their objectives, reviewing their MCO contracts, and evaluating the role of CM in supporting members with SCD.

Effective CM programs typically advance four essential objectives:

1. Assess member needs.
2. Leverage data to ensure access to services.
3. Support the plan of care through training and education.
4. Build trust.

Programs that are poorly designed or inadequately managed or that lack robust data infrastructure will likely fall short of these goals, failing to deliver meaningful quality improvements for beneficiaries or payers. Successful CM programs begin by establishing open communication and inviting dialogue with members. Acknowledging a fundamental truth—few individuals, regardless of health status, want to be “managed” by their health plan—is key. Instead, enrollees and their families seek accurate information to make informed decisions as well as timely and reliable access to high-quality services. Before proposing solutions or services, CM teams must prioritize listening to the member’s experience of care. An approach rooted in appreciative inquiry helps uncover both positive and negative encounters, the unique challenges faced by individuals with SCD, and their specific needs from their health plan and providers.

For MCOs looking to launch or revitalize a CM program, conducting focus groups or structured interviews is key to uncovering enrollee experiences related to access, timeliness of care, provider expertise, transportation, and respect for the patient journey.[36] The insights gathered should inform the design of an SCD-specific CM program that genuinely reflects enrollee needs, fostering both trust and meaningful outcomes.

CM program element 1: assess member needs

It is common for CM programs to become bogged down by home-grown assessments and questionnaires. These tools can yield poorly structured data sets that can quickly complicate data analysis.

When conducting assessments, strong CM programs use statistically validated survey instruments. For SCD, this can include tools such as the Sickle Cell Disease Functional Assessment, which can provide valuable insights on the impact of SCD on functional, cognitive, and psychosocial status, as well as comorbidities and appropriate medication use.

Sharing assessment findings with providers ensures that care coordination services are both informed and actionable. As an example, CM programs that integrate assessments with a regional or statewide health information exchange (HIE) can efficiently collaborate with providers to identify enrollee needs and opportunities to enhance care. Examples of linking assessed needs to services could include initiating HU treatment during an inpatient admission, addressing gaps in preventive care, or connecting enrollees with an outpatient specialty provider prior to discharge.

SICKLE CELL CARE MANAGEMENT
ACTION ITEMS FOR MEANINGFUL RESULTS

TRAINING AND EDUCATION

- Health equity and disparities awareness.
- Evidence-based clinical practices.
- Programs for community health workers and peer navigators.
- Plan benefits, formulary, prior authorization.

BUILD TARGETED CARE NETWORKS

- SCD-trained primary care providers.
- Hematologists.
- Behavioral health specialists representing multiple licensures.
- Community health workers and navigators.
- Community-based programs and advocacy groups.

PROGRAM OPERATIONS

- Use care gaps, service delays, and consumer pain points to evaluate performance.
- Measure CM effectiveness using outcomes-based performance metrics.
- Track and trend access, quality of care, and utilization for pediatric, adolescent, and adult populations.

SEAMLESS ACCESS TO SERVICES

- Stress test organizational workflows to determine how seamless services are.
- Scrutinize opportunities for information sharing; leverage health information exchanges.
- Implement authorization-free zones.

OFFERING SUPPORTIVE BENEFITS

- Offer easily accessed add-ons such as QR-code enabled medic alert documentation, biometric wearables, and specialized SCD applications for mobile devices.

CM program element 2: leverage data to ensure access to services

Well-run CM programs leverage data to understand how members are accessing available services. These programs have robust reporting capabilities that easily, consistently, and accurately evaluate service utilization, including MCO provider networks, emergency services, telehealth, and primary and specialty care. This process ensures that the MCO is equipped to meet the unique needs of individuals with SCD.

Exploring service access may create opportunities to incorporate alternative care models, such as day treatment or infusion centers, which can enhance access to timely evaluation and treatment. Evidence suggests that these models can improve pain management and quality of life while reducing hospitalization rates, contributing to both clinical and operational efficiencies. Another approach is to target services for older adolescents moving from pediatric care to adult providers. Evidence suggests that during this sensitive transition, young individuals with SCD experience higher rates of potentially avoidable acute care utilization. Programs geared toward reducing the

36 Phillips, S., Chen, Y., Masese, R., Noisette, L., Jordan, K., Jacobs, S., Hsu, L. L., et al. (2022). Perspectives of individuals with sickle cell disease on barriers to care. PLoS One, 17(3), e0265342. Retrieved February 24, 2025, from https://doi.org/10.1371/journal.pone.0265342.

interval between ending pediatric service and beginning adult service can support appropriate utilization and better outcomes.[37,38]

In parallel with a strong CM program, states and MCOs should consider investing in services that leverage advisory boards, social media platforms, and remote meeting capabilities to engage with SCD affinity groups, Medicaid Advisory Committees, or similar bodies. These structures can improve outcomes by identifying care facilitators as well as barriers to care. Mobile applications that support independence, self-efficacy, and patient engagement, particularly among adolescents, can further enhance management and improve outcomes for individuals living with SCD.

Finally, MCOs can strengthen support for individuals with SCD by fully leveraging the provisions outlined in section 712(a) of the 2004 American Jobs Creation Act (AJCA), as detailed in the September 29, 2005, State Medicaid Director letter.[39] AJCA offers a range of targeted provisions for SCD, including access to genetic counseling, chronic blood transfusions, increased reimbursement for specialized care and services, and the availability of matching funds. Maximizing these resources can significantly enhance the quality of care for enrollees.

CM program element 3: support the plan of care through training and education

Before initiating outreach and enrollment for a CM program, it is essential to ensure that all team members and their partners are adequately trained and prepared to address the plan of care (POC). A comprehensive and effective POC will consider and address both the clinical and psychosocial impacts of SCD. Training to support the POC should encompass a broadly defined CM team, including licensed professionals, support staff, provider networks, and affiliated departments such as pharmacy and utilization management (UM). All stakeholders, including CM team members, provider groups, and internal business units, must have a clear understanding of the program's goals and objectives.

A comprehensive training curriculum is critical to this preparation. The content should cover the role of specialty providers and treatment centers, formulary benefits, and UM requirements, with the goal of equipping all involved to navigate the complexities of care. Additionally, training should emphasize strategies for identifying and mitigating internal barriers to care, streamlining services, and adopting a consumer-focused approach to operations. With thorough preparation and alignment, the CM program can deliver meaningful support to individuals living with SCD.

CM program element 4: build trust

If, at the end of a lengthy CM assessment or educational sessions, members still face barriers to care such as prolonged UM processes, inadequate provider networks, or failure to receive needed services, they may very well determine CM to be of little value and decline the next contact from the plan. Effective CM programs are in constant contact with all business units in the MCO and regularly evaluate processes and program outcomes to ensure that their efforts are effective and value-added. CM programs must break internal barriers. It is not enough for them to document challenges they encounter with processes, whether they are related to network gaps, prior authorizations, or other barriers. Instead, they must proactively raise these issues with leadership and collaborate on methods to address them. A program that fulfills its mission will engender the trust needed to support positive outcomes.

37 Howell, K. E., Kayle, M., Smeltzer, M. P., Nolan, V. G., Mathias, J. G., Nelson, M., Anderson, S., et al. (2024). Gaps during pediatric to adult care transfer escalate acute resource utilization in sickle cell disease. Blood Advances, 8(14), 3679–3685. https://doi.org/10.1182/bloodadvances.2023011268.

38 Calhoun, C., Luo, L., Baumann, A. A., Bauer, A., Shen, E., McKay, V., Hooley, C., et al. (2022). Transition for adolescents and young adults with sickle cell disease in a US Midwest urban center: A multilevel perspective on barriers, facilitators, and future directions. Journal of Pediatric Hematology/Oncology, 44(5), e872–e880. Retrieved February 24, 2025, from https://doi.org/10.1097/MPH.0000000000002322.

39 Centers for Medicare and Medicaid Services. (September 29, 2005). Letter to State Medicaid Directors. Retrieved February 24, 2025, from https://www.medicaid.gov/federal-policy-guidance/downloads/smd092905.pdf.

The road ahead

CM programs for SCD hold the potential to significantly improve patient outcomes and may even drive cost savings by reducing avoidable acute care utilization. However, their success depends on thoughtful design, effective management, and a person-centered approach. Medicaid managed care plans should invest in both quantitative analysis to measure the impact of their existing CM programs and qualitative reviews to ensure these programs deliver high-quality results while staying true to their intended design. For beneficiaries with SCD, targeted CM can play a vital role in connecting individuals with providers who have the expertise necessary to address the complexities of SCD, foster better health outcomes, and enhance quality of life.

Caveats and limitations

CGTs are an emerging therapeutic subject to modification over time. Consequently, the information presented in this analysis reflects the information available at the time of writing. The material in this paper represents the opinion of the authors and is not representative of the view of Milliman. Milliman is not advocating for or endorsing any specific views contained in this paper related to CGTs and case management for SCD.

The information in this paper is designed to provide insight into SCD treatments and the use of case management to support individuals with SCD. We do not intend this information to benefit any third party that receives this work product.

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milliman.com

CONTACT

Shelley Perino
shelley.perino@milliman.com

Rachel Ferguson
rachel.ferguson@milliman.com

Jim Davidson
jim.davidson@milliman.com