MILLIMAN WHITE PAPER

CMS Cell and Gene Therapy Access Model

Exploring the benefits, limitations, and considerations for expansion

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The introduction of the Cell and Gene Therapy Access Model by CMS presents a promising option for Medicaid programs, aiming to address the complexities and financial uncertainties associated with these therapies.

Cell and gene therapies (CGTs) represent a revolutionary frontier in modern medicine. In contrast to most traditional therapies that treat symptoms of the disease, CGTs work by targeting and repairing or replacing abnormal genes or cells, thus treating the origin or root cause of the condition. These therapies have short or one-time administrations associated with treatment while (potentially) providing years of clinical benefit. Benefits may include delay or prevention of disease progression, symptom alleviation, and/or improvements in quality of life.

While these therapies are a promising treatment option for certain patients with rare diseases, the cost of CGTs has been record-setting. As of March 2024, the current single-administration gene therapies approved by the U.S. Food and Drug Administration (FDA) were priced between $850,000 and $4.25 million. All of the gene therapies, except Luxturna, were priced at or above $2.2 million. Single-administration cell therapies were priced lower than gene therapies, ranging between $338,000 and $543,000 (1). However, the episodic cost associated with administration and monitoring can add significant financial uncertainty, with some cell therapies reported to have cost of care (excluding the drug cost), exceeding $1 million (2).

To address the cost and clinical uncertainties associated with CGTs, the Centers for Medicare and Medicaid Services (CMS) proposed the CGT Access Model in January 2024. This new model intends to enable access to outcomes-based agreements (OBAs) for state Medicaid programs. This white paper delves into the CGT Access Model, including an overview and timelines, how the Access Model does (or does not) address historical challenges associated with CGTs and OBAs, and considerations for expansion of the CGT Access Model.

Historical challenges

The currently available CGTs are primarily indicated for rare diseases. They often have stringent eligibility criteria, such as age, disease severity, and/or specific gene mutation(s), which restrict the pool of eligible treatment recipients. Consequently, the limited number of potential patients poses challenges for payers to accurately identify, forecast, and budget for anticipated utilization in upcoming plan years.

Due to the frequently debilitating nature of these rare diseases, many of the patients requiring CGT treatment are insured through Medicaid. Consequently, state Medicaid programs have increasingly voiced the need for enhanced transparency regarding costs and reimbursement, as well as improved systems for monitoring and forecasting spend. Additionally, there is a growing call for rigorous evaluation of patient outcomes to ensure optimal allocation of resources based on the treatments' efficacy.

The six- to seven-figure up-front costs combined with clinical and durability uncertainties are significant contributors to the complexity associated with CGTs, creating a mismatch between when costs are incurred and when the long-term benefits are realized. Additionally, when these treatments receive approval, they usually have fewer than 10 years of clinical trial data from a small group of treated individuals. This limited data can lead to uncertainties about the treatment's long-term effectiveness or durability in a broader, real-world setting. To address this challenge, some manufacturers have announced or offered new contracting options, such as OBAs, to provide full or partial financial protection against the risk of failure in efficacy or longer-term durability of the CGT.

Outcomes-based agreements can be a valuable option to alleviate some of the budgetary impact for cases in which the treatment does not perform to the expected level. However, smaller state Medicaid programs may not have the resources or utilization volume leverage to execute competitive OBAs with pharmaceutical manufacturers. The administrative burden in implementing OBAs and the operational complexity of overseeing them further discourages Medicaid programs from engaging in them. The administration and tracking requirements of OBAs may also require financial and human capital investments, thus

further disincentivizing already resource-scarce Medicaid programs.

Cell and Gene Therapy Access Model

The CGT Access Model, developed by CMS in response to President Biden's Executive Order 14087, Lowering Prescription Drug Cost for Americans, has the potential to address some of the barriers and challenges outlined above that are faced by state Medicaid programs (3). Announced in January 2024, the stated aim of this model is to increase access to CGTs and OBAs for state Medicaid programs, thereby helping to mitigate the inherent complexities and financial uncertainties associated with CGTs. Insights from key stakeholders—including states, patient advocacy groups, manufacturers, and providers—were taken into consideration during the model design process. It is important to note that the CGT Access Model is a voluntary initiative; states and manufacturers may choose to participate beginning in January 2025.

Currently, the CGT Access Model is only applicable to gene therapies for sickle cell disease (SCD). However, the model is intended to run for 11 years and may expand to other diseases and CGTs.

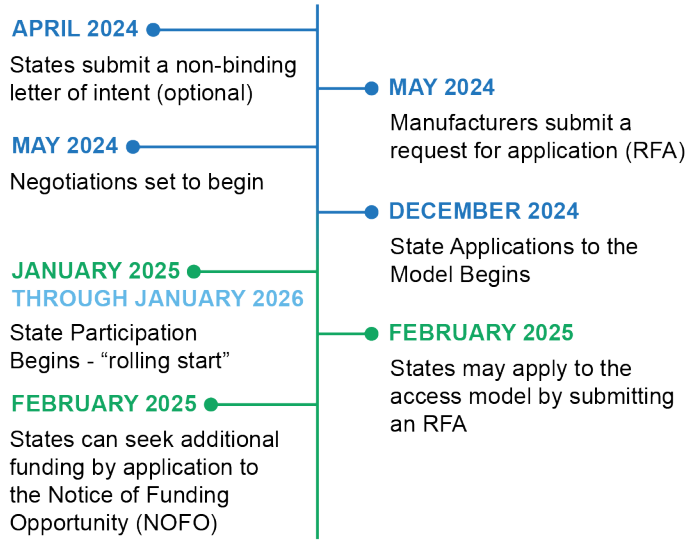
The CGT Access Model reflects the alignment of state, CMS, manufacturer, and patient interests to improve access to potentially life-altering treatments.

CGT ACCESS MODEL PROCESS AND TIMELINE

The CGT Access Model reflects the alignment of state, CMS, manufacturer, and patient interests to improve access to potentially life-altering treatments for Medicaid enrollees in fee-for-service (FFS) and managed Medicaid. The following are key steps in the process associated with this model, with Figure 1 displaying the timeline:

- **Negotiation.** CMS will have the ability to utilize pooled, multistate bargaining leverage to conduct confidential negotiations of key terms and agreements for OBAs with the manufacturers. In exchange for a standard access policy across all participating states, the SCD gene therapies will be provided at a discounted rate through supplemental rebates, some of which would be tied to patient outcomes. Note that state Medicaid programs may negotiate and enter into their own OBAs independently of this model, as participation in the CGT Access Model is voluntary (4).
- **Participation.** All states and territories that participate in the Medicaid Drug Rebate Program (MDRP) can participate in the Access Model, including Medicaid FFS and managed Medicaid enrollees as well as beneficiaries with Children's Health Insurance Program (CHIP)-funded Medicaid expansion. At the time of publication, it is unclear whether beneficiaries with CHIP standalone coverage will be included in the model. For manufacturers to participate in the CGT Access Model, they must also participate in MDRP and market an FDA-approved or -licensed SCD gene therapy. Beneficiaries with a SCD diagnosis who are treated with a SCD gene therapy of a participating manufacturer (and for whom Medicaid is the primary payer) qualify for model inclusion.
- **Financing.** Currently, state Medicaid programs have access to the MDRP statutory rebate. However, the potential rebate structure under the Access Model could also allow states to access guaranteed rebates, volume discounts, and/or outcomes-based rebates via a supplemental rebate agreement (4). CMS intends to link manufacturer rebate payments to specific predefined clinical endpoints. In addition to the discounted pricing structure for CGTs, CMS will offer optional funding to states to support activities promoting equitable access to care. Under the CGT Access Model, OBA administration requires the drug claim to be unbundled from the diagnosis-related group (DRG) or Enhanced Ambulatory Patient Grouping (EAPG). This unbundling would reflect the cost of the drug as a separate line item from the associated costs of administration to meet the covered outpatient drug (COD) definition (5) (6), thus allowing applicable rebates to be paid for the drug if the intended clinical outcomes are not met.
- **Implementation.** States will be responsible for implementing the negotiated contract, including outcomes monitoring, which can leverage the existing Transformed Medicaid Statistical Informational System (T-MSIS) and/or patient registry infrastructure. Operational support will be offered to states for technical assistance and data collection on clinical and claims outcomes. States may choose to begin with only their FFS program and expand to their managed Medicaid entities during the rolling start period between January 1, 2025, through January 1, 2026.

FIGURE 1: CGT ACCESS MODEL KEY DATES



An evaluation of existing Medicaid policies for CGTs (not covered by the new CGT Access Model) found that coverage varied from state to state, often with additional restrictions and criteria narrowing the eligible population from the labeled indication (7). From a manufacturer's perspective, the CGT Access Model could provide an opportunity to have consistent or increased access across multiple Medicaid states in exchange for offering an OBA under the program. And while states can still choose to enter into an OBA directly with a manufacturer, the CGT Access Model can streamline the contracting and outcomes tracking processes.

Sickle cell disease gene therapies

SCD gene therapies are currently the only treatments eligible for coverage under the CGT Access Model. SCD is a life-threatening, inherited red blood cell disorder that affects approximately 100,000 Americans. SCD decreases life expectancy by over 20 years. Additionally, vaso-occlusive crises (VOC), a hallmark of SCD, lead to severe pain and life-threatening complications, resulting in drastic increases in healthcare resource utilization, significant impacts on morbidity, and poor quality of life for the patient (8).

SCD gene therapies are one-time treatments that edit the genome in certain cells to mitigate disease expression. If successful, these treatments provide patients with the opportunity to have a lifetime of benefits, including reduction of VOCs, and can potentially alter the disease course.

SCD presents as an ideal candidate for the CGT Access Model due to inherent multifaceted challenges, including:

- **Health disparities**. SCD disproportionately impacts Black individuals. A recent study using the National Inpatient Sample database found that 93.4% of patients hospitalized for SCD were Black followed by 4.8% Hispanic, and 1.8% white (9). Additionally, compared to white patients, Black patients had higher odds of having a VOC (9).
- **Access barriers.** While comprehensive care is essential for avoiding hospitalizations, there is less access to it for SCD than for other genetic disorders like cystic fibrosis and hemophilia, due to lack of funding (10). Access to qualified treatment centers (QTCs) that are approved to administer one of the two SCD gene therapies is crucial for individuals to obtain treatment. At the time of publication, there were approximately 50 qualified or approved treatment centers nationwide, distributed across several states (11) (12). However, certain SCD hotspot states either lacked a QTC within state lines or only had one, necessitating travel for patients and their caregivers residing further away. This requires state-funded patient assistance for costs related to travel, housing, and meals for the patient and in some cases either a parent or caregiver (11) (12).

  An additional access barrier for SCD patients or caregivers and parents is employment conditions. Of the approximately 100,000 Americans with SCD, approximately 52,000 were Medicaid enrollees in 2021 (13). Medicaid enrollees are often employed in shiftwork, such as agriculture, construction, retail, or hospitality, which may not be amenable to or offer employment security for significant time off to accommodate the lengthy gene therapy treatment process (14). Greater access may help begin to promote health equity and ultimately lower healthcare expenditures in the long term.
- **Racial bias and inequity in treatment of SCD.** VOCs frequently drive patients to seek urgent care in emergency rooms (ERs) due to their severe and debilitating pain. However, the journey for SCD patients seeking medical assistance for pain and respiratory distress is fraught with widespread marginalization and dismissal (15). Amid the backdrop of the opioid crisis, SCD patients often encounter accusations of drug-seeking behavior, leading to inadequate treatment and increased suffering (16). The stress associated with perceived racial stigma further dissuades many from seeking care altogether, exacerbating the risk of life-threatening complications (10). Additionally, the personalized nature of pain management, tailored to patients' previous experiences and effective medications, can inadvertently lead to misconceptions of "drug-seeking" behavior, further widening existing disparities in care, particularly given the predominance of Black SCD patients (17).

- **Cost.** SCD not only impacts individuals and families but also reverberates throughout the healthcare economy, necessitating comprehensive care. SCD results in high healthcare utilization encompassing medications, emergency room visits, and inpatient hospitalizations. It is a major public health concern and estimated by CMS to cost $2.98 billion annually (8).

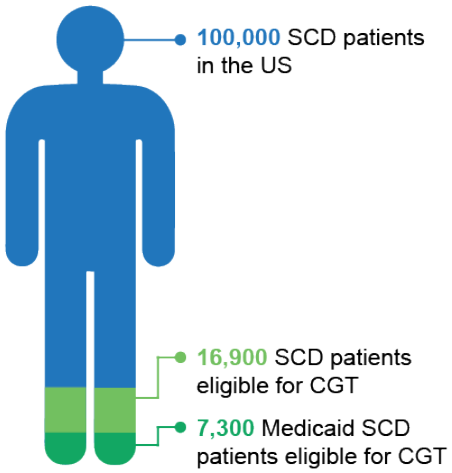
Financial barriers, the need for significant time off to prepare for CGT, the need to travel for care, and lack of treatment centers in SCD hotspots are all factors that contribute to bias and inequity in access to CGTs.

For SCD, there are currently two marketed cell-based gene therapies: Casgevy and Lyfgenia. These therapies focus on the reduction of VOCs. VOCs occur because of sickled red blood cells blocking blood flow. This leads to impairment in oxygenation and subsequent cell or tissue death, triggering an inflammatory response which is associated with significant pain (18). VOCs are an important endpoint for SCD as they not only cause significant pain and drive ER visits and hospitalizations (19) (20) but are also associated with significantly higher morbidity and mortality (21). At the time of publication, the wholesale acquisition costs for the therapies are $2.2 million for Casgevy and $3.1 million for Lyfgenia.

Patients are eligible for treatment with Casgevy or Lyfgenia if they are over 12 years of age and have a history of recurrent VOCs. Patients undergo an extensive process prior to and after receiving these treatments, marked by multiple hospitalizations. First, they undergo a process for collecting stem cells from the body. The cells are then utilized to manufacture the gene therapy. Prior to receiving the gene therapy, patients require chemotherapy to prepare the body. After treatment administration, patients are closely monitored in a hospital setting and then discharged for follow-up care to continue for 15 years. The entire process of CGT can take months to a year to complete and is associated with significant healthcare resources and costs. Thus, in addition to the cost of the treatment itself, the associated administration and monitoring costs can be significant (22).

Figure 2 displays the estimated SCD population eligible for a CGT in the United States. While approximately 7,300 individuals with Medicaid may be eligible for an SCD CGT, it is anticipated that far fewer individuals will opt for pursuing treatment. Uptake of these therapies will be driven by a multitude of factors, including access disparities (as outlined above), payer coverage criteria, manufacturing capabilities, provider preference, and patient willingness to undergo the extensive treatment process.

FIGURE 2: ESTIMATED SCD POPULATION SIZE



Source: Milliman DNA Gene and Cell Therapy Forecasting. Dual-eligible patients are excluded from the Medicaid estimate above. The number of CGT-treated patients is anticipated to be much lower than the number of CGT-eligible patients.

Considerations for expansion of the CGT Access Model

CELL AND GENE THERAPY OUTLOOK

Beyond SCD, there are several other disease states that have CGTs that CMS could consider for expansion of the CGT Access Model. According to Milliman DNA Gene and Cell Therapy Forecasting, a total of 19 single-administration CGTs are approved by the FDA as of March 2024, with some approved to treat multiple conditions. The current CGTs are approved to treat 19 therapeutic areas, representing oncology (13 CGTs), hematology (six CGTs), neuromuscular disease (four CGTs), ophthalmology (one CGT), and an immunological condition (one CGT) (1). In addition to conditions with existing CGT therapies, the pipeline of new and expanded indications include:

- 12 CGT therapies with imminent FDA review (these therapies have anticipated approval dates in 2024)
- An additional 50 single-administration CGTs and/or indication expansions that may be approved in the next three years

Medicaid plays an important role in developing access and delivery models to ensure equitable access to current and future CGTs. The expansion of the CGT Access Model into other

therapeutic areas would be a key driver for patient access (7). Treatments with associated hardship (both financial and lifestyle) may have a lower uptake rate among Medicaid beneficiaries, further exacerbating the health disparities. Therefore, adoption of models that holistically support patients will be an important feature driving CGT utilization.

THERAPEUTIC AREA CONSIDERATIONS

A key consideration for expansion of the CGT Access Model is the selection of therapeutic areas that have measurable OBA metrics. CGTs can generally be categorized into three types:

- **Therapies that have a clear, definable, and measurable outcome that is easily captured in retrospective claims or patient registry data.** SCD is a prime example of this, as VOCs are coded in claims data via ICD-10 and procedure codes. Other examples include hemophilia, or transfusion-dependent beta thalassemia, which have clearer outcomes or "failure" markers, making outcomes easier to track for an OBA.
- **Therapies with difficult-to-quantify therapeutic endpoints.** Examples may include oncology therapies that target disease stability or maintenance of remission, which are more subjective endpoints that may not be consistently coded in claims data because they lack correlating diagnosis codes. For inclusion in the CGT Access Models, these disease states may require agreement on surrogate endpoints, such as addition of adjunctive agents for symptom management or procedures or surgeries indicative of disease progression.
- **Therapies with poorly defined or subjectively measurable outcomes.** Examples may include therapies that target behavioral or functional disabilities, such as spinal muscular atrophy or Duchenne muscular dystrophy, by stopping or delaying disease progression. Outcomes for these conditions may be harder to reliably capture in claims data or could rely on subjective assessments. If surrogate endpoints for efficacy cannot be determined, then therapies for these types of conditions may not be good candidates for an OBA.

Selection of therapeutic areas that have measurable OBA metrics is critical for the success of the CGT Access Model.

DATA CONSIDERATIONS

A key component related to OBAs is identifying measurable outcomes and having the data available to track and identify when treatment failure has occurred. According to CMS, the CGT Access Model will use a combination of patient-level sales data submitted by manufacturers and claims data from states in the T-MSIS to track outcome measures. However, the data quality of the T-MSIS is inconsistent across states, with 17 states not meeting all of the targets reported in the data quality progress assessment (23). These states include the six largest states by population and nine of the 10 largest cities in the United States. This inconsistency could make it difficult to identify a treatment failure if outcomes are developed and measured against unreliable data. Additionally, it is not yet known whether an OBA can transfer if a patient leaves their state or goes off Medicaid. This may lead to data integrity issues as outcomes and follow-up data may be lost upon patient movement.

Conclusion

The advent of CGTs represents a significant breakthrough in the treatment of certain diseases. However, the high costs associated with these therapies, compounded by uncertainties surrounding the long-term effectiveness, can present significant challenges to payers. To address these issues, outcomes-based contracting options have been proposed by some manufacturers. However, negotiating, contracting, and implementing OBAs can be difficult, particularly for payers that may lack the necessary resources.

The introduction of the CGT Access Model by CMS represents a promising option for Medicaid programs. By increasing access to CGTs and OBA contracts for state Medicaid programs, this model aims to address the complexities and financial uncertainties associated with CGTs. However, the model is currently only applicable to gene therapies for SCD, and it remains to be seen whether it will be expanded to other disease states and CGTs.

There are several other conditions that currently have CGTs approved for treatment, with more than 60 CGTs in the three-year pipeline. If CMS considers expanding the CGT Access Model, the selection of therapeutic areas that have measurable OBA metrics will be crucial. Furthermore, the success of the CGT Access Model will depend on the ability to identify measurable outcomes and track treatment failures, as well as the willingness of states to take on the administrative burden associated with implementing and tracking outcome measures. As such, while the CGT Access Model represents a significant step forward, further work is needed to ensure equitable access to these potentially life-altering treatments.

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