COMMERCE DEPARTMENT

Evaluation of HF XXXX – Coverage for Gene Therapy Treatment for Sickle Cell Anemia

Report to the Minnesota Legislature Pursuant to Minn. Stat. § 62J.26

January 28, 2025

Report Prepared By

This report was prepared by the American Institutes for Research (AIR) at the request of the Minnesota Department of Commerce. AIR created this document for internal use by the Minnesota Department of Commerce pursuant to Contract No. 216732. The document assumes reader familiarity with the proposed mandated health benefits currently under consideration by the Minnesota State Legislature. The document was prepared solely to assist the Minnesota Department of Commerce. No other use of this document or the information or conclusions contained herein is authorized. The period of data collection for any policies and literature analyzed for the proposed mandate ended on December 31, 2024.

Defrayal analysis completed by the Minnesota Department of Commerce is independent of AIR's evaluation.

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Upon request, this material will be made available in an alternative format such as large print, Braille or audio recording. Printed on recycled paper. A 508 compliant version of this report is forthcoming.

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Executive Summary

If enacted, this proposed mandate would require a health issuer to provide coverage for single administration gene therapies approved by the United States Food and Drug Administration (FDA) to treat sickle cell anemia (SCA). Additionally, Medical Assistance would be required to provide coverage for single administration gene therapies if the drug manufacturer does not enter into a value-based arrangement with the Commissioner of Human Services, or if the State does not obtain federal approval required for entering into such an arrangement.

While the language of this proposed mandate concentrates on SCA, research and federal programs focus on sickle cell diseases (SCD) as a whole. Due to this, information in this evaluation is often related to SCD, except where SCA-specific data is indicated.

SCD is an umbrella term that refers to a larger group of inherited blood disorders, the most common of which is SCA. In 2021, there were an estimated 959 Minnesotans living with SCD, of which 96% were African American and over half were covered by Medicaid. Individuals with SCD are estimated to have a 20-to-30-year shorter lifespan compared to the general United States population. However, this gap is closing with the development of new treatments, including gene therapies. In 2023, two single administration gene therapies were approved by the FDA for treatment of SCD in individuals 12 years and older (Casgevy and Lyfgenia). While these gene therapies are estimated to cost between $2 million and $3.3 million per patient, research indicates that they can improve quality of life and increase lifespan for individuals with SCD.

There are several federal and state laws related to the proposed coverage. Under the Centers for Medicare & Medicaid's Cell and Gene Therapy Access Model, state Medicaid agencies participating in the model will be required to provide coverage for all components of gene therapy, fertility preservation services, and ancillary services (e.g., travel expenses and case management) to qualifying enrollees seeking gene therapy for SCD. Multiple state Medicaid programs and commercial issuers have established coverage for Casgevy and/ or Lyfgenia for qualifying enrollees. In Minnesota, Minn. Stat. § 62Q.451 prohibits issuers from restricting treatment of rare diseases or conditions to only in-network providers. This statute enables individuals with rare diseases, such as SCD, to seek specialized care from providers or at treatment centers that may otherwise not be covered.

Public comments were largely supportive of this proposed mandate and stated that, if enacted, it would have positive health equity considerations and improve access to care for individuals with SCD. Respondents noted that the services required to be covered under this proposed mandate are unclear. Several commercial issuers stated that they already provide coverage for gene therapy for SCA.

An actuarial analysis was not feasible for the proposed mandate due to the recent FDA-approval of the treatments included in the proposed coverage. The potential utilization, cost trends, costs associated with manufacturer agreements and otherwise are not readily accessible from the available data.

The potential state fiscal impact of this mandate is as follows:

- There is no estimated cost for the State Employee Group Insurance Program because gene therapy for SCA is covered in the program's medical benefit package.

- There are no estimated defrayal costs associated with this proposed mandate.
- This proposed mandate would apply to Minnesota Health Care Programs (e.g., Medical Assistance and MinnesotaCare) and may have a cost.

Introduction

In accordance with Minn. Stat. § 62J.26, the Minnesota Department of Commerce (Commerce), in consultation with the Minnesota Department of Health (MDH) and Minnesota Management and Budget (MMB), performs an evaluation of benefit mandate proposals. For evaluation criteria and required evaluation components, please review the Evaluation Report Methodology, available at https://mn.gov/commerce/insurance/industry/policy-data-reports/62j-reports/.

Bill Requirements

House File (HF) XXXX is sponsored by Representative Liz Reyer. At the time Commerce received the request for evaluation, the bill had not yet been introduced.

If enacted, this bill would require a health issuer to provide coverage for single administration gene therapies approved by the United States Food and Drug Administration (FDA) to treat sickle cell anemia (SCA). The restrictions for accessing the treatment cannot be stricter than those imposed for other medical treatments covered by the health issuer, such as requirements for prior authorization or step therapy.

Additionally, Medical Assistance would be required to provide coverage for single administration gene therapies if the drug manufacturer does not enter into a value-based arrangement with the Commissioner of Human Services, or if the State does not obtain federal approval required for entering into such an arrangement.

This proposed mandate would apply to fully insured small and large group commercial health plans, individual market plans, the State Employee Group Insurance Program (SEGIP), and Minnesota Health Care Programs (e.g., Medical Assistance and MinnesotaCare). This would not apply to self-insured employer plans, grandfathered plans, and Medicare supplemental policies.

This bill would create Minn. Stat. § 62Q.511 and amend Minn. Stat. § 256.969, by adding a subdivision.

Related Health Conditions and Associated Services

While the language of this proposed mandate concentrates on SCA, research and federal programs focus on sickle cell diseases (SCD) as a whole. Due to this, information in this evaluation is often related to SCD, except where SCA-specific data is indicated.

SCA is an inherited blood disorder, and one type of SCD. SCD impacts the shape of red blood cells, causing them to be shaped like crescent moons and become rigid and sticky which can slow blood flow.[1] This can result in a vaso-occlusive crisis (VOC), where blood flow to a body part is obstructed by the sickled blood cell.[2] This

obstruction can occur in the limbs, organs, joints, etc. The effects of occlusion can result in a variety of symptoms and outcomes, including but not limited to severe pain and organ failure.

Two gene therapies for SCD, Casgevy and Lyfgenia, were approved by the FDA in December 2023. These gene therapies are approved for patients 12 years or older. Both treatments follow a similar regimen which includes but is not limited to the following treatment steps:[3,4]

- Pre-treatment, including blood transfusions and/or mobilization medicine;
- Collection of an individual's stem cells which are used to make the treatment;
- Chemotherapy, to clear cells from bone marrow and make room for the treatment;[5]
- Stem cell transplantation with gene therapy infusion;
- Recovery and monitoring in hospital for 4-6 weeks; and
- Long-term monitoring and follow-up.

Patients with these treatments may experience a significant reduction in symptoms associated with SCA, with primary outcomes for these therapies targeting "freedom" from severe VOCs.[6]

Related State and Federal Laws

This section provides an overview of state and federal laws related to the proposed mandate and any external factors that provide context on current policy trends related to this topic.

Relevant Federal Laws

There are no federal laws directly requiring coverage for gene therapy treatment for SCA. The Orphan Drug Act of 1983 was enacted to provide incentives and reduce barriers to promote research and development of orphan drugs, which are typically unprofitable and otherwise unpursued novel therapies used to treat rare diseases, including SCD.[7] The FDA has granted orphan drug designation to multiple treatments for SCD, including Lyfgenia in 2014[8] and Casgevy in 2020[9]. These designations assisted in the development of each treatment and led to their dual approvals as the first cell-based gene therapies for SCD in December 2023.[6]

In October 2022, President Biden issued an executive order[a] on lowering prescription drug costs for Americans, which included the implementation of a new health care payment and delivery model for innovative drug therapies for Medicare and Medicaid enrollees.[10] In response to this order, the Cell and Gene Therapy (CGT) Access Model was created by the Centers for Medicare & Medicaid Services (CMS) to increase access to transformative treatments for Medicaid enrollees with rare and severe diseases by forming outcomes-based agreements between state Medicaid agencies and drug manufacturers.[11] The first type of gene therapy approved under this model is for SCD. State Medicaid agencies participating in the CGT model will be required to provide coverage for all components of gene therapy, fertility preservation services, and ancillary services (e.g.,

[a] President Trump issued an executive order on January 21, 2025 revoking Executive Order No. 14087.

travel expenses and case management) to qualifying enrollees. The manufacturers participating in the CGT model with SCD therapies are Vertex Pharmaceuticals which produces Casgevy and Bluebird Bio, Inc. which produces Lyfgenia.[12] Participation in the CGT model begins on a rolling basis in 2025.

The Sickle Cell Data Collection Program, administered by the Centers for Disease Control and Prevention (CDC), focuses on improving quality of life and health outcomes for those living with SCD through data such as the newborn screening program, hospital and emergency room data, and Medicaid claims.[13] There are currently 16 states, including Minnesota, that are participating in this program. Additionally, the Minnesota Department of Health recently received a 5-year grant from the CDC to further Sickle Cell Data Collection efforts toward understanding the impact of SCD in Minnesota.[14] The data collected through the Sickle Cell Data Collection program and CDC grant will allow researchers to better understand SCD, the population impacted, SCD effects on health, and future treatment opportunities.

Relevant Minnesota Laws

Minn. Stat. § 62Q.451 prohibits issuers from restricting where enrollees can receive services for the diagnosis, monitoring, and treatment of rare diseases or conditions.[15] Prohibited restrictions include, but are not limited to prior authorization, preauthorization, and increased fees. This statute enables individuals with rare diseases, such as SCD, to seek specialized care from providers or at treatment centers that may otherwise not be covered.

Minn. Stat. § 256.969, subd. 32 states that if Minnesota receives federal approval to enter into a value-based arrangement with a drug manufacturer, the Commissioner may provide reimbursement for treatments relating to cell or gene therapy for rare diseases if they occur in the inpatient hospital setting.[16] This reimbursement is contingent upon the drug manufacturer entering into a value-based agreement with the Commissioner and using the outpatient methodology for biological products.

In April 2024, HF 5428 was introduced in the Minnesota legislature to require the Commissioner of Human Services to conduct an annual review of all treatment modalities and services for SCD covered by Medical Assistance.[17] The review would determine whether the currently covered medications, treatments, and services are adequately meeting the needs of enrollees with SCD, or if additional options should be covered. If HF 5428 is passed, coverage for gene therapy for SCD may be assessed annually.

State Comparison

State coverage of gene therapy for SCD is rapidly evolving due to the recent FDA-approval for Casgevy and Lyfgenia. As the one-year anniversary of the approvals approaches, it is likely there will be additional policy changes across states to include gene therapy in coverage requirements for SCD, especially with the initiation of the CGT Access Model for state Medicaid agencies in 2025. Currently, there are no state mandates requiring coverage for gene therapy for SCD.

While current coverage for gene therapy varies by state, all commercial plans and state Medicaid programs cap coverage at one treatment per lifetime. Eligible enrollees are required to meet medical necessity criteria and complete prior authorization protocols before receiving coverage for gene therapy treatment. Some prior

authorization protocols include a requirement for enrollees to have exhausted other treatment options (e.g., stem cell transplant) prior to receiving authorization for gene therapy.

Several commercial issuers have added coverage for gene therapy for SCD to their qualifying enrollees. Some Blue Cross Blue Shield plans (e.g., Kansas,[18,19] Louisiana,[20,21] Massachusetts,[22] and North Dakota[23,24]) provide coverage for both Casgevy and Lyfgenia. Cigna Healthcare currently provides coverage for both gene therapies, with the Children's Hospital of Philadelphia being the current participating in-network provider for both treatments as of September 2024.[25–27]

Multiple state Medicaid programs have established coverage for Casgevy and/ or Lyfgenia for qualifying enrollees. Two states (Kansas[28] and Nevada[29]) provide coverage for both gene therapies through their Medicaid preferred drug list. Ohio provides coverage for both gene therapies and all medically necessary inpatient or outpatient hospital claims associated with treatment under the Ohio Medicaid Fee-for-Service medical benefit, inclusive of Medicaid Managed Care.[30] Tennessee provides coverage for both gene therapies through Medicaid Managed Care Organizations.[31] Michigan was the first state to sign an outcomes-based agreement with Bluebird Bio, Inc., which will provide qualifying Medicaid enrollees with coverage of Lyfgenia.[32]

Public Comments Summary

Commerce solicited public input on the potential health benefit mandate through a request for information (RFI) posted to Commerce's website and the Minnesota State Register. The summary below represents only the opinions and input of the individuals and/or organizations who responded to the RFI.

Key Stakeholder Comment Themes

For this proposed mandate, Commerce received RFI responses from four commercial health issuers, one health care organization, three advocacy organizations, and one health care provider.

Coverage Inclusion and Health Equity. One respondent expressed that comprehensive coverage of gene therapy for SCD should also include associated inpatient hospital stays, long-term follow-up, and fertility services. They noted the proposed mandate would make gene therapy for SCD more affordable and increase access to treatment options for eligible enrollees. Two respondents noted that the proposed mandate would promote health equity for those disproportionately affected by SCA, such as African Americans, and would increase access to treatment that may otherwise be too costly.

Current Coverage and Limiting Factors. Multiple health issuers indicated that gene therapy for SCA is already a covered service included in their health plan, but expressed concern that the proposed mandate would limit their ability to update medical and coverage policies in response to the rapidly evolving medical evidence base and current market trends. They also mentioned that limiting coverage to SCA may create coverage barriers and inequities relative to other conditions with FDA-approved gene therapies.

Cost and Long-Term Outcomes. Two respondents noted that while gene therapy has a high up-front cost, the potential savings due to treating the underlying cause of disease, reducing the severity of illness, and decreasing

health care utilization make gene therapy for SCA cost-effective. However, another respondent expressed concern that while there is strong evidence on the clinical benefits of gene therapy for SCA in the short-term, long-term effectiveness is less known. Some respondents expressed concerns that the proposed mandate would require coverage for enrollees that may not be appropriate for gene therapy, potentially increasing premiums. Another potential increase to premiums was linked to Minn. Stat. § 62Q.451, which prohibits issuers' ability to require in-network providers for treatment of rare diseases.

Parity in Public and Private Insurance. One respondent highlighted the need for further discussions with the Department of Human Services regarding participation in federal coverage models for Medical Assistance and MinnesotaCare, to ensure parity in coverage between public and private insurance in Minnesota.

General Comments. One respondent highlighted Minnesota's implementation of Minn. Stat. § 62M.07, effective January 1, 2026, which prohibits prior authorization for certain medical conditions, including outpatient mental health or substance use disorder treatment, antineoplastic cancer treatment per National Comprehensive Cancer Network® guidelines (excluding medications), preventive services, pediatric hospice care, neonatal abstinence program treatment by pediatric pain or palliative care specialists, and chronic condition treatment. The respondent suggested that many of this year's proposed mandates fall under this new statute and expressed concerns that removing prior authorization could increase health care costs and negatively affect health outcomes for Minnesotans. Several respondents agreed that without prior authorization for gene therapy for SCA, the proposed mandate would increase premiums.

Another respondent noted that all of the proposed health benefit mandates have the potential to broadly improve health outcomes for Minnesotans by enhancing their quality of life, supporting individuals, families, and caregivers, and increasing workforce participation, while also benefiting the broader health care system.

Cost Estimates Provided in Stakeholder Comments

Stakeholders and MMB provided the following cost estimates related to the proposed benefit mandate:

- MMB does not estimate any state fiscal impact to the state plan, as SEGIP currently provides coverage for gene therapy for SCA in its medical benefit package (see State Fiscal Impact section).
- Several commercial health insurance plans in Minnesota currently provide coverage for gene therapy for SCA. According to one respondent, if enacted, there would be no immediate cost impact as the proposed mandate aligns with current coverage. However, another respondent noted that if coverage is expanded (e.g., inpatient stays are included in coverage), there would be an increase in premiums as these expenses are not currently integrated into reimbursement methodologies.

Stakeholders' results may or may not reflect generalizable estimates for the mandate, depending on the methodology, data sources, and assumptions used for analysis.

Evaluation of Proposed Health Benefit Mandate

Methodology

The following section includes an overview of the literature review and actuarial analysis performed to examine the potential public health and economic impact of the mandate. The literature review includes moderate- to high-quality relevant peer-reviewed literature and/or independently conducted research with domestic data that was published within the last 10 years and is related to the public health, economic, or legal impact of the proposed health benefit mandate. For further information on the literature review methodology, please reference https://mn.gov/commerce/insurance/industry/policy-data-reports/62j-reports/.

Public Health Impact

SCD is the most common inherited blood disorder in the United States.[33] SCD is an umbrella term that refers to a larger group of disorders caused by a gene mutation in the *β-globin* gene on chromosome 11. This mutation results in the production of abnormal hemoglobin, which is a part of red blood cells that help carry oxygen, known as hemoglobin S (HbS).[34] Individuals that inherit one HbS gene and one normal gene have a condition called sickle cell trait. Individuals with sickle cell trait are considered carriers and do not display symptoms of SCD but can pass the HbS gene on to children. Individuals with SCD have two abnormal β-globin genes, which can range in type and severity (see **Table 1**).[35]

Table 1. Common Types of Sickle Cell Disease

Type	Gene Mutations	Severity of Disease
HbSS (Sickle Cell Anemia)	2 HbS genes	Severe
HbSC	1 HbS gene & 1 HbC gene	Mild
HbS beta thalassemia (“Zero” and “Plus” types)	1 HbS gene & 1 beta thalassemia gene	“Zero” type: severe “Plus” type: mild

Prevalence and Newborn Screening. It’s estimated that up to 100,000 Americans have SCD.[36] SCD disproportionately affects populations with ancestral origins in sub-Saharan Africa, the Mediterranean, the Middle East, and parts of India and Southeast Asia due to sickle cell trait’s protective effect against malaria.[34,37] Because of this, 1 in 365 African American births and 1 in 16,000 Hispanic-American births result in a SCD diagnosis.[38,39] Due to this disparity, prevalence rates vary across states, with the highest rates of SCD reported in states with larger African American populations.[34]

The CDC recommended universal newborn screenings for inherited blood disorders, such as SCD, starting in 1988.[38] MDH implemented a newborn screening program in 1964, and following the CDC recommendation started screening for the three most common types of SCD (see Table 1) in 1988.[40,41] In 2021, 101 newborns screened positive for SCD in Minnesota and 2,776 screened positive for sickle cell trait through the newborn screening program.[42] In total, there are an estimated 959 Minnesotans living with SCD as of 2021. Of these Minnesotans, 55% were female and 84% were below the age of 50.

Symptoms, Hospitalizations, and Life Expectancy. Individuals with SCD typically start experiencing symptoms between 5 months to one year of age.[35] These symptoms can range in severity and lead to delayed growth and development in children. Some of the most common symptoms include fatigue, anemia, stroke, organ damage, and increased susceptibility to infections.[34,43] VOCs, which occur from obstruction of blood flow by sickled blood cells and limit oxygen delivery to tissues, are the most common symptom. VOCs can cause severe pain, organ damage, and death.[6] VOCs can also weaken blood vessel walls, which leads to a reoccurrence of VOCs.[6,44] Because of their serious and often frequent nature, VOCs are the most common reason for hospitalization for individuals impacted by SCD.[45,46]

Approximately 50% of individuals living with SCD experience one or more emergency department (ED) visit(s) in a year, and 88% have at least one of these visits during a 10-year timeframe.[47] These types of visits peak in early adulthood and may be attributed to the lack of primary care providers specializing in SCD as individuals transition from pediatric to adult care.[37] Across the United States, approximately 250,000 ED visits and 90,000 hospitalizations were due to SCD complications in 2014.[37] Due to the lack of primary care providers specializing in SCD, individuals may frequent the ED and hospital.[34] This may be detrimental to individuals with SCD as individuals experiencing VOCs in the ED had wait times 70-75 minutes longer than the guideline recommendations for treatment, which can result in irreversible tissue damage, inflammation, and extended length of pain.[37] The most common VOC treatment received in the ED is pain management, which can include opioids and non-steroidal anti-inflammatory drugs (NSAIDs).

Due to the beforementioned complications, individuals living with SCD have a lower quality of life than the average American, and may impact the ability of individuals with SCD to stay employed or attend school.[36] Individuals with SCD are estimated to have a 20-to-30-year shorter lifespan compared to the general U.S. population.[37,43] Deaths related to SCD most commonly occur due to acute events (e.g., infection or cerebrovascular events) in younger individuals and from chronic complications (e.g., chronic cardiac complications or renal disease) in older individuals.[43]

SCD Trends. Increased understanding of SCD has led to improved treatment and increased lifespan. In 1979, the median age at death for individuals with SCD was 28 years and by 2017 the median age at death was 43 years.[43] Survival rates for children with SCD under the age of 18 have improved with 94% of individuals with SCD surviving to adulthood in 2010 compared to an 86% survival rate in 2004.[37] However, this shift in lifespan has increased mortality rates for young adults, specifically those between the ages of 20 to 24, due to the transition from specialized pediatric care to the more limited adult care setting.[37]

Standards of Care. The American Society of Hematology produced guidelines in 2020 for SCD prevention, SCD diagnosis, pain management related to SCD, and treatment for cerebrovascular disease in children and adults.[48,49] Standard medical care for SCD varies widely depending on the individual's needs and can include preventive care, medications, complication-specific treatment, and disease-modifying therapy. Preventive care typically includes lifestyle behaviors such as ensuring adequate fluid intake, avoiding extreme temperatures, preventive medical screenings, and blood transfusions.[34] Medications can include hydroxyurea or L-glutamine to reduce frequency of VOCs and opioids or NSAIDs for pain management.[34,37] However, all of these medications are typically under-prescribed and individuals with SCD report barriers related to access, price, and prior authorization.[37,45] Complication-specific treatment can range from antibiotics, to transfusion therapy, or

pulmonary hypertension management.[34] Bone marrow and stem cell transplants are potential curative options for SCD, however these treatments are restricted to individuals with severe SCD due to their complexity and risks.[34,44] Complications include graft rejection, infertility, and increased short-term risk of mortality.[36] Additionally, both treatments require a matched donor which may be difficult to identify.[39] Treatments other than FDA-approved cell and gene therapies are not covered by the proposed mandate.

Gene Therapies for Sickle Cell Disease. On December 8, 2023, two single administration gene therapies were approved by the FDA for treatment of SCD in individuals 12 years and older: Exagamglogene Autotemcel (Casgevy) and Lovotibeglogene Autotemcel (Lyfgenia). [6,50,51] Casgevy is the first one-time gene therapy that uses CRISPR/Cas9 gene editing technology to receive FDA approval across inherited blood disorders.[44] This gene editing technique prevents the sickling of red blood cells and improves oxygen delivery, thereby reducing the mortality and morbidity associated with SCD. Casgevy uses an individual's own modified blood stem cells to increase normal hemoglobin levels and improve the production of red blood cells. This treatment ultimately reduces the number of VOCs in treated individuals, and in some cases eliminates VOCs entirely. Casgevy was approved to treat individuals 12 years of age and older living with SCD and experiencing recurring VOCs.[50]

Lyfgenia is also a one-time gene therapy, but it works by genetically altering an individual's blood stem cells through adding functional copies of the *β-globin* gene to help the body make anti-sickling hemoglobin.[51] This can potentially decrease or stop VOCs leading to an increased quality of life. Lyfgenia was approved by the FDA to treat individuals living with SCD ages 12 and above that have a history of VOCs.

Both Casgevy and Lyfgenia utilize a six step system for their treatment that can take approximately nine months to a year to complete.[50,51] For both gene therapies, these steps include pre-treatment, stem cell collection from the individual with SCD, creation of individually tailored Casgevy or Lyfgenia in a laboratory, conditioning chemotherapy, infusion of either Casgevy or Lyfgenia, and recovery with long-term follow-up. As of January 2025, the M Health Fairview University of Minnesota Medical Center is the only authorized treatment center for Casgevy and there are no authorized treatment facilities for Lyfgenia in Minnesota. Residents seeking Lyfgenia treatment would need to travel out of state for some treatment steps. If enacted, there may be additional authorized treatment facilities by the time the mandate goes into effect.

Gene Therapy Side Effects. As Casgevy and Lyfgenia are administered in similar manner, they have many overlapping side effects. Common side effects include mouth sores, low platelet and white blood cell levels, and febrile neutropenia.[44] Specific to Casgevy, individuals reported nausea, musculoskeletal pain, abdominal pain, vomiting, headache, and itching.[6] Specific to Lyfgenia, individuals reported low blood pressure and hot flushes.[51]

Casgevy and Lyfgenia both use chemotherapy as part of their treatment plans, which can lead to infertility.[50,51] Individuals considering gene therapy may elect to use fertility preservation options prior to receiving chemotherapy to mitigate this. Additionally, due to the nature of these gene therapies, individuals that receive this treatment are not able to donate blood, organs, tissues, or cells post-treatment.[50,51] Some individuals that received Lyfgenia have reported receiving a diagnosis of blood cancer.[44] Because of this risk, it is recommended individuals treated with Lyfgenia be monitored at least every 6 months for a minimum of 15 years.

Gene Therapy Clinical Effectiveness. Casgevy's clinical trial included 35 participants with severe SCD, defined as having at least two severe VOCs in each of the two years prior.[6] After treatment, 93.5% of participants did not have a severe VOC for 12 consecutive months and 100% of participants were not hospitalized for severe VOC for 12 consecutive months.[50] The average length of time without a severe VOC was 22.2 months. Overall, participants reported improved quality of life (e.g., physical, social, and emotion wellbeing) during the 18-month follow-up period.[36]

Lyfgenia's clinical trial started in February 2015 and included 45 participants with a history of VOCs between the ages of 12 and 50 that were not able to effectively use other treatment modalities for management (e.g., hydroxyurea or hematopoietic cell transplant).[6,36,51] After treatment, 88% of participants did not experience a VOC in the following 6 to 18 months and 94% of participants did not experience a severe VOC in the following 6 to 18 months.[51] Additionally, Lyfgenia was found to lower the average hospital days and admissions for participants at a 24-month follow-up.[36] Overall, participants reported improved quality of life from baseline. The clinical trial found no clinically meaningful differences in safety or efficacy between adolescents and adults.

Health Equity. Overall, individuals with SCD face systemic racism, including disparities in access to care, and underfunding for treatment research.[36] Genetic counseling and carrier screening programs are crucial in identifying individuals who have an elevated risk of having children with SCD to allow for informed family planning decisions. However, African Americans consistently face difficulty in accessing these preventive services.[34] When it comes to treatment, there is a lack of available centers and specialized providers which creates additional barriers to care, especially in low-income and rural areas.[37] This gap ultimately leads to poorer outcomes for individuals with SCD who are unable to access specialized care. Another gap is access to opioids and other medications for pain relief. In 2014 the National Heart, Lung, and Blood Institute recommended opioids for severe SCD pain; however, many individuals with SCD that request this treatment are stigmatized and face access barriers due to increased restrictions and oversight of opioids resulting from the opioid epidemic.[37] In 2019, CMS released a policy statement recommending Medicare enrollees with SCD be exempt from any opioid restrictions due to the need to treat their severe pain. SCD is also under-researched and underfunded compared to other rare diseases.[37] This inequity prevents further research into alternative therapies for a population that already faces discrimination in the health care setting.[52] The degree to which the proposed coverage might address health equity considerations for individuals living with SCD has not been specifically evaluated in the current literature.

Economic Impact

Due to the wide range of treatments for SCD, costs vary from person to person. In the United States, direct medical costs for all individuals living with SCD are estimated to be nearly $3 billion annually.[36] Lifetime medical costs for an individual with SCD are estimated to be between $1.1 million to $1.7 million.[37,46] It is estimated that individuals may pay up to $44,000 in out-of-pocket expenses related to SCD in their lifetime.[46] Many of these costs are associated with related complications (e.g., VOCs), which can occur more frequently due to decreased access to specialty care, and can often require ED visits.[52] The specific costs for Minnesota are not readily accessible from the available data.

Gene Therapy Costs. Total costs for Casgevy and Lyfgenia, including all six steps of treatment, are estimated to be between $2 million and $3.3 million per patient.[36,53,54] Women with SCD who receive gene therapy are estimated to have an increased 9.8 quality-adjusted life years (QALYs) compared to women who receive standard of care treatment, and this results in a $1.8 million increase in treatment cost.[54] Men with SCD who receive gene therapy are estimated to have an increased 8.9 QALYs compared to men who receive standard of care treatment, and this results in a $1.6 million increase in treatment cost.[54] These estimates do not consider downstream savings or the estimated $454,483 increase in lifetime earnings for individuals who receive Lyfgenia.[53]

Insurance Coverage. The majority of individuals with SCD are publicly insured through state Medicaid programs or Medicare.[37] Nationally, the average Medicaid enrollee with SCD is 28.5 years old and 58.2% are female.[45] When looking at annual utilization in this population, 29.5% received blood transfusions, 24.9% used hydroxyurea, and 70.7% received prescription opioids. Of Medicaid enrollees with SCD, 48.1% experienced acute complications and 47.5% had chronic complications annually. An estimated 55% of enrollees had one or more VOCs requiring a health care visit in a year, with the majority of these managed in the inpatient setting (46.1%), followed by the ED (35%) and the outpatient setting (19%).[45] The total annual all-cause health care cost for enrollees with one VOC is $29,880.[45] Medicaid enrollees with SCD face additional barriers to accessing care due to limitations on coverage for specialized health care. While more individuals with SCD have Medicaid coverage compared to commercial coverage, it has been shown that fewer Medicaid enrollees visit a hematologist compared to their commercial counterparts, which can result in negative health outcomes.[37,39]

The average Medicare enrollee with SCD is 48.2 years old and 59.6% are female.[45] Approximately 77.4% of this population are enrolled in Medicare under age 65 due to disability status. More than a third (34.3%) received blood transfusions annually, 22.6% used hydroxyurea annually, and 66.8% received prescription opioids annually.[45] Of Medicare enrollees with SCD, 65.3% experienced acute complications and 70% of enrollees had chronic complications annually. Approximately 64% of this population had one or more VOCs requiring a health care visit in a year, with 37.7% occurring in the in-patient setting, 32.2% in the out-patient setting, and 30.1% in the ED.[45] The total annual all-cause health care cost for Medicare enrollees with one VOC is $29,250.[45] Of the treatment settings, inpatient was the most expensive.

The typical commercially-insured enrollee with SCD is 36.7 years old and 61.4% are female.[45] In this population, 6.3% received blood transfusions annually, 9.7% used hydroxyurea annually, and 45.4% received prescription opioids annually.[45] Commercial enrollees experiences the lowest percent of acute complications at 36.7% and experienced chronic complications at 36.8% annually. Nearly 36% of enrollees experienced one or more VOC requiring a health care visit in a year, with 37.4% being treated in the in-patient setting, 36.2% treated in the out-patient setting, and 26.4% treated in the ED.[45] The total annual all-cause health care cost for enrollees with one VOC is $27,194.[45] As seen by the lower treatment rates compared to the Medicaid and Medicare populations, individuals that are commercially-insured tend to have fewer complications, which suggests that this population is healthier or has less severe forms of SCD.

Due to Casgevy and Lyfgenia's recent FDA approval, there is limited information regarding coverage for these gene therapies. Under the Patient Protection and Affordable Care Act (ACA) commercial payers are required to

cover routine patient care costs for enrollees participating in clinical trials, such as those for gene therapy for SCD.[39] This requirement does not apply for individuals insured through Medicaid.

Limitations

A more comprehensive impact assessment of the proposed coverage is not readily available from the literature, given the relative novelty of the gene therapies and current coverage environment for individuals with SCD. Casgevy and Lyfgenia were approved in December 2023, so there is limited research currently available on these treatments. Their clinical trials included small sample sizes and limited follow-up timeframes which may lead to uncertainty regarding the long-term safety and durability of these gene therapies.[36] Their trials did not directly compare Casgevy or Lyfgenia to other established treatments, such as stem cell transplantation, so it is unclear when one treatment type may be more appropriate for a given individual. It is likely that more research related to cost and clinical effectiveness will be available in the future as the treatment becomes more widely available to the SCD population across the United States.

Additionally, it is unclear whether the coverage in the proposed health benefit mandate includes all associated treatment steps (e.g., fertility preservation) and the potential long-term follow-up care required for single-administration gene therapy for SCD. It is also unclear whether travel costs would need to be considered for the proposed mandate.

Data Limitations

Due to the recent FDA-approval of the treatments included in the proposed coverage, an actuarial analysis to estimate the potential economic impact of the mandate is not feasible. Actuarial analysis of claims in the Minnesota All Payer Claims Database requires that covered treatments from a period greater than three years be available at the time of evaluation to ensure accuracy of the analysis. Additionally, the potential utilization, cost trends, costs associated with manufacturer agreements and otherwise are not readily accessible from the available data related to the proposed coverage.

State Fiscal Impact

The potential state fiscal impact of this proposed mandate includes the estimated cost to SEGIP as assessed by MMB in consultation with health plan administrators, the cost of defrayal of benefit mandates as understood under the ACA, and the potential impact to Minnesota Health Care Programs.

- This proposed mandate is estimated to have no fiscal impact on SEGIP.
- There are no estimated defrayal costs associated with this proposed mandate.
- The proposed mandate would apply to Minnesota Health Care Programs (e.g., Medical Assistance and MinnesotaCare) and may have a cost.

Fiscal Impact Estimate for SEGIP

MMB does not estimate any state fiscal impact to the state plan, as SEGIP currently provides coverage for gene therapy treatment for SCA.

Patient Protection and Affordable Care Act Mandate Impact and Analysis

States may require qualified health plan issuers to cover benefits in addition to the 10 essential health benefits (EHBs) defined by the ACA but must defray the costs, either through payments to individual enrollees or directly to issuers, and can partially defray the costs of proposed mandates if some of the care, treatment, or services are already covered in the state's benchmark plan or mandated by federal law, pursuant to section 1311(d)(3)(b) of the ACA. For further defrayal requirements and methodology, please visit https://mn.gov/commerce/insurance/industry/policy-data-reports/62j-reports/.

If enacted, HF XXXX would not constitute an additional benefit mandate requiring defrayal, as it does not relate to any new requirements for specific care, treatment, or services that are not already covered by Minnesota's benchmark plan. Minnesota's benchmark plan includes coverage for outpatient services, specialist visits, specialty drugs, laboratory testing, chemotherapy, and infusion testing, which broadly cover the administration and pre-administration stages of the approved treatments.[55]

Fiscal Impact of State Public Programs

This proposed mandate would apply to Minnesota Health Care Programs (e.g., Medical Assistance and MinnesotaCare) and may have a cost. Medical Assistance and MinnesotaCare cover all FDA-approved cell and gene therapies,[15] but cost may be incurred from the specific coverage requirements. However, a fiscal estimate has not yet been completed on this proposed mandate.

Appendix A. Bill Text

Section 1. **[62Q.511] GENE THERAPY; SICKLE CELL ANEMIA.**

A health plan must provide coverage for single administration gene therapies approved by the U.S. Food and Drug Administration (FDA) for the treatment of sickle cell anemia. A health plan must not apply more restrictions to enrollee access for this treatment than are applied to other medical treatments covered by the health plan, including, but not limited to, prior authorization or step therapy requirements.

EFFECTIVE DATE. This section is effective January 1, 2026, and applies to health plans offered, issued, or renewed on or after that date.

Sec. 2. Laws 2024, chapter 127, article 54, section 5, is amended to read:

Sec. 5. Minnesota Statutes 2022, section 256.969, is amended by adding a subdivision to read:

Subd. 32. **Biological products for cell and gene therapy.**

(a) Effective July 1, 2025, and upon necessary federal approval of documentation required to enter into a value-based arrangement under section 256B.0625, subdivision 13k, the commissioner may provide separate reimbursement to hospitals for biological products provided in the inpatient hospital setting as part of cell or gene therapy to treat rare diseases, as defined in United States Code, title 21, section 360bb, if the drug manufacturer enters into a value-based arrangement with the commissioner.

(b) The commissioner shall establish the separate reimbursement rate for biological products provided under paragraph (a) based on the methodology used for drugs administered in an outpatient setting under section 256B.0625, subdivision 13e, paragraph (e).

(c) If federal approval of the required documentation to enter into a value-based arrangement under paragraph (a) is not obtained, or if a drug manufacturer does not enter into a value-based arrangement with the commissioner for single administration gene therapies for the treatment of sickle cell anemia, medical assistance coverage of gene therapy must meet the requirements of section 62Q.511, effective January 1, 2026.

Appendix B. Key Search Terms for Literature Scan

Beta-Globins

Casgevy

Cell and gene therapy

Chemotherapy

Clinical trials

Gama-Globins

Gene editing

Gene therapy

Genetic therapy

Genetic vectors health disparities

Hemoglobin

Lyfgenia

Severe vaso-occlusive episodes cost-effectiveness

Sickle cell

Single gene therapy

Stem cell therapy

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