



Access to New Cures & Innovative Care for Medicaid Patients

Examining Challenges and Opportunities
for Cell and Gene Therapies in Medicaid

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TABLE OF CONTENTS

- ACKNOWLEDGMENTS..... 3**
- EXECUTIVE SUMMARY..... 4**
- METHODOLOGY 6**
- INTRODUCTION..... 7**
- BACKGROUND 8**
 - Understanding Cell and Gene Therapies8
 - Cell and Gene Therapies on the Market Today9
 - The Pipeline of New Cell and Gene Therapies10
 - Medicaid Provides Health Coverage and Support for Millions of Americans.....13
 - How Medicaid Patients Access Cell and Gene Therapies13
 - Payment Approaches for Medicaid-Covered Drugs15
- CURRENT CHALLENGES.....16**
 - A Pandemic and a Recession.....16
 - Increasing Demands on Medicaid Program Leaders16
 - The High Cost of Innovative Cures and Therapies.....17
 - Lack of Visibility of CGT Candidates in Development.....19
 - Variance in the Use of Clinical Evidence19
 - Geographic Barriers to Accessing Health Care Providers20
 - Qualified Health Care Providers.....21
 - Health Care Disparities and Structural Racial Inequities22
 - Coverage of Supportive Wraparound Services22
 - Medicaid Managed Care Challenges23
 - Barriers to Value-Based Payment Arrangements for CGT24
- MODERNIZATIONS TO REALIZE THE PROMISE OF CELL AND GENE THERAPY27**
- RECOMMENDATIONS PROPOSED BY STAKEHOLDERS.....27**
 - Recommendations to Improve Patient Access to Supportive Wraparound Services.....27
 - Recommendations to Advance Value-Based Payment and Reduce Costs.....28
 - Recommendations to Improve State Medicaid Program Leader Capacity29
 - Recommendations for Ongoing Research on Medicaid and CGT.....29
 - Recommendations to Help Ease State Medicaid Financing Challenges Due to Recession30
 - Recommendations to Address the Lack of Visibility on the CGT Pipeline.....31
 - Recommendations to Address Racial Inequities.....32
 - Recommendations to Address the Social Determinants of Health.....32
 - Recommendations to Address Access Barriers Related to Geography33
 - Recommendations on Patient-Prioritized Outcomes and Evaluations of Therapy Success.....33
- CONCLUSION.....34**
- SOURCES36**

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TAF is a nonprofit 501(c)(3) independent charitable assistance organization that helps patients by providing financial assistance with copayments, coinsurance, deductible, and other health-related expenses. TAF currently manages over 70 disease programs, all of which cover FDA-approved medications that treat a specific disease. TAF is committed to improving the lives of patients by easing the burden of high-cost therapies, including cell and gene therapies, and supporting policies which will improve access to these life-saving treatments over time. For more information, please visit www.tafcares.org.

Leavitt Partners acknowledges the valuable insights and perspective of the more than 45 experts whom we interviewed as part of the research for this project. The individuals we interviewed provided insightful observations and thoughtful recommendations on the wide array of challenges and diverse opportunities related to the coverage and reimbursement of cell and gene therapies in Medicaid.



EXECUTIVE SUMMARY

Cell and gene therapies (CGTs) are some of the most promising and exciting medical advancements taking place today. Some existing CGTs treat previously untreatable rare diseases, and there are hundreds of CGTs in clinical development to treat various types of cancer, hemophilia, sickle cell and other blood disorders, Alzheimer's disease, and numerous rare conditions. The prospect of curative therapies which stop a disease in its tracks or even reverse the damage caused by the disease has the potential to change the course of medicine and improve the lives of millions of people. However, these new treatments also come with new complexities, one of the most pressing of which is price.

As a safety net program, Medicaid is responsible for providing care to some of America's most needy populations. Enrollees in the Medicaid program have the potential to benefit greatly from CGTs on the market today and those to come in the next few years. Many patients with rare diseases and chronic life-threatening conditions and their families are eager to access these groundbreaking therapies. But for the Medicaid program, there are multiple challenges that states must navigate to ensure access to medically necessary therapies while also being good stewards of the taxpayer dollar and ensuring a sustainable program for all patients served by Medicaid. There is an urgent and ongoing need for new tools and approaches in Medicaid's coverage and payment of CGT to provide patients with access to breakthrough cures.

Leavitt Partners provides in-depth analysis of the challenges in CGT coverage and payment in Medicaid, as well as opportunities for improvement, including concrete recommendations to improve coverage and payment. Leavitt Partners also helps patients access CGTs. Over 45 experts from stakeholders including state Medicaid directors and experts, providers, Medicaid health plans, manufacturers, and federal policymakers were consulted in outlining these challenges and moving toward solutions.

In this white paper, Leavitt Partners provides an overview of the CGT landscape in Medicaid. The paper starts by reviewing the science of CGTs, the pipeline of future therapies, and the basics of the FDA review process. Next, the paper explains how Medicaid currently covers and pays for CGTs and identifies various value-based and other payment arrangements being used by states.

Based on a landscape assessment of existing literature and analysis, as well as original interviews with more than 45 subject matter experts representing a wide range of Medicaid stakeholders, the paper provides in-depth analysis of the challenges in CGT coverage and payment in Medicaid. Finally, the paper identifies areas of opportunity identified by the stakeholders, highlighting concrete recommendations to improve the Medicaid policy and program context to support more sustainable coverage and payment of CGT for Medicaid patients.

About 7,000 rare diseases impact humans, of which only a few hundred have any treatment. Although each rare disease affects fewer than 200,000 Americans in total, these illnesses affect an estimated 30 million people in the United States. Since rare diseases often are difficult to diagnose, it can take years to obtain an accurate diagnosis. Even after a proper diagnosis, treatment often is unavailable, because only about 5 percent of rare diseases have a treatment approved by the FDA.



Using the landscape assessment and original interviews, the white paper identifies multiple challenges to the timely, sustainable provision of CGT for Medicaid patients. Such challenges include, but are not limited to, the following:

- ✓ The COVID-19 Pandemic and Recession
- ✓ Increasing Demands on Medicaid Program Leaders
- ✓ The High Cost of Innovative Cures and Therapies
- ✓ Lack of Visibility of CGT Candidates in Development
- ✓ Variance in the Use of Clinical Evidence
- ✓ Geographic Barriers to Accessing Health Care Providers
- ✓ Qualified Health Care Providers
- ✓ Health Care Disparities and Structural Racial Inequities
- ✓ Coverage of Supportive Wraparound Services
- ✓ Medicaid Managed Care Challenges
- ✓ Barriers to Value-Based Payments for CGT

Based on these challenges identified by stakeholders, the white paper makes recommendations in 10 core areas, offering dozens of actionable ideas for policymakers, researchers, and Medicaid stakeholders to improve the sustainability of access to CGT in Medicaid. These areas include recommendations to:

- ✓ Improve Patient Access to Supportive Wraparound Services
- ✓ Advance Value-Based Payment and Reduce Costs
- ✓ Improve State Medicaid Program Leader Capacity
- ✓ Help Ease State Medicaid Financing Challenges Due to Recession
- ✓ Research on Medicaid and CGT
- ✓ Address the Lack of Visibility on the CGT Pipeline
- ✓ Address Racial Inequities and Social Determinants of Health
- ✓ Address Access Barriers Related to Geography
- ✓ Patient-Prioritized Outcomes and Evaluations of Therapy Success



METHODOLOGY

This white paper provides insights, analysis, and recommendations based on two components: (a) a landscape assessment, and (b) interviews with subject matter experts.

The landscape assessment surveyed existing literature, research, and analysis from a wide array of publicly available sources. Such sources included, but were not limited to, the following:

- ✓ Academic, non-profit, and professional society articles, research, and publications
- ✓ State Medicaid program policies
- ✓ Media coverage and press reports from national and trade outlets
- ✓ Policy proposals, guidance, and analysis from the Centers for Medicare and Medicaid Services (CMS), the Food and Drug Administration (FDA), the Medicaid and CHIP Payment and Access Commission, and other federal sources
- ✓ Other publicly available sources such as interviews, surveys, and presentations.

Leavitt Partners also conducted interviews with select subject matter experts, including more than 45 experts on cell and gene therapy and Medicaid. These individuals represented a wide range of views representative of the perspectives of:

- ✓ **Patient advocacy groups (including advocates for patients with rare diseases)**
 - Six patient advocacy groups, including four with a rare disease focus and one focused on cancer
- ✓ **Medicaid managed care organizations**
 - Four large national managed care plans
- ✓ **State Medicaid programs (pharmacy and state program leadership)**
 - Four former Medicaid directors from different states, a pharmacy director
- ✓ **Drug manufacturers**
 - Five manufacturers, all involved in the development of current cell and gene therapies or such products under development
- ✓ **Associations and researchers working on cell and gene therapy issues**
 - Two national associations focused on cell and gene therapy
 - Researchers focused on value-based payment for cell and gene therapy
- ✓ **Health care providers**
 - An expert knowledgeable in cell and gene therapy coverage and reimbursement challenges for hospitals
- ✓ **Federal policymakers and researchers**
 - Congressional staff from both the House and Senate

Leavitt Partners also spoke with a knowledgeable policy staff employed by trade associations representing a number of the organizations and sectors listed above.

Interviews covered a wide range of topics, including challenges observed in access to, coverage of, and payment for cell and gene therapies; insights on potential opportunities for improvement in those areas; and specific recommendations on value-based purchasing arrangements and policy changes to better facilitate access to cell and gene therapies. Through these interviews, Leavitt Partners obtained first-hand accounts of the complexities surrounding Medicaid's role in ensuring patient access to cell and gene therapies that served as core basis for the content, conclusions, and proposed stakeholder recommendations in the report.

The research in this white paper was financially supported by The Assistance Fund. Leavitt Partners maintained editorial control and independence throughout the writing of this white paper.

INTRODUCTION

Today, there are about 7,000 rare diseases impacting humans, and only a few hundred treatments addressing those conditions. While each rare disease affects fewer than 200,000 Americans, in total these illnesses affect an estimated 30 million people in the United States.¹ Many of these patients, as well as others with special needs and chronic diseases, are served by the Medicaid program.

The Medicaid program plays a critical role as a safety net by helping to provide health care and long-term care supports for some of the nation's most vulnerable patients. Today, state Medicaid programs collectively provide services to roughly one in four Americans each year. If Medicaid were a single insurance product, it would be the largest health plan in the world.

This year, Medicaid programs have endured the twin threats of the COVID-19 pandemic and a precipitous economic disruption that triggered a recession. Yet despite the current challenges, bright potential for many Medicaid enrollees is visible on the horizon. In the last few years, new cell and gene therapies have been approved that hold phenomenal promise to roll back the tide of disease, offering new cures and innovative therapies. With the approval of the U.S.' first gene therapy in 2017, and subsequent breakthrough therapies making their way to the market, a new frontier of medicine has opened, bringing curative therapies that can correct blindness, thwart and sometimes even reverse the advancement of degenerative diseases, and prevent premature death altogether.²

The approved therapies are just the tip of the iceberg; there are currently 18 approved cell and gene therapies, with another 363 in clinical development. These therapies involve treatments for 100 diseases and 132 therapies for rare diseases. The promise these therapies hold for patients is one of the most exciting and promising fields of medical science.

And yet today, many Medicaid programs struggle to provide enrollees with timely access to new therapies. The difficulties Medicaid programs face are not due to a lack of goodwill or desire; rather, they involve a complex, multi-faceted series of dynamics related to Medicaid program policies, payments, funding, authorities and tools at the federal, state, and local levels, as well as public and private sector organizations.

Understanding and examining these challenges requires patience, dedication, and humility. Thinking about new ways to tackle these challenges requires creativity, a recognition of the legitimacy and importance of each stakeholder's perspective and experience, and a multi-sector effort. In many respects, work in this spirit has already begun. Yet as the number of approved therapies grow, so too does the need for patients, payers, providers, and Medicaid programs to bring their perspectives, experiences, and insights together in this important space.³



With many challenges comes the need for collaborative efforts to help think about how to modernize a 20th-century payment model for 21st-century therapies and cures. New medical approaches to diseases require new systems and payment approaches to treatments. Every stakeholder impacted by the program today has the potential to be part of a future-oriented constructive path forward. Progress requires a focus on policies, practices, and payments that impact the program – and ultimately, patients.

Medicaid has a special role in helping extend access and provide treatments and cures to our country's most vulnerable populations. Improvements can be made so more patients can access cell and gene therapies in a sustainable, equitable, and timely manner. Policies and reforms must identify specific problems and solve for the entire value chain.

This white paper outlines research in three core areas. First, the paper outlines some of the greatest challenges currently facing the Medicaid program in providing for cell and gene therapies. Next, it identifies areas where there are opportunities for improvement in coverage and payment that could increase enrollee access. Finally, the paper offers concrete, actionable recommendations for policymakers at the state and federal levels, based on the insights of experts.

There are no perfect or simple solutions, but there are meaningful and actionable steps that will help to bring timely access to 21st-century treatments and cures to patients and their families. The millions of Americans with rare diseases, and the Medicaid program that serves many of them, need solutions to ensure the availability of innovative care and new cures for the future.

BACKGROUND

Understanding Cell and Gene Therapies

While cell and gene therapies have been a focus of scientific research and development for decades, the first such therapy was only approved by the FDA in 2017. Cell and gene therapies represent a groundbreaking advancement in the ability of medical science to roll back, and in some cases fully conquer, human disease. Because cell and gene therapies are a relatively new reality in the health care system, it is critically important that Medicaid stakeholders understand the basic science underpinning recent advancements.

The science enabling gene therapy came about in the late 1970s as a result of the development of recombinant DNA technology. The first gene therapy in the U.S. was approved in 2017.⁴

By contrast, insights into cell therapies date back to the first blood transfusions during the 1940s and have advanced with organ and bone marrow transplant in the 1960s and 1970s. Today, cell therapy products are advancing to treat cancer through lymphocyte transfer and potentially hold the ability to use stem cells to repair injured organs.⁵

Cell therapies. Cell (or cellular) therapy refers to the transplantation of live cells into a patient to heal or replace damaged tissues or cells. The cells can come from the patient themselves (known as autologous cells) or from a donor (known as allogenic cells).⁶ Cellular therapy products such as cellular immunotherapies, cancer vaccines, and other types of cells like stem cells hold great promise to alter the course of certain diseases.

With many challenges comes the need for collaborative efforts to help think about how to modernize a 20th-century payment model for 21st-century therapies and cures.

PROVIDING PATIENTS WITH HOPE

Cell and gene therapies have already shown promising results for patients with rare, life-threatening diseases. There is now an FDA-approved gene therapy for spinal muscular atrophy (SMA) type 1, which is a genetic disease that is characterized by the progressive loss of motor neurons, which causes muscle weakness and atrophy. Patients with SMA type 1 exhibit symptoms early, usually at birth or by six months of age, and about 82% do not live to see their fourth birthday. In a Phase 3 trial of the gene therapy, patients showed improved motor function in the months following treatment, and five out of six patients who reached the age of 18 months by the end of the trial were able to sit independently for brief periods.

Currently, the most commonly used cell therapy is hematopoietic stem cell transplantation (otherwise known as a bone marrow transplant), which is used to treat various blood cancers and hematologic conditions. Other applications for cell therapies include treating cancer, autoimmune disease, urinary problems, and infectious diseases. Cell therapies may also be able to help repair joint problems, spinal injuries, neurological disorders, and weakened immune systems.⁷

Gene therapies. Gene therapies are products that seek to “modify or manipulate the expression of a gene to alter the biological properties of living cells for therapeutic use.”⁸ More simply put, gene therapies alter a person’s genes to treat a disease. There are numerous types of gene therapy products, including plasmid DNA, viral and bacterial vectors, human gene editing technologies, and patient-derived cellular gene therapy products. Plasmid DNA genetically engineers DNA molecules to transport therapeutic genes to human cells. Viral and bacterial vectors can alter a virus’s or bacteria’s ability to cause illness by carrying therapeutic genes to the cell. Gene editing products disrupt harmful genes and repair mutated genes, while patient-derived cellular gene therapy products take cells that are removed directly from the patient and modify them before returning them to the patient.

Gene therapies hold promise for treating various conditions, including inherited disorders, some cancers, and some viral infections.⁹ Because of their gene editing capabilities, gene therapies can address the root cause of a disease and some have the potential to provide a long-term, one-time treatment.¹⁰ Experts have characterized gene therapies as a tool that can be used to change the course of medicine “away from a chronic disease management approach toward disease interception and prevention.”¹¹ Former Food and Drug Administration (FDA) Commissioner Scott Gottlieb said that he believes “gene therapy will become a mainstay in treating, and maybe curing, many of the most devastating and intractable illnesses.”¹²

Throughout this report, cell and gene therapies will be referred to generally as “CGTs.” Where appropriate, specific cell or gene therapy products and the diseases they treat may also be noted.

Cell and Gene Therapies on the Market Today

There are several CGTs available to patients today. As of July 24, 2020, FDA’s Office of Tissues and Advanced Therapies (OTAT) lists 18 approved CGT products, including 11 cell therapies and 5 gene therapies.¹³ The treatments on the market address a range of diseases, including cancers, blood disorders, tissue abnormalities, and rare diseases. The table below (Figure 1) lists the approved treatments, types of treatment (cell or gene therapy and mechanism), and the diseases each therapy is designed to treat.

FDA has granted approvals for gene therapies in recent years, with the first three approvals made in 2017, one in 2019, and the most recent in July 2020. More gene therapies are expected in the coming years.¹⁴ Thus far, CGTs on the market today have come with significant price tags. They range in cost from thousands of dollars to over \$2 million per treatment, with the most expensive being gene therapies designed to treat rare conditions.¹⁵

While many Medicaid stakeholders are excited about the scientific advancement and promise of cures and therapies for Medicaid enrollees, there is also great concern about the costs and sustainability of access for patients. The high cost of CGTs is due in part to the intense scientific research and development needed for the creation of the therapies as well as the fact that some CGTs only apply to rare diseases where there are relatively few patients. Additionally, some CGT have high costs, but are curative.¹⁶ These considerations and other dynamics contribute to the pricing of upcoming cell and gene therapies.



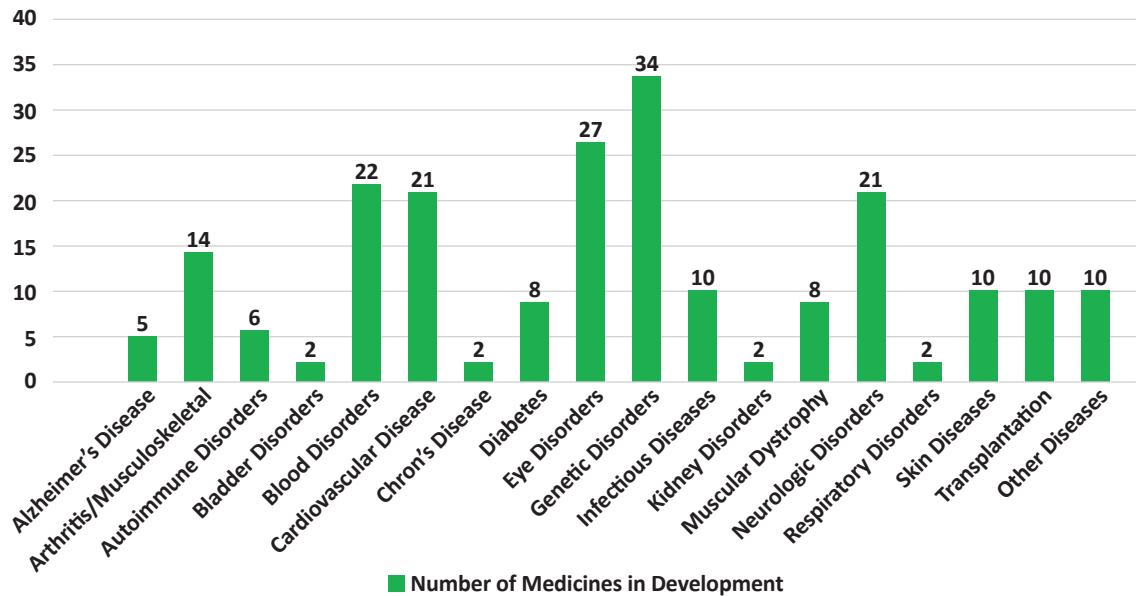
For a list of CGT approved by the FDA and on the market currently, please see Appendix 1 on page 35.

The Pipeline of New Cell and Gene Therapies

The number of CGT products in the development pipeline continues to grow at a quick pace, with numerous products in clinical development.¹⁷ While there are currently only a handful of CGTs on the market, FDA is receiving hundreds of applications for ongoing clinical studies and expects to make many more approvals in the coming years.¹⁸

In early 2019, FDA estimated there would be between 10 to 20 CGTs by 2025 each year. Former FDA Commissioner Gottlieb and Center for Biologics Evaluation and Research (CBER) Director Peter Marks stated in 2019 that they have seen a “large upswing” in investigational new drug applications (INDs) and said that they anticipate by 2020 they will receive over 200 INDs per year.¹⁹ Since that statement, FDA has issued 9 guidance documents on CGTs, including on gene therapies for hemophilia, rare diseases, and retinal disorders.²⁰

Figure 1 –Medicines in Development by Disease Type



173

In addition to these medicines in development, there are **173 medicines in development** to treat or cure cancer.

*Development is inclusive of any medicine in clinical trial: Phase 1, Phase 2, Phase 2, or Application Submitted
Source: <https://www.phrma.org/en/Report/Medicines-in-Development-for-Cell-and-Gene-Therapy-2020>





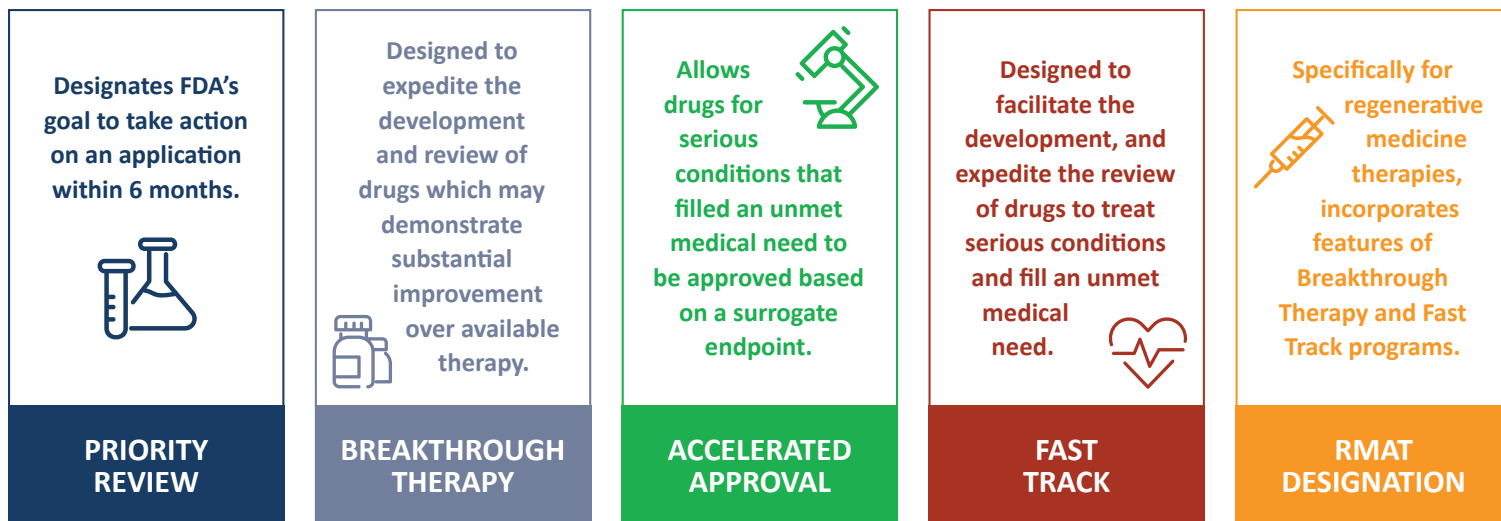
Others who have examined the scope of CGT products that could potentially receive approval have estimated a similarly robust pipeline.

- The Alliance for Regenerative Medicine (ARM) said in September 2019 that over 20 CGTs are expected to be filed or receive approval in the next year and half.²¹
- The Massachusetts Institute of Technology's (MIT's) NEW Drug Development Paradigms (NEWDIGS) program conducted an analysis in 2018 to project new product launches for CGTs in the United States through 2030, and found that 40 to 60 launches could be expected through 2030, with at least 15 to 30 launched by 2022.²² NEWDIGS also projected that about 500,000 patients would be treated with CGTs by 2030. These numbers present a significant change for the health care sector, with a paradigm shift toward one-time, curative products.
- In March 2020, the Pharmaceutical Research and Manufacturers of America (PhRMA) released a report on the current pipeline, including detailed information on types of treatments to expect in the coming years. In the report, PhRMA noted that there are currently 363 CGTs in clinical development by US biopharmaceutical companies, up from 289 in 2018.²³ The report notes that more than 100 diseases are being explored for potential treatment, with more than 132 therapies in development for treatment of rare diseases. By the numbers, oncology has the largest number of therapies in the pipeline, with 173 in application submitted or phase I-III clinical trials.²⁴ Others include blood disorders, cardiovascular diseases, eye disorders, genetic disorders, and neurological disorders.

A number of experts we interviewed highlighted the potential for CGTs in late stage development to better treat hemophilia, expand CAR-T to target malignant myeloma, and fundamentally alter the harmful impacts of sickle cell disease. Experts noted concerns with expensive CGTs that treat larger populations coming to market. While many of the CGTs on the market today treat relatively rare conditions, the pipeline presents therapies that could have a much larger reach. These therapies have the potential to make a significant economic impact on the health care market, based on the prevalence of the condition and the cost of the CGT.²⁵ According to a recent report, in 2018, the CGT market was valued globally at \$1.07 billion. It is projected to grow by over \$8.95 billion by 2025.²⁶ The growth in the cell and gene therapy market holds great promise for patients since while about 7,000 rare diseases impact humans, only a few hundred have treatment – leaving roughly 30 million Americans suffering from rare diseases each year. CGTs are generally regulated by the Center for Biologics Evaluation and Research (CBER) at FDA, and this regulation covers the products themselves as well as certain related devices. CBER regulates clinical studies of CGTs and also provides scientific and regulatory product development advice for researchers and manufacturers.²⁷

The FDA uses various methods to prioritize review of products where there is an urgent medical need, and in the case of CGTs it has used Priority Review, Breakthrough Therapy, Accelerated Approval, Fast Track designations and Regenerative Medicine Advanced Therapy (RMAT) pathways.

Figure 2 – FDA Expedited Review Routes



<https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review>
<https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/regenerative-medicine-advanced-therapy-designation>

- ✓ **Priority Review.** A priority review designation indicates that FDA aims to take action on an application within 6 months, as opposed to the 10 months it is statutorily permitted under standard review.²⁸ Each application gets either a designation of priority or standard review.
- ✓ **Breakthrough Therapy Designation.** Manufacturers may also request breakthrough therapy designation, which comes with all the same benefits as fast-track designation, in addition to guidance as early as phase I on the drug development program and FDA organizational commitment to development and approval. Breakthrough therapy designation is reserved for those therapies that can demonstrate substantial improvement over other treatments on a clinically significant endpoint.²⁹
- ✓ **Accelerated Approval.** Accelerated approval permits FDA approval based on a surrogate endpoint,³⁰ which can speed the drug approval process by allowing a therapy to be approved where there is reasonable likelihood of a real clinical benefit. Through this process, FDA can grant approval prior to clinical benefit being confirmed, and allow confirmatory trials to be performed post-approval. Approval may be withdrawn if the therapy does not demonstrate a clinical benefit or is discovered to have significant risks.³¹
- ✓ **Fast Track Designation.** Manufacturers may opt to request fast-track designation at any point in the drug development process and receive a decision within 60 days. This designation allows for the manufacturer of a therapy with an unmet medical need to have more frequent meetings with FDA to discuss the development plan, more frequent communications with FDA, eligibility for priority review and accelerated approval, and rolling review of parts of the BLA and NDA by FDA.³²
- ✓ **RMAT Designation.** In 21st Century Cures, Congress enacted the “regenerative medicine advanced therapy” (RMAT) designation. This designation enables sponsors with qualifying therapies to benefit from the features included in the breakthrough therapy as well as the fast track programs.

These review processes have allowed FDA to bring CGTs to the market and to patients more quickly than the traditional drug development process may allow, and sometimes with more limited evidence from smaller clinical trials. As we will discuss, some experts have noted that while this expedited process has brought CGTs to the market faster, it has also contributed to some difficulties for states and payers that are making decisions about coverage based on clinical evidence.

Medicaid Provides Health Coverage and Support for Millions of Americans

Medicaid is a critically important safety net program for millions of Americans. The Medicaid program plays a major role in providing CGT access, coverage, and reimbursement. Through covering patients with rare diseases and serious life-threatening conditions, Medicaid has become responsible for covering not only basic medical expenses, but also expensive, ground-breaking therapies that have the potential to enhance, improve, or extend the lives of enrollees. Medicaid's role as a safety net program operated by states on limited budgets, combined with the expensive nature of CGTs, poses issues for states in paying for therapies that enrollees medically require. To address these issues, the Centers for Medicare and Medicaid Services (CMS) and state Medicaid programs have been exploring innovative approaches to paying for therapies while ensuring financial stability in the future.

The Medicaid program is a federal-state safety net program that has historically provided coverage to low-income children, pregnant women, people with disabilities, elderly individuals, and parents with dependent children.³³ The Patient Protection and Affordable Care Act (ACA) authorized states to expand Medicaid eligibility to adults under age 65 with an income of up to 138% of the federal poverty level (FPL), and 39 states have expanded coverage to that population.³⁴ In May 2020, more than 66 million people were enrolled in Medicaid.³⁵ The Congressional Budget Office estimates that more than 94 million Americans will be enrolled in FY2020.³⁶

Medicaid is jointly financed by the state and federal governments, with the federal contribution determined by a formula (the federal medical assistance percentage, or FMAP). FMAP allows states with lower per capita incomes relative to the national average to pay for a lower percentage of Medicaid costs.³⁷ There is no cap on federal contributions to a state's Medicaid funds, as Medicaid is an open-ended entitlement for states.

Medicaid has two primary delivery systems to provide enrollees with health care benefits: fee for service (FFS) and managed care. In FFS, the state Medicaid program directly pays providers for services rendered to Medicaid enrollees. In managed care, the state contracts with one or more managed care organizations (MCOs) to provide services to enrollees. The state typically pays MCOs a capitated rate based on number of enrollees in the plan for provision of health care services. Over time, the majority of states have shifted to a managed care delivery system, with more than two-thirds of enrollees now covered by an MCO.³⁸

How Medicaid Patients Access Cell and Gene Therapies

Health care benefits available to Medicaid enrollees vary state to state. There are some mandatory benefits that states must provide, while other benefits are optional.³⁹ State Medicaid programs are required to cover a list of mandatory benefits, including inpatient and outpatient hospital services, physician services, rural health clinic and federally qualified health center services, nursing facility and home health services, laboratory and X-ray services, transportation to medical care, and early and periodic screening, diagnostic, and treatment services (EPSDT) for children.⁴⁰ Many other benefits are optional in the program, including prescription drugs and other diagnostic, screening, preventative, and rehabilitative services.⁴¹

EPSDT. The EPSDT provisions ensure that children receive "all Medicaid coverable, appropriate, and medically necessary services needed to correct and ameliorate health conditions."⁴² For treatment, EPSDT requires that "necessary health care services must be made available for treatment of all physical and mental illnesses or conditions discovered by any screening and diagnostic procedures." States can establish guidelines for medical necessity decisions in EPSDT, but those parameters cannot be more restrictive than the federal statute.⁴³ EPSDT is especially relevant to the discussion of CGT coverage, as these requirements require states to cover therapies for certain rare conditions that are often discovered in children.⁴⁴ However, it is important to note that states may place limitations on coverage for purposes of utilization control, require prior authorization for certain services, and consider cost-effectiveness as part of its evaluation on prior authorization.⁴⁵ States may also limit access to experimental treatments or treatments outside acceptable medical practice. While "experimental" is not defined by the provisions, CMS says that states should use the "latest scientific informational available."⁴⁶

Outpatient Prescription Drugs. Although Medicaid drug coverage is optional, all states provide outpatient drug coverage for Medicaid patients.⁴⁷ Outpatient prescription drugs include those that are prescribed by a provider and dispensed by a pharmacy, not medications provided as part of an inpatient or nursing facility stay.

States may provide the pharmacy benefit in FFS or through MCOs. States can contract with vendors, such as MCOs, in carrying

out the pharmacy benefit, and many MCOs in turn subcontract with pharmacy benefit managers (PBMs) to manage the pharmacy benefits. States that “carve in” the pharmacy benefit make MCOs responsible for pharmacy administration and costs within their capitated rate, while states that “carve out” the benefit opt to keep the pharmacy benefit in FFS and handle administration outside of the MCO. Managed care is becoming increasingly responsible for covering prescription drugs, but some states have opted to carve out or carve certain drugs out in recent years.⁴⁸ States have also increasingly used a combination of carve in and carve out to handle specialty high-cost therapies, like CGTs.⁴⁹ Reimbursement for prescription drugs may occur under either managed care or FFS, but states vary in reimbursement rates.⁵⁰ Congress created the Medicaid Drug Rebate Program to ensure that Medicaid would receive prescription drugs at the lowest or best price at which manufacturers sold the drug.⁵¹ In order to participate in the Program, manufacturers agree to enter into a drug rebate agreement with HHS in order to have their drug reimbursed by the Medicaid program.⁵² In return, states receiving prescription drugs at the discounted rate must generally agree to cover the manufacturer’s products for FDA-approved indications. However, states are permitted to limit access to off-label indications and subject the drug to other limitations such as preferred drug lists (PDLs), prior authorization, quantity limits, and utilization management.⁵³

The federal rebate amounts collected are shared to states based on their current FMAP and a unit rebate amount (URA) times the number of units paid for the drug during the rebate period. To determine the URA, CMS utilizes separate rebate formulas for brand and generic drugs, which account for a basic rebate amount and an inflationary component. For brand name drugs, the rebate is 23.1% of Average Manufacturer Price (AMP) or AMP minus the “best price,” which is the “lowest price available from the manufacturer during the rebate period to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity within the United States...”⁵⁴ For drugs specifically provided for pediatric indications, the rebate is 17.1% of AMP or AMP minus best price.⁵⁵ The rebate formulas for brand and pediatric-specific drugs ensures that the Medicaid program receives the lowest price for outpatient prescription drugs.

In addition to the rebates provided under the Medicaid Drug Rebate Program, most states have negotiated supplemental rebates with manufacturers.⁵⁶ Manufacturers typically provide these rebates to receive placement on the state’s PDL. Supplemental rebates are calculated by subtracting the federal rebate and guaranteed price from the benchmark price.⁵⁷ More information on supplemental rebates is included with information on payment models in the next section.

Cell and Gene Coverage in Medicaid. Our research showed variation in whether CGTs are covered through inpatient drugs or through the pharmacy benefit in Medicaid. To address coverage for CGTs and other high-cost therapies, states and MCOs use several methods to ensure appropriate and medically necessary use of the therapy. Many states use advisory boards, known as Pharmacy and Therapeutics Committees (P&T Committees) and Drug Use Review (DUR) boards, to advise the Medicaid program. While the formality and responsibilities of these boards vary state to state, states generally use these boards for oversight and administration in Medicaid pharmacy benefits.⁵⁸

States use DUR programs to aid in ensuring that outpatient drug prescriptions are appropriate, medically necessary, and unlikely to result in adverse health outcomes.⁵⁹ In order to develop a formulary, states must use a DUR board or equivalent body of experts in determining which drugs are added.⁶⁰ DUR boards also support activities such as retrospective review, DUR standards, pharmacy and prescriber interventions, and corrections for clinical misuse, incorrect dosage, and duplicate prescriptions.⁶¹

States may also use a P&T Committee in review and development of coverage decisions for new therapies and preferred drug list (PDL) placement.⁶² There is variance across states in the DUR board and P&T Committee’s roles in areas such as step therapy, prior authorization, review of utilization management tools,



and review of drugs approved through expedited review processes.⁶³ State-contracted MCOs may also use their own versions of P&T Committees, which can opt to provide more coverage for a therapy than the state.⁶⁴

States use coverage criteria, along with PDLs and formularies, as methods to manage the access and use of CGTs, ensure appropriate utilization, and manage risk. Some states are statutorily limited on prior authorization requirements that can be placed on certain classes of therapies.

Specialty Pharmacy. CGTs are a special class of therapies due not only to their high cost, but also to the complexities needed to administer the therapies. As described above, states

sometimes carve out CGTs from managed care, and MCOs will sometimes also utilize special coverage policies for dealing with CGT administration. One method utilized by states and MCOs is specialty pharmacy. Specialty pharmacies are “distinct from traditional pharmacies in coordinating many aspects of patient care and disease management. They are designed to efficiently deliver medications with special filling, storage, and distribution requirements with standardized processes that permit economies of scale.”⁶⁵ States utilize preferred specialty pharmacies for the distribution of CGTs in FFS or carve-out drugs, and MCOs also have specialty pharmacy networks to handle specialty pharmacy products.⁶⁶

Site of Service. Given the expertise needed in certain diseases that require CGTs, sometimes providers are focused in academic medical centers (AMCs) and what are known as Centers of Excellence (CoEs). CoEs are providers or groups of providers within health care institutions that “supply exceptionally high concentrations of expertise and related resources centered on particular medical areas.”⁶⁷ The CoE model for CGTs aims to standardize specialized care for CGTs and ensure consistent quality,⁶⁸ but it can also mean more limited access to CGT administration for Medicaid beneficiaries who do not live close to a CoE and must travel to access treatment.⁶⁹

Payment Approaches for Medicaid-Covered Drugs

Even before the pandemic, Medicaid directors stated that covering expensive therapies like CGTs was a major concern and began exploring alternative financing models to help pay for these therapies. To address the costs of pharmaceutical drugs, several states, MCOs, and manufacturers have worked to develop payment strategies to find new ways to pay for the expensive therapies. Much of this work began several years ago and focused on specialty drugs, and over time, several strategies have emerged which show promise: subscription models, outcome-based models, and supplemental rebate agreements.

Subscription Models. Subscription models, also informally referred to as “Netflix” models, allow for a state to enter into an agreement with a manufacturer to pay a negotiated flat price for a certain volume of a drug (potentially unlimited) for a specified period of time, rather than paying per unit of that drug.⁷⁰ Benefits of this structure include predictability for state Medicaid budgets on cost to the program, and an exemption of the additional rebated amount from manufacturers from being included in the calculation of Medicaid best price. The benefits to the state may be particularly notable where the therapy is curative, as those for hepatitis C are, and where the state has a large population of individuals with the disease to cover.

Two states thus far have utilized this payment structure in covering hepatitis C treatments for their Medicaid populations. CMS approved a state plan amendment (SPA) for Louisiana to utilize a subscription model to cover hepatitis C treatments for its Medicaid and correction populations.⁷¹ Louisiana then contracted with a manufacturer, agreeing to pay a lump sum in exchange for the number of therapies needed to treat patients from 2019-2024.⁷² CMS also approved a SPA for Washington,⁷³ which then contracted with another manufacturer using a similar contract.⁷⁴



Supplemental Rebate Agreements. Supplemental rebates are another approach that allows states to seek deeper discounts from manufacturers. CMS permits states to enter into supplemental rebate agreements provided that the “agreements achieve drug rebates equal to or greater than the drug rebates” set forth in the Medicaid Drug Rebate Program.⁷⁵ States often use a prior authorization program as leverage in seeking a supplemental rebate from the manufacturer. Currently, 46 states report using supplemental rebates, with many utilizing a purchasing pool to handle negotiations with manufacturers.⁷⁶ 30 states have entered into multi-state purchasing pools in an effort to increase negotiating leverage.⁷⁷ States also allow MCOs and PBMs to negotiate supplemental rebates.

Outcomes-Based Models. States have also begun to receive CMS approval for value-based arrangements for supplemental rebates to handle the cost of expensive therapies. Oklahoma,⁷⁸ Michigan,⁷⁹ Colorado,⁸⁰ and Massachusetts⁸¹ all received approval for SPAs that allow the state to enter into value-based purchasing arrangements with a manufacturer that could produce supplemental rebates if clinical outcomes are not achieved.

CURRENT CHALLENGES

A Pandemic and a Recession

State Medicaid programs across the country are filled with many talented leaders and dedicated public servants. Yet this year has tested many Medicaid program staff in unprecedented ways. The scope and breadth of challenges facing many state Medicaid programs today has perhaps never been greater. Hammered by the twin crises of the COVID-19 public health emergency and a precipitous drop in state revenues due to reduced economic activity, state Medicaid program staff have been triaging problems and working around the clock for months. Many of these staff have been working to adjust policies and program requirements to help shore up the delivery systems and payment policies that enable Medicaid patients to continue receiving needed care.

States are taking actions to shore up their Medicaid provider networks, leverage telehealth, and help ensure patients receive care – all while the total number of patients Medicaid programs are responsible for continues to increase. Recent data from CMS shows that about 4 million more individuals enrolled in Medicaid in the first few months of the pandemic.⁸² While the massive increases in Medicaid enrollment projected at the outset of the pandemic have not materialized at the rate expected due to a range of factors, many experts expect enrollment will continue to increase in coming months.⁸³

While the COVID-19 public health and economic crises have placed unique strain on state Medicaid program leadership, even in the best of times, states face a range of operational and programmatic challenges that can constrain program leaders’ ability to drive positive change. Medicaid programs have limited resources due to state budget and federal rules that match half of administrative costs. Efficient management and lean overhead expenses are admirable goals, but budget and political dynamics can make it more challenging for states to sufficiently invest in the knowledge, capacity, and staff that oversee the program. With Medicaid programs often constituting about one in every four state dollars in the state budget, building capacity by investing in expert staff and program administrators is a responsible investment.

Increasing Demands on Medicaid Program Leaders

According to a 2019 survey by the National Association of State Medicaid Directors (NAMD), only about half of the Medicaid directors previously worked in the program before taking on their role.⁸⁴ As a result, less than half of directors reported having “very extensive” knowledge of Medicaid before becoming a director, and one-third would only characterize their knowledge as “moderate.” Many directors reported that it would have been helpful to better understand several dynamics before starting their job, including CMS waivers and authorities, Medicaid financing details, and the Medicaid agency structure, function, and processes.

Medicaid directors often benefit from a dedicated leadership team that helps them oversee their state’s program. According to the 2019 survey, more than half of Medicaid directors reported that their leadership team included a Medical Director, Deputy Director, Policy Director, Managed Care Director, Chief Financial Officer, and Information Technology (IT) Director. While working with a team of direct reports to help manage the program is important, the quality of that team can come up short. For example, even though managed care is a dominant form of the Medicaid delivery system today, the majority of Medicaid directors reported that their leadership team had only a moderate, mixed, or even low level of experience in managed care procurement.

In this environment, many Medicaid program leaders find it challenging to think beyond the next 12-18 months, but many are trying.⁸⁵ The 2019 NAMD survey reported that Medicaid directors' top strategic program management priorities were "1) delivery system and payment reform; 2) behavioral health reforms, including integration with medical care and managed care; and 3) Medicaid Management Information System (MMIS) and eligibility systems implementation and operations."⁸⁶ These priorities certainly are "multi-year, transformative efforts that require sustained effort, staff, and financial resources," but hidden beneath the headlines is directors' growing awareness of the burgeoning pipeline of CGT and what it may mean for their Medicaid program.⁸⁷ Many directors articulated the important goal of "strategic sustainability" of their program as well – which is a critically important dynamic to consider specifically for CGTs in the Medicaid program.⁸⁸

The High Cost of Innovative Cures and Therapies

Perhaps one of the most clear and persistent challenges that surfaced in our interviews was the subject of the price of CGT, and the cost to the Medicaid program. During the interviews for this white paper, it was acknowledged that pricing was a challenge for Medicaid programs – both with regard to the high cost of individual CGTs and with regard to ensuring sustainable program access for Medicaid patients to future CGTs. Experts underscored the need to modernize the 20th-century Medicaid payment policies so that state Medicaid programs are able to provide access to 21st-century innovative cures and treatments. They drew from their insights and general experience with high-cost curative drugs in Medicaid (such as recently approved drugs to cure Hepatitis C), as well as their specific experience with the handful of CGTs on the market.

Interview subjects consistently expressed appreciation for the value of many new therapies for curing disease and improving the lives of Medicaid patients, while also voicing concern about the price of such drugs and the costs to the program. Researchers at the Duke-Margolis Center for Health Policy have noted two acute challenges for state Medicaid programs. First, "state Medicaid programs may recognize the downstream health benefits of broader access to a drug, but tight budget constraints may nonetheless limit their ability to pay more now – even if the up-front payments are linked to long-term reductions in Medicaid costs from avoided complications."⁸⁹ Second, CGTs could create a cumulative strain on the budget: as the number of cures and groundbreaking therapies available to Medicaid patients continues to grow, the program costs will likely accumulate higher and higher over time as well. Duke-Margolis noted that "State budgets (including a state's Medicaid budget) are set in advance for one- to two-year periods by legislative vote, and many states cannot effectively run annual deficits, so even a small number of patients requiring high-cost transformative treatments could potentially require states to divert funds from other important public priorities in order to provide coverage for new therapies."⁹⁰

Experts we interviewed stressed the same dynamics. They emphasized the need for policy and payment solutions that recognize the equities and needs of each Medicaid stakeholder. As the MIT NEWDIGS initiative has succinctly summarized, "understanding the payer perspective and the challenges they face in delivering affordable healthcare coverage while ensuring access to medical innovation is critical to the sustainability of research and development of new cures."⁹¹

Experts noted that Medicaid program leaders are often drawn to work in the Medicaid program out of a sense of public service and personal mission – they want to make a difference and help improve the lives of their neighbors in their communities and across their states. Yet given the cost of many new groundbreaking drugs, they also bear a weighty responsibility to ensure that the Medicaid program budget remains adequate to fund the health coverage and long-term care of thousands of other patients who do not benefit from CGT. In the eyes of program leaders, the intertwined issues of cost and access are particularly acute in the realm of Medicaid, which cares for some of the most vulnerable patients with rare conditions and diseases who could benefit from CGT. Several interview subjects observed irony in the reality that drug manufacturers set a price while Medicaid bears the requirement to cover all FDA-approved drugs. In some cases, the high costs of innovative CGTs, when applied to a large number of patients, can amount to a substantial program cost that begins to compete with other state Medicaid policy priorities, as well as with state non-Medicaid policy priorities (e.g., other areas of significant state expenditures, such as the criminal justice system, infrastructure, education, and transportation).

Manufacturers and researchers we interviewed highlighted the challenges of trying to price a new CGT while navigating the labyrinth of policy and payment considerations such as the role of rebates, prices in different market segments, the role of Medicaid best price in impacting non-Medicaid prices, and other dynamics. Many experts pointed out the fundamental difference between the economics of supporting the time and money invested in research and development for a drug that would be widely prescribed to millions of Americans, and the economics of funding a CGT that may cure a rare disease but only apply to a few hundred or thousand individuals

nationwide. Several experts noted that CGTs currently in the pipeline to treat sickle cell disease or relatively common cancers present fundamentally bigger challenges to the economics of Medicaid drug coverage.

One especially challenging dynamic that experts discussed was differing views of “value” for the price of a CGT. In some cases, a curative CGT may be life-giving for an individual patient. However, any medical savings or economic benefit from that patient being healed accrues to that patient’s community or workplace, or even society more generally, but not to Medicaid. There are some cases in which curative CGTs benefit pediatric populations, and they may reduce projected Medicaid costs that would otherwise be associated with a specific child who would remain on Medicaid if left untreated. But generally, when drug manufacturers set the metrics for value of a CGT, they are often assessing the broader general effects rather than the more narrow and specific savings that might accrue to the Medicaid program. General economic arguments or value-of-life arguments have their merit and place to be sure, but such economic arguments are not often calibrated to reflect the *costs or savings to Medicaid*. Moreover, other “value” assessments, “such as comparative effectiveness and incremental cost-effectiveness, cannot be determined for first and only treatments for a condition, which may be a relevant issue for gene therapies.”⁹²

However, more broadly, experts interviewed generally underscored the intrinsic value of each patient life. They agreed patients need access to CGT and underscored that the value of a particular therapy to a specific patient could be life-giving and transformative. Several experts stressed that these realities also have to be held in balances with the operational budget realities of running a program.

Several experts talked about the importance and challenges of leveraging existing claims data from clinical trial patients to better build out a data-driven assessment of what other associated medical or long-term care costs that are borne by Medicaid might be recouped or reduced if a patient receives a CGT. Finally, a challenge that drug manufacturers face is adopting a pricing strategy that enables some return on investment and even reinvestment in new R&D without creating a price barrier that ultimately results in a delay in patients accessing CGT. Ultimately, the benefits of CGT will not be realized unless patients have access to them. “A treatment that is unavailable to patients who need it has no value at all.”⁹³



Lack of Visibility of CGT Candidates in Development

One of the persistent challenges identified through our interviews with experts is that many Medicaid programs lack consistent and accurate visibility into the CGT development pipeline. While public information on the pipeline does exist, it requires proactive, dedicated, consistent monitoring of the complexities of emerging products in order to generate meaningful insights about CGTs in the long term. While some programs undertake this challenge, this longer-term focus on products under development (some of which may fail in a clinical trial and not be approved) is often beyond the planning horizon of Medicaid programs.

Many Medicaid programs focus on a 12 to 24-month time horizon built around state budget and program procurement cycles. They often find it challenging to dedicate time to maintain visibility on an individual CGT product's progression through clinical trials, much less wrap their heads around the potential impacts of the growing CGT pipeline. Also, with faster approval time frames for therapies, Medicaid directors have less time to factor high-cost therapies into the state's Medicaid budget. "The current coverage and reimbursement system is focused on a 12-month cycle and is not structured to recognize interventions with value that accrues over years or decades... precision financing tools that target the specific challenges of each payer segment will be needed. These tools will be facilitated by addressing regulatory and operational barriers."⁹⁴

Variance in the Use of Clinical Evidence

While speedier FDA reviews of new medical products are important to some, including patients, since they can accelerate access to new cures and therapies, experts we talked with explained how the increasing use of expedited review and approval pathways presents novel challenges. For example, in some cases a new therapy may receive approval well in advance of Medicaid program anticipation, and the need to cover the new drug is disruptive to current budgets or capitated arrangements with Medicaid MCOs.



Some experts also discussed how greater use of surrogate endpoints presents an unintended challenge from a Medicaid program perspective for the coverage of some therapies for rare diseases. FDA-approved drugs receive approval through a traditional clinical trial's endpoints (which measure the outcomes in the trial), or through "surrogate endpoints," which are used when the clinical outcomes might take a long time to study or are otherwise well understood.⁹⁵ When surrogate endpoints are used in approving a drug, Medicaid clinical experts may be left playing catch-up in order to understand the drug's label, its efficacy in a clinical trial, and any pharmacogenomic implications.

Research has indicated that "the most important aspects of value (for managed care executives) that would drive their decisions about covering gene therapies, are the magnitude of effect on key treatment endpoints (i.e., efficacy and/or benefit), duration of the effect, safety, and cost. Payers are also interested in seeing improvements in productivity and reduced care burden."⁹⁶ Furthermore, because many CGTs are intended to treat or cure rare conditions (which inherently only affect relatively few Americans), the clinical trials for such approvals may be relatively small compared to traditional Phase III trials. In such cases, Medicaid pharmacy and medical leaders may only have a few dozen people in a clinical trial to inform their understanding of the drug's effects. This smaller clinical trial can result in states having a harder time feeling comfortable with broad conclusions for coverage and payment – especially when it comes to rare conditions.

The results of one survey of payers reported that "fast-tracked therapies were noted as being accepted with, what is viewed as, an incomplete evidence package, particularly in rare disease or protected product class scenarios," which often leads to "much greater emphasis on how the product would be managed in terms of step therapies and other access restrictions."⁹⁷ These payers also reported that there may be "delays associated with uncertainties in product assessment that have the potential to delay decisions by 6 to 12 months."⁹⁸

Certainly, differences over how to best interpret and act on the available clinical evidence when a drug is approved remains a major challenge in Medicaid programs. As previously noted, although Medicaid programs are required to cover all FDA-approved drugs,

there is wide variation in how and when those drugs are covered. The same drug for the same patient populations in two different states can result in two very different levels of access to that drug.

Medicaid program and plan perspectives often stress the need for detailed clinical information to ensure appropriate utilization of new cures and therapies. They emphasize that such insight is especially important given the economic incentives for manufacturers to get drugs covered and the lack of lower-cost competitors for new drugs on the market.

Many manufacturers and patient advocates, on the other hand, point to the curative effects and life-transforming benefits of new CGTs. They worry about state programs and Medicaid plans using tools like prior authorization, special formularies, and fail-first methods that too often restrain timely access to new treatments for some patients.

Medicaid plan and program experts highlighted the challenge of sorting through competing claims on the appropriate target population, estimated disease burden in a given state, amount of pent-up demand, and durability of the curative treatments for Hepatitis C. Experts across the spectrum of Medicaid stakeholders pointed to the need for drug manufacturers to collect and share as much information as possible on the durability of specific therapies and drugs with Medicaid programs.

Additionally, several experts noted that FDA uses more than just limited clinical trial data when developing the label, but that information is often not shared with states. As a result, some states' clinical process may inadvertently be redoing some of the analysis that FDA already conducts.

Geographic Barriers to Accessing Health Care Providers

It is widely understood that certain geographic dynamics can effectively create barriers to timely access to care in the health care system. For example, a perennial focus of policymakers is ensuring patients in rural and underserved areas have access to care. While these dynamics exist in health care generally, the challenges are exacerbated for Medicaid patients needing access to CGT.

Many CGTs may be administered through a Centers of Excellence (CoE) model, which relies on health care providers delivering CGT and associated care at a few specific locations that are streamlined to provide specialized services. For example, in many cases, CGTs may be administered at academic medical centers (AMCs) where health care providers have the appropriate training and resources to ensure the patient receives a successful treatment. While AMCs provide access to highly qualified health care providers, they are often centered only within major cities in a given state – potentially leaving sick Medicaid patients in other parts of the state in a “care desert” for their condition. Such patients face the challenges of substantial travel time and cost (including overnight stays) in order to receive care. In addition to experts we spoke with, MIT NEWDIG's FoCUS Project analysis included broad patient access to CGT “regardless of geography” as a major challenge for CGTs.⁹⁹

For patients seeking to access a CGT in a state other than where they reside, the complexities are multiplied. In many cases, while individual state Medicaid programs may have reciprocal agreements with neighboring state Medicaid programs for providing routine care to Medicaid patients, states find it extremely challenging to maintain multiple arrangements for CGT with AMCs and children's hospitals across numerous other states.

Individual state Medicaid programs are required to screen and enroll health care providers in Medicaid according to federal and state rules. These rules are designed to exclude providers who do not meet minimum standards and protect programs from fraud, waste, and abuse. Yet, these important requirements also inadvertently increase the administrative time and expense necessary to ensure that patients in need of CGT treatments in a neighboring state can receive it. Importantly, the increased administrative time and costs are borne not only by state programs, who must have arrangements in place with providers, but also by the many AMCs and children's hospitals that must maintain arrangements with states.

Further complicating this issue is the fact that states and hospitals often find it necessary to make multiple arrangements with one another, each related to a specific CGT therapy for a specific number of patients. In some cases, states and providers even have a “single case agreement” – a highly tailored contractual arrangement designed just to enable a single patient to receive the benefit of a CGT.

Administrative challenges are real, but the CoE model also comes with significant structural challenges. There are a limited number of locations where CGT treatments are provided in a high-quality manner and a limited number of sites that run trials effectively.

Thus, potentially even more challenging than the barrier that a CoE model may represent for an individual Medicaid patient, is the strain this delivery system model will face in accommodating future CGTs that will involve substantially higher patient volumes (such as potential treatments for sickle cell and cancer that are in the pipeline). Already, institutional tensions sometimes arise between Medicaid programs, managed care plans, AMCs, and children’s hospitals over reimbursement rates and payment models. Increased numbers of patients being driven through CoEs could further exacerbate those tensions.

More broadly, the very nature of Medicaid’s state-by-state administration presents challenges. Many experts noted that the state-by-state variation creates a near inability to scale payment and coverage improvements across multiple states – whether they are trying to scale a simple coverage policy or a specific value-based arrangement. In some cases, the unique nature of each state Medicaid program’s specific requirements for CGT (including prior authorization, travel, etc.) can prevent Medicaid patients from receiving access to CGT in as timely a manner as similar patients enrolled in commercial coverage.

CMS has at times acknowledged the challenges of ensuring appropriate, coordinated care for patients across state lines. In January 2020, CMS issued a Request for Information (RFI) regarding “coordination of care from out-of-state providers for Medicaid-eligible children with medically complex conditions.”¹⁰⁰ While CMS’s focus in this RFI is on pediatric populations (not patients on CGT *per se*), many of the insights and observations provided in response to the RFI could be used to help CMS and states ensure more coordinated care for patients accessing CGT outside the state in which they reside.

Qualified Health Care Providers

The delivery of CGT medicine often requires on-site administration and cannot be easily provided off campus. Outside of a CoE model, many health care providers may lack the sophistication and training necessary to be successful in delivering high-quality care and providing CGT to patients. Even talented medical professionals need a mix of specific training and a supportive infrastructure of staff, facilities, and revenue streams to enable them to provide CGT. Many hospitals find the provision of CGT to be challenging to resource, operationalize, and sustain, as there are many extra internal steps in the delivery of care as well as externalities which must be addressed.

Another challenge is that for a period, new CGTs often lack reporting and billing codes that are specific to the new therapy. “Irrespective of the potential impact of a therapy, if it does not fit into existing coding and payment systems, this can represent a substantial acceptance and uptake hurdle for manufacturers, providers and patients.”¹⁰¹ Absence of timing specific codes was “noted as a challenge for novel CAR-T therapies” even though “requirements for using a non-specific code, can also result in underpayment and risk to providers and manufacturers alike.” Under such conditions, hospitals take a significant risk in providing these therapies where (a) reimbursement is uncertain and (b) not all aspects of procedural expense may be sufficiently paid, even if the product is reimbursed.¹⁰² Thus, providers face an unfavorable choice: wait to get the right codes in place, which may result in delayed care for patients, or proceed with providing CGT for a patient and risk a denial of reimbursement under existing codes until new codes are assigned. Even large, sophisticated health systems may struggle with these dynamics.

Additionally, hospitals face reimbursement challenges in the provision of CGT, since their margin on an inpatient bundle may be smaller than if it were provided in an outpatient setting.¹⁰³ Yet payers also report paying substantial markups that can be significantly higher than a provider’s acquisition cost if providers purchase a drug and then bill the payer for the drug at a higher rate that builds in the cost of administration.



Health Care Disparities and Structural Racial Inequities

In a year in which the COVID-19 public health emergency has laid bare many preexisting inequities in our health care system, numerous experts we interviewed voiced concerns that current structural disparities and racial inequities may prevent Medicaid patients from receiving equitable access to CGT. In the worst-case scenario, health care disparities and structural racial inequities may prevent thousands, even millions, of Americans in communities of color from receiving timely, fair, and equitable access to CGT.

This troubling dynamic is especially worrisome in the case of sickle cell disease, which affects about 100,000 Americans and disproportionately impacts black Americans.¹⁰⁴ There are numerous promising CGT candidates in the development pipeline that hold promise to roll back the worst effects of sickle cell disease. Yet if current practices and trends are allowed to persist, structural inequities and implicit bias could prevent thousands of Americans from receiving needed treatment.



Coverage of Supportive Wraparound Services

Many patients who have identified a qualified health care provider operating a CoE to administer a CGT for their disease face logistical challenges, such as affordable lodging and family transport, loss of income during time away from work, or inability to stay for multiple days. Patients also frequently lack access to decision support tools, including information specific to their disease or condition that might improve their understanding and adherence to follow-up care. Currently, Medicaid patients and their families are forced to pay out of pocket for the costs of many support services, or to rely on charitable assistance from non-profits, friends, or family. The cost of support services may be modest in some cases, but can quickly add up for patients needing to stay overnight or over a period of days, or who must frequently return to the health care provider for related follow-up care. Compared with the cost of the therapy given to the patient, support services may cost a tiny fraction of amount but help increase patient adherence to follow-up care protocols, avoid infections or complications, and provide greater piece of mind.

Experts identified the current web of rules under the federal Anti-Kickback Statute and related regulations as a barrier to patients receiving the help they need. The combined effect of such rules pertaining to federal health care programs is to essentially prohibit health industry stakeholders from financially assisting patients with covering the costs of valuable support services.

Many patients who receive CGT must be monitored over time. This monitoring may be required as part of the FDA's post-market surveillance, a value-based payment arrangement, a patient registry, or it may be the clinical standard of care to avoid complications. In some cases, the CoE where the patient received the care may not have especially cost-effective or accessible primary care services. Additionally, there are often challenges in determining which providers are responsible for the follow-up monitoring, tracking responsibilities, and costs – whether these fall to the state, a research-based organization, or some other entity. MCOs can also find it challenging to cover the costs of support services, based on whether such services are classified as administrative expenses or directly tied to the medical benefits of the patient.

Medicaid Managed Care Challenges

Today, about two-thirds of Medicaid patients are enrolled in managed health plans (or managed care organizations, MCOs).¹⁰⁵ Experts we interviewed underscored notable differences between the challenges faced by smaller regional MCOs compared to those faced by large national MCOs with respect to coverage of and payment for CGTs. The challenges of both large and small MCOs are noteworthy because while a handful of large national plans cover roughly half of the lives enrolled in Medicaid MCOs, there are a large number of small regionally based plans that provide care for millions of Medicaid patients.

Some research suggests that the process for evidence assessment for Medicaid MCOs who are large national plans essentially tracks the same process it does for their commercial plans. However, large MCOs may have more resources to commit to develop value-based payment (VBP) arrangements.¹⁰⁶ Large national plans may also have the market leverage and sophistication needed to work with a state to drive economies of scale for VBP, while smaller plans lack these assets.¹⁰⁷ Furthermore, whereas larger MCOs may only see a handful of patients each year with a rare condition that is treated by a CGT, smaller Medicaid MCOs may see even fewer and find it more challenging to establish the capabilities to manage them. Smaller MCOs may have an advantage when it comes to forming close relationships with local health care providers across a specific geography. Yet they may struggle to develop the internal capacities needed to effectively contract with the state, manufacturers, or providers around VBP.

Another potential challenge for Medicaid MCOs is that small regional plans in a particular state may be disproportionately impacted by the emergence of a CGT for a patient population that is especially prevalent in that geography. For example, it is not too difficult to imagine that when a successful CGT arrives on the market to cure or rollback sickle cell disease, Medicaid MCOs will be impacted differently based on their patient populations.¹⁰⁸

A perennial challenge for the Medicaid program and MCOs remains the significant number of Medicaid patients who drop in and out of eligibility based on changes in income. Research in recent years has “highlighted the potential for adults with incomes near the ACA’s Medicaid eligibility threshold to experience changes in insurance coverage as they transition between qualifying for Medicaid and qualifying for subsidized private insurance offered through health benefit exchanges.”¹⁰⁹ While this churning in and out is not a new phenomenon for Medicaid, as a program for which eligibility is based largely on income levels, the reality of the churn presents several challenges with respect to MCOs covering and paying for CGT.

We will highlight three challenges briefly. First, as the MIT NEWDIGS research has noted, “Medicaid payers are least likely to reap the reward of medical cost offsets resulting from the use of durable therapies because members of the plan are often transient.”¹¹⁰ Second, patients who receive CGT in Medicaid and then exit the program to a private source of health coverage could see an increase in their out-of-pocket costs for such treatment, a change in their network of providers, or a change in coverage policy altogether. Third, Medicaid patients benefitting from CGT who churn in and out of the program may be harder to track for follow-up care or monitoring to assess outcomes tied to a VBP arrangement.

Several experts we interviewed discussed the importance of reinsurance and risk corridors as tools that MCOs can use to address the actuarial uncertainty that may accompany new CGTs. Experts stressed that these financial levers are simply tactical tools that enabled MCOs a bit more stability, not long-term strategies sufficient to address broader program concerns about how to appropriately ensure sustainability and access over time. On the one hand, reliance on commercial reinsurance over a longer period would likely just drive up the premium and rate structure.¹¹¹ On the other hand, reliance on a state to act as a reinsurer, essentially as a backstop for MCOs, is likewise unsustainable since this approach saddles the state with escalating costs. Both Medicaid program and MCO experts stressed the challenge of actuarial imprecision when a new CGT has been approved, since there is little experience with the treatment, and it has not been made widely available to beneficiaries.

Tied closely to general concerns over the high cost of CGTs are apprehensions about how durable the benefit of a new CGT may be. MIT’s NEWDIGS, which has published meaningful insights and analysis of the challenges created by CGT, highlighted this concern among Medicaid MCOs and other payers. In the results of a payer survey, MIT NEWDIGS noted that payers were roughly as concerned about a drug’s effectiveness and durability as they were about the total cost to the MCO of the drug itself. They also ranked concerns about the actuarial risk being very high.¹¹² At the intersection of these issues, payers expressed concern that the offsets (based on reducing other spending associated with the patient in Medicaid within a specific timeframe) might not offset the high cost of the treatment itself. In a 2019 survey reported earlier this year, more than three-fourths of Medicaid MCO leaders said their level of concern over managing the financial risk and impact of high-cost durable therapies like CGT was “high” or “extremely high.”¹¹³

As a result of all these concerns, many Medicaid MCOs institute utilization protocols that are more restrictive than the FDA label. In reporting the findings from one of their surveys, MIT NEWDIGS noted that 54% of Medicaid plans reported utilization management that was more restrictive than the label, with 44% covering as specified in the label.¹¹⁴ MACPAC research has found that Medicaid applies utilization management tools at a rate similar to or higher than other payers.¹¹⁵ However, in some cases, Medicaid may have patients receiving a CGT who are more vulnerable than patients covered by other payers – either because such Medicaid patients have a more fragile socioeconomic position or because they face significant barriers to care related to the social determinants of health.



Barriers to Value-Based Payment Arrangements for CGT

VBP arrangements are important for CGT in two key ways. First, they enable the alignment of payment based on value (cost, quality, outcomes) for a specific CGT and can also help generate evidence for value over time. Second, VBP arrangements help reduce some of the budgetary pressure on the Medicaid program by only paying for specific outcomes over time. Experts we interviewed broadly agreed that VBP arrangements were a very important tool for Medicaid programs to help enable access to CGT. Thus, in addition to the broad range of challenges identified thus far, it is important to examine a few other specific challenges to Medicaid's use of VBP for CGT.

Medicaid Paying Over Time. One of the most fundamental challenges to VBP is that there is no simple way for Medicaid programs to pay over time for CGT. Today, states can enter into supplemental rebate agreements with drug manufacturers that build upon the requirements in the existing Medicaid drug rebate program. The details are usually addressed between the state and manufacturer and while supplemental rebate agreements require CMS approval, additional savings to the state does not trigger the requirement in federal statute that drug manufacturers provide Medicaid their best price. While these supplemental rebate agreements are necessary and important, they cannot adequately address the need under VBP for a state to be able to pay a manufacturer over time for a particular CGT.

Medicaid Best Price. On a related subject, experts widely identified Medicaid's best price requirement as a structural challenge in the greater adoption of VBP for CGT. Congress created the Medicaid Drug Rebate Program in 1990 to ensure that Medicaid would receive a net price as low as the lowest or "best price" for which manufacturers sold the drug to any wholesaler, retailer, provider, or paying entity (except for certain governmental payers).¹¹⁶ The best price requirement is included in the Medicaid drug rebate (for brand drugs) such that if a brand drug's "best price is lower than 23.1% below AMP, then the best price generates a higher basic rebate which applies to all Medicaid utilization of the drug" in that quarter of the year.¹¹⁷ Importantly, in contrast to other aggregate calculations, the calculation of Medicaid's best price requirement applies to each of the drug manufacturer's products and contacts with payers or providers. This means that a change in a single contact could trigger a change in Medicaid best price and affect a manufacturer's liability to pay across the entire Medicaid program.

While the Medicaid best price mechanism may have represented an attempt to ensure that the safety net program is an economical payer, it has been widely viewed as hampering manufacturers of CGT from entering into VBP arrangements with Medicaid and other payers. Medicaid's best price requirement is viewed as such a barrier to VBP that CMS has released a regulatory proposal which would redefine "best price" with the goal of enabling more VBP.¹¹⁸ The proposed regulation has received more than 30,000 comments.¹¹⁹

Researchers from the Duke Margolis Center for Health Policy explained that "if total discounts on any unit of the drug involved in a VBP arrangement result in a MBP that is lower than 23.1 percent below AMP, the manufacturer would be required to extend that discount to all of Medicaid."¹²⁰ Put simply, "to fully align payment for a product with that product's actual value, VBP arrangements likely need to offer substantial rebates; however, implying that a product's failure to perform in one patient may effectually lower pricing across all markets may prove to be an unsustainable pricing practice." They provided an example scenario to illustrate why the best price requirement is such a challenge: imagine "an arrangement between a drug manufacturer and a payer wherein the manufacturer agrees to a tiered rebate structure that depends on the drug meeting a range of agreed-upon clinical outcomes."¹²¹ "Different combinations of outcomes could yield different rebates, based on negotiations between the manufacturer and provider/payer... But any rebate greater than 23.1 percent would require the manufacturer to offer the same rebate in all Medicaid contracts, even though the VBP arrangement was intended to be limited and offered in conjunction with new opportunities for value creation..."¹²²

The Anti-Kickback Statute. Another major barrier to VBP arrangements for CGT in Medicaid identified by experts we interviewed was the Anti-Kickback Statute (AKS). Under this statute, it is a felony for a person to knowingly and willfully offer, pay, solicit, or receive anything of value ("remuneration") in return for a referral or to induce generation of business reimbursable under a federal health care program.¹²³ While the AKS does include some limited safe harbors, it was created decades before the emergence of VBP and presents a challenge for "implementation of VBP arrangements since their potential for increased value often depends on some degree of coordination and sharing of resources between the contracting parties."¹²⁴ Experts we spoke with explained the AKS is a barrier to manufacturers that are financially supporting systems and processes important for VBP, such as electronic health records, patient monitoring efforts, software and analytics, data tools, and other materials.



In addition to these significant challenges in federal policy, experts were virtually unanimous in highlighting the need for stronger outcome assessment data for CGT, in order to more accurately gauge value when new therapies come to market, and better inform ongoing coverage and payment efforts. Specifically, payers, providers, patients, plans, and state Medicaid programs often want more granular and specific information on how efficacious a drug’s curative or transformative effect is among specific patient subpopulations, as well the durability of this effect. More robust outcomes data for each CGT is challenging to trace and collect in many cases because of variation in how this data is tracked by states or in new patient registries.

While VBP for CGT holds promise for more closely linking Medicaid program payment to patient outcomes, there is a real tension between the long-term benefit to an individual patient and the high, upfront cost to the program. Many experts stressed that the complexity, uncertainty, and imprecision of trying to design a VBP that would track outcomes and pay accordingly over a four-year or five-year period led them to conclude that the most VBP arrangements could stretch would be two, maybe three years. Experts noted the challenges of patients churning in and out of Medicaid, tracking patient outcomes over a long-time horizon, and other challenges.

The emphasis on a nearer-term contract period tracks with the views of payers, as well. Releasing the results earlier this year from a survey of financial and clinical health plan leaders (including many Medicaid MCOs), the MIT NEWDIGS Initiative found that, in general, “payers are motivated to manage the financial risk associated with high-cost durable one-time treatments differently, making this a high priority.”¹²⁵ The survey found that “payers were most interested in short-term milestone-based contracts, defined as contracts of less than two years duration where the therapy is paid for upfront and the plan receives refunds tied to performance.”¹²⁶

Yet one of the persistent challenges in outcomes-based contracts is identifying concrete outcomes that are clinically relevant, measurable, and that can be identified in the near term. Experts we talked with stressed that there are few appropriate short-term metrics that measure long-term outcomes. “Increased lifespan” or “greater quality of life” is too nebulous and non-specific of an outcome on which to base payment. There is a need to track patient-centered outcomes (such as improvements with activities of daily living, greater reported quality of life, increased rest and alertness, etc.) along with program-centered outcomes (such as reduced inpatient hospital length of stay, reduced utilization of the emergency room, reduced use of other funded support services, etc.).



Challenges to Achieving Scale. Finally, experts stressed the problem that many VBPs for CGT are one-off agreements between a plan or provider and a manufacturer, or between a state and a provider. There are challenges to achieving scale in VBP and accumulated shared learnings that allow the Medicaid program and MCO to drive VBP forward at scale. While researchers from MIT NEWDIGS and the Duke Margolis Center for Health Policy are conducting important work to examine “aspects of value assessment and payment models and some manufacturers are advancing new payment models (e.g., multi-year payback periods), the reality is that the next wave of therapies may enter in greater numbers into a system that has not developed payment models to handle them in volume. Based on the evidence of early uptake of the initial vanguard of therapies, more work is warranted to move away from one-off solutions to more predictable and broadly applicable payment approaches.”¹²⁷

MODERNIZATIONS TO REALIZE THE PROMISE OF CELL AND GENE THERAPY

In light of the many and varied operational, policy, financial, cultural, administrative, technological, and programmatic challenges presented regarding sustainable access to CGT for Medicaid patients, it can be daunting to trace a path forward. Experts we interviewed expressed the sentiment that stakeholders interested in improving the access to and sustainability of CGT for Medicaid patients must simultaneously keep their feet grounded in the details of very real structural and situational challenges, while also keeping their eye on the promise of CGT. CGT is a new frontier of science, and these treatments have opened a new world of hope and help for many Americans served by Medicaid.

One goal that leaders across the range of Medicaid stakeholders articulated is to collaborate with peers to identify and move forward on actionable, incremental improvements to address the many challenges facing patients and stakeholders in the program. Through patient work and quiet dedication by a cross-sector group of health care leaders, specific actions can be taken that will show benefit over time. These actions can accumulate and even gather momentum over time, helping transition a 20th-century coverage and payment model into one that keeps pace with the scientific advancement of the 21st century. Collaborative action can make improvements, strengthen systems, and modernize programs.



RECOMMENDATIONS PROPOSED BY STAKEHOLDERS

Recommendations to Improve Patient Access to Supportive Wraparound Services

- ✓ The federal Anti-Kickback Statute has limited safe harbors that enable health care industry stakeholders to pay for a patient's travel. Last year, the HHS Office of the Inspector General proposed expanding the travel safe harbor,¹²⁸ but this expansion is limited. The travel safe harbor has mileage limits, advertisement limits, and vehicle limits, among other constraints. Some patients participating in certain clinical trials also face limitations in their travel being covered. Congress should work on a bipartisan basis to understand and broaden the current and proposed safe harbor related to travel-related costs, lodging, etc., to ensure that access to care for Medicaid patients is not jeopardized.
- ✓ State Medicaid programs should adopt provider payment strategies to ensure that patients receiving CGT receive their follow-up care (as clinically appropriate) and primary care from providers who are paid economical rates.

Recommendations to Advance Value-Based Payments and Reduce Costs

One of the most challenging elements of VBP approaches for CGT identified by experts has been the complexity and time required in their design and implementation. A number of specific policies and actions can help address this dynamic to enable VBPs to be more rapidly created and scaled.

- ✓ HHS should finalize its 2019 proposed rule that would modernize “safe harbor protections under the Federal anti-kickback statute for certain coordinated care and associated value-based arrangements between or among clinicians, providers, suppliers, and others that squarely meet all safe harbor conditions.”¹²⁹
- ✓ Congressional committees should, after the HHS 2019 rule is finalized, further evaluate perspectives from stakeholders on bipartisan legislative proposals that further modify the Anti-Kickback Statute in a manner that codifies (key provisions or the entirety of) the final rule and includes additional improvements to allow financial support from industry stakeholders for important elements of VBP such as infrastructure for patient registries, data and analytics, information technology, patient monitoring and patient-reported outcomes, etc.
- ✓ CMS should, before potential finalization of its rule, pursue further notice-and-comment rule making regarding the component of its June 2020 proposed rule that would effectively permit the calculation of multiple “best prices” for Medicaid-covered outpatient drugs that “could be made available by the manufacturer for a particular drug based on the drug’s performance (such as the case with VBP arrangements that use evidence or outcomes-based measures) in a quarter.”¹³⁰ While experts we spoke with were generally supportive of efforts to support VBP, given the level of detail in CMS’s proposal, there remain important unanswered questions from many Medicaid stakeholders. For example, there are questions about how possible changes to best price calculations could impact:
 - Manufacturers’ overall liability for Medicaid drug rebate calculations
 - Uniform data reporting and collection, as well as unintended consequences or gaming in pricing decisions
 - Overall Medicaid program spending for drugs (including CGT)
 - Incentives for VBP within Medicaid for drugs (including CGT, especially for rare conditions)
 - Medicaid patient access to drugs and CGT
 - Continued incentives for investment in research and development for CGT for Medicaid patients

The best way for CMS to address these complexities and concerns is through additional transparent notice-and-comment rule making.

- ✓ Congress should adopt the bipartisan policy, which would “add an option for states under SSA Section 1927 to pay for certain covered outpatient drugs through risk-sharing value-based agreements,” through which “states would be able to use the risk-sharing value-based agreements with drug manufacturers for covered outpatient drugs that are potentially curative treatments intended for one-time use.”¹³¹ This new option for states would allow payments for new VBP agreements to be “structured as installment-based payments with the state paying equal installments of the total installment year amount at regular intervals over the period of time.”¹³²
- ✓ CMS should evaluate how it can further support the development of public and private sector efforts to accelerate VBP models for state Medicaid programs related to CGT.
- ✓ Private sector research initiatives and cross-sector collaboration to identify and propose new approaches to entrenched policy challenges are very important and should continue. Experts noted that states need modular VBP contractual options that can be tailored and scaled, rather than developed *ex nihilo* in single-case agreements with manufacturers, providers, and Medicaid MCOs. Collaborative efforts could help provide states with consistent approaches and reduce the development time required for VBP, while helping preserve appropriate flexibility for gaining efficiencies as new data becomes available.

Recommendations to Improve State Medicaid Program Leader Capacity

- ✓ Federal policymakers should support and encourage collaborative work among state Medicaid programs, researchers, and others to periodically catalogue states' financing models for VBP that support CGT. Such work could serve as a policy and technical resource to identify the necessary components of VBP in each successful state model, as well as identify proven or promising practices for other states to consider. These identified best practices should be gathered and disseminated over time to benefit states.
- ✓ Congress should provide state Medicaid programs with capacity development grants to support Medicaid program leadership and staff by improving their ability to (a) understand and prepare for a greater number of CGTs on the market and (b) adopt VBP models tying payment to clinical outcomes. Such capacity grants could help improve program management and oversight; inform negotiations with providers, Medicaid MCOs, and manufactures; and better equip Medicaid staff with fresh insights. Capacity grants could include a wide range of allowable activities that could be eligible for funding, including:
 - Professional development opportunities for Medicaid staff to learn about CGT, FDA approval pathways, evidence collection in clinical trials, etc.
 - Hiring and employing staff or paying contractors with needed subject matter knowledge, skills, or capabilities
 - Providing actuarial support for rate development and analysis, analytical support during procurement, and development or purchase of risk adjustment tools
 - Supporting information technology improvements
 - Improving monitoring and oversight
 - Quality measurement and state evaluation activities, development and deployment of survey tools, costs of accessing, transferring, and analyzing data
- ✓ Congress should evaluate legislative proposals that would provide enhanced federal financial support for the recruitment and retention of top-performing, senior leadership in state Medicaid programs. Such evaluation could include requests for information, committee hearings, or a series of structured conversations with Medicaid stakeholders.

Recommendations for Ongoing Research on Medicaid and CGT

Interviewees broadly expressed concerns that the high costs of many CGTs are exacerbated by the current COVID-19-related recession and fragile financial situation of state Medicaid programs. They noted that greater financial support for states could help avoid a scenario where states respond to the economic turmoil by restricting access to high-cost CGT or making deep reductions in other parts of their Medicaid program. Several experts we talked with expressed conceptual support for the countercyclical Medicaid financing proposal originally outlined by the Government Accountability Office (GAO) and reviewed by MACPAC.¹³³

- ✓ Congress should hold a series of hearings examining the recent research on countercyclical financing proposals. Such hearings would be a useful venue for members to understand the issues of program data, precision and timing, and budgetary impacts, as well as to evaluate potential legislation. Such hearings would also be an appropriate time to hear testimony from economists, budget experts, Governors, Medicaid directors, and other state leaders.



Recommendations to Help Ease State Medicaid Financing Challenges Due to Recession

Many experts were familiar with the analytical work in recent years from the Duke Margolis Center for Health Policy, MIT NEWDIGS, and other related research efforts. Experts underscored the continued need for critical analysis and targeted research to develop promising policy concepts and surface new ideas related to CGT issues in Medicaid. They stressed the importance of cross-sector collaborations that tackle big challenges in Medicaid policy pertaining to CGT by addressing the equities, interests, and views of each Medicaid stakeholder. What follows are recommendations on specific research topics or approaches that merit consideration.

- ✓ Research focused on policy development should be presented in a manner that is accessible to federal and state policymakers. In many cases, such policymakers may understand one element of a particular policy or program challenge, but not have full visibility into all the other component elements or contingencies related to that challenge. Existing research should be packaged in a manner that is easily accessible in order to educate federal and state policymakers through visual, auditory, and interactive means.
- ✓ Stakeholders should continue to invest in ongoing and new cross-sector efforts that incubate research and development of payment and policy concepts for the public and private sectors – with special attention to Medicaid CGT issues, especially to patients with rare conditions.
- ✓ Because of the significant number and potential of CGT products in development, stakeholders suggested that new, targeted federal financial support that helps states bear risk could be a significant mechanism to help maintain sustainable access to CGT. This may be especially warranted due to the unique market conditions of CGT for rare conditions. Further research could help explore what approaches could support states in a focused manner without inadvertently encouraging higher launch prices.
- ✓ Research addressing the prevalence of rare diseases across Medicaid patient populations can help policymakers connect CGT products in development with the footprint of patient populations in a specific state.
- ✓ Research related to how frequently individuals in Medicaid who receive CGT change sources of coverage would be of significant value. Such research could examine topics such as:
 - How frequently do Medicaid patients who receive CGT change sources of health coverage? How frequently and for what period of time do they:
 - Transition into private sector/commercial coverage?
 - Churn and come back into the Medicaid program?
 - Transition out of federally funded health coverage (e.g., Medicare, other Medicaid coverage within a different state or a different MCO within the same state, CHIP, qualified health plan coverage sold on the Exchanges, etc.)?

Such research could help policymakers and other assess the “practicality of including risk adjustment for prior transformative therapies (and the existence of a long-term VBP contract) in Medicare Advantage or other insurance choice systems.”¹³⁴

- ✓ Congress should work together on a bipartisan basis to identify top research and data questions related to Medicaid CGT. Congress could then pursue its research agenda by requesting analytical work from Congressional advisory and analytical entities (MACPAC, GAO, CBO, CRS, etc.) designed to equip policymakers with more granular information.
 - For example, MACPAC has examined several issues related to Medicaid’s coverage of and payment for specialty drugs. In 2018, MACPAC heard about different approaches states are taking to address the challenges of high-cost specialty drugs.¹³⁵ In 2019, MACPAC hosted a conversation that identified some key challenges for specialty drugs and discussed some potential policy solutions.¹³⁶ MACPAC could undertake additional work¹³⁶ to specifically consider the challenges and opportunities pertaining to Medicaid coverage and payment of CGT and implications for Medicaid patients and stakeholders.
- ✓ Duke Margolis researchers identified the need for ongoing research to inform policymaking in three critically important areas:
 - First, “more research on best methods for tracking long-term outcomes data related to a therapy’s impact through post-market registries or suitable claims data systems, improvements in targeting treatments to appropriate patients, and the ability to address unmet needs through more rapid and better-targeted access as a result of these risk-sharing approaches.”¹³⁷

- Second, “additional economic and actuarial modeling could help predict the influx and financial impact of new, approved therapies.” The researchers noted that “by clarifying the costs associated with developing and administering contracts, these economic and actuarial models may add clarity to why VBP arrangements may be worth their additional administrative complexity transformative therapies ideal for exploring VBP approaches.”¹³⁸
- Third, more research is needed to identify promising “strategies for collecting appropriate longer-term outcome measures.”¹³⁹ This could include “conducting registry or post-market studies of intermediate performance measures to validate long-term outcomes,” or “linking the long-term outcome payments to measures included in registries in order to strengthen the support and quality of existing and planned transformative therapies registries.”¹⁴⁰

Recommendations to Address the Lack of Visibility on the CGT Pipeline

MACPAC has recommended that Congress amend the Social Security Act to allow states to exclude or otherwise restrict coverage of a covered outpatient drug for 180 days after a new drug or new formulation of a drug has been approved by the FDA and entered the market.¹⁴¹ MACPAC explained their recommendation sought to address the concern that “current law does not provide sufficient time to assess the effectiveness of a drug or determine appropriate coverage and prior authorization criteria, especially when the drug under review is a first-in-class or novel, complex treatment.”¹⁴² They concluded that “giving states time to review the literature regarding safety, efficacy, and clinical outcomes helps prevent potential drug-related harm and would not likely create undue access restrictions.”¹⁴³

While this recommendation is a well-intended effort to allow program processes to be prepared for the arrival of a new drugs, including CGT, there are understandable concerns that this approach could limit access to life-saving, life-improving CGTs. Such delays could impact any patient who is a candidate for a CGT, posing serious problems for patients with progressive degenerative conditions like spinal muscular atrophy.

- ✓ MACPAC should reexamine their recommendation that Congress amend the Social Security Act to allow states to exclude or otherwise restrict coverage of a covered outpatient drug for 180 days after a new drug or new formulation of a drug has been approved by the FDA and entered the market.
 - MACPAC should work with patient advocates and researchers to evaluate alternate approaches to address the program concerns without an overly broad approach that could inadvertently create a barrier to timely patient access. One possible area for exploration could focus on identifying and removing barriers to more robust pre-approval communications between manufacturers and Medicaid programs.
- ✓ Drug manufacturers should engage state Medicaid programs 12 to 18 months before the anticipated approval of a CGT product to provide states with comprehensive information about a CGT candidate product in clinical trials. Manufacturers should provide as much information as possible on what is known regarding the following:
 - Clinical evidence on efficacy and durability of the CGT candidate product within Medicaid populations and subpopulations
 - Clinical evidence to support coverage within the expect FDA label
 - Disease burden of the condition or disease within each specific state (state-specific information)
 - Insights on what types of providers and sites of care are necessary
 - Insights on what types of support services, follow-up care, and other linkages may need to be made in a patient’s care journey to ensure adherence with clinical protocols and successful treatment
 - Opportunities for value-based payment approaches tied to patient outcomes



Recommendations to Address Racial Inequities

Working to confront and erase racial inequities in health care is a very important and complex task. It is also important that stakeholders acknowledge that racial inequities present in health care overall are present in Medicaid and in access to CGTs in Medicaid. Thus, each Medicaid stakeholder has a responsibility to seek to be informed about current challenges and active within such stakeholder's sphere of influence to confront this reality and remove barriers to care.

- ✓ In general, federal and state policymakers working to confront and erase racial inequities in health care should consider how to leverage the important role Medicaid has to play as a regulator and payer.
- ✓ Congressional leaders seeking to understand the endemic persistence of the challenges they seek to tackle could benefit from marshalling available research. For example, Congressional Committees tasked with jurisdiction over the Medicaid program and the FDA could:
 - Request that the Congressional Research Service produce reports on issues and considerations regarding Medicaid, CGT, and racial inequities.
 - Solicit ideas from major stakeholders and from the public through a public open letter process to help them evaluate to what degree there may be appropriate, bipartisan ways to leverage the important role Medicaid has to play as a regulator and payer in confronting racial inequities in health care.
- ✓ Manufacturers of CGT should continue their efforts to ensure that clinical trials for CGT are diverse and include the full participation of the patient communities that would benefit from them.

Recommendations to Address the Social Determinants of Health

- ✓ To help address the social determinants of health (SDOH) that are a challenge for many Medicaid patients who need CGT, CMS should take several steps using their regulatory and administrative authority.¹⁴⁴ Some of these steps include:
 - Consolidate approved guidance to states and establish a learning collaborative for states addressing SDOH through their Medicaid programs.
 - Provide ongoing, direct technical assistance and guidance to state Medicaid programs in developing, implementing, and evaluating programs that incorporate SDOH interventions.
 - Provide guidance to states surrounding inducements and gifts, and how SDOH activities may fit within "safe harbor exceptions."
 - Outline provisions of the Medicaid managed care regulations that can be used to address SDOH and encourage states to use these flexibilities.
 - Release a Request for Information on mechanisms through which CMS could address "premium slide" concerns raised by MCOs and states. Premium slide could occur if medical costs declined so significantly such that capitated rates also declined and inadvertently reduced the ability of MCOs to continue further investing in SDOH interventions.
 - Encourage states to establish capitation rates that support SDOH interventions as quality improvement activities.
 - Support efforts to make available template language for states to use for MCO contracts addressing SDOH.
- ✓ Experts expressed support for Congress ensuring there is funding for adequate surveillance and screening (including newborn screening and whole exome sequencing) for rare and genetic diseases, especially for pediatric populations. Patient advocates have discussed the challenges many patients and their families may face in receiving an accurate, timely diagnosis for a rare condition. In many cases, a diagnosis provides a way to connect to a specific patient community. Additionally, with so many CGTs in the pipeline for rare diseases and the potential for further clinical studies, parents need an accurate assessment for their child's condition, so they can receive the best care.



Recommendations to Address Access Barriers Related to Geography

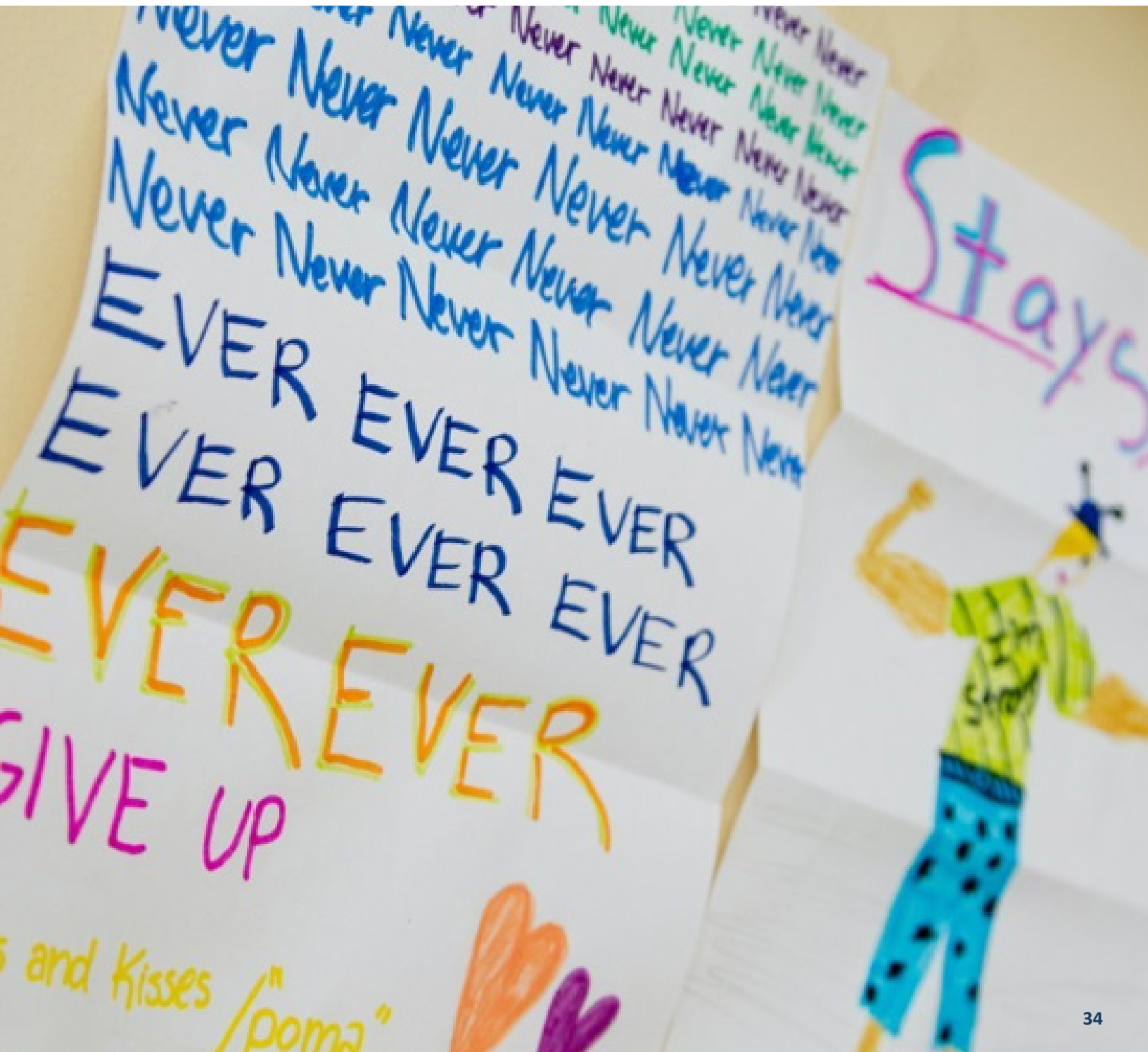
- ✓ Congress should pass bipartisan legislation that would reduce barriers for Medicaid patients receiving CGT in a state other than the state in which they reside. This legislation should:
 - Respect a state program’s authority over health care providers
 - Allow interested states to participate in an arrangement by which providers in another state have a streamlined fast-track process for being credentialed or enrolled in the state
 - Include safeguards to prevent waste, fraud, and abuse
 - Be designed to include pediatric providers and providers most likely to provide CGT (such as a center of excellence or academic medical center).
- ✓ The Accelerating Kids’ Access to Care Act, a piece of bipartisan Senate legislation that was recently introduced, appears to meet these criteria, and it merits further development and passage by Congress.¹⁴⁵
- ✓ CMS should work with states to identify best practices for enrolling out-of-state providers in a timely and economical manner that safeguards program integrity. Proven and promising practices should be shared with the states via a State Medicaid Director letter or program information bulletin.
 - CMS should examine whether the responses to CMS’s January 2020 Request for Information regarding “coordination of care from out-of-state providers for Medicaid-eligible children with medically complex conditions” are of sufficient detail and value to form the basis for such communication.¹⁴⁶
- ✓ State Medicaid program leadership for neighboring states, or states which see a significant number of Medicaid patients traveling between such states, should examine to what degree aligning on coverage and payment criteria would reduce administrative costs for the state program and Medicaid MCOs in both states.

Recommendations on Patient-Prioritized Outcomes and Evaluations of Therapy Success

- ✓ Manufacturers should collect data during CGT clinical trials sufficient to help inform Patient-Reported Outcome Measures (PROMs) or Goal-Attainment Scaling outcomes that effectively serve as, or correlate with, endpoints for rare conditions.
 - “PROMs are standardized, validated questionnaires that are completed by patients’ during the perioperative period to ascertain perceptions of their health status, perceived level of impairment, disability, and health-related quality of life” that “allow the efficacy of a clinical intervention to be measured from the patients’ perspective.”¹⁴⁷
 - Goal-Attainment Scaling “is an instrument that is intended to evaluate the effect of an intervention by assessing change in daily life activities on an individual basis.” The tool is “most useful if improvement can be assessed in functional terms. The key element of GAS is the difference that a patient notices, which can also be assessed more or less objectively by an independent assessor. In some cases this could be measured objectively, even with a validated high quality Patient Reported Outcome Measure (PROM) or function test, but in many cases the patient’s individual goals cannot be captured in an existing validated PROM or other measurement instrument.”¹⁴⁸
- ✓ Payers should consider CGT clinical trial endpoints for rare conditions that may be atypical measures of efficacy but could represent more easily measurable standards of the functional benefits conferred by CGT.¹⁴⁹
- ✓ As appropriate, manufacturers should collect and make available to state Medicaid programs real-world data on how caregivers of patients receiving CGT experience a secondary benefit from the patient receiving CGT (such as reduced levels of stress and better ability to sleep, fewer missed work days, greater earnings, etc.) While such data may not in many cases identify positive benefits to caregivers that are hard costs for Medicaid, it is an important data point and could (for non-rare conditions) have a material impact on Medicaid-related costs.
- ✓ State Medicaid programs should work with Medicaid MCOs and providers to utilize patient survey data in developing metrics of success pertaining to the delivery and receipt of CGT.

CONCLUSION

While some health care challenges and their potential solutions polarize stakeholders and policymakers and thus are never overcome, there are others where consensus emerges and a problem once perceived as unconquerable is solved. Based on our conversations with experts from different parts of the health care ecosystem and levels of government, we believe that Medicaid coverage for cell and gene therapies, especially those for rare conditions, carries the potential to become one of those areas where consensus on the challenges and solutions could develop. The challenges surrounding this issue are significant. However, according to the experts interviewed, so are the consequences of failing to work together to find and implement solutions. Consideration and pursuit of the recommendations detailed above (and others that will emerge) could enable these challenges to be overcome, thus ensuring timely access to 21st-century treatments and cures for patients in the Medicaid program.



APPENDIX 1

FDA-Approved CGTs on the Market Today

Trade Name	Type of Therapy	Used to Treat
HPC Cord Blood Therapies <ul style="list-style-type: none"> • ALLOCORD • CLEVECORD • Ducord • HEMACORD • HPC, Cord Blood • Other names as well 	Allogeneic cord blood hematopoietic progenitor (cell therapy)	For use in unrelated donor hematopoietic progenitor cell transplantation procedures in conjunction with an appropriate preparative regimen for hematopoietic and immunologic reconstitution in patients with disorders affecting the hematopoietic system that are inherited, acquired, or result from myeloablative treatment. ¹⁵⁰
GINTUIT (allogenic cultured keratinocytes and fibroblasts in bovine collagen)	Allogeneic cellularized scaffold product (cell therapy)	Treatment for topical (non-submerged) application to surgically created vascular wound bed in the treatment of mucogingival conditions in adults. ¹⁵¹
IMLYGIC (talimogene laherparepvec)	Genetically modified oncolytic viral therapy (cell therapy)	Local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery. ¹⁵²
KYMRIAH (tisagenlecleucel)	Genetically modified autologous T-cell immunotherapy (gene therapy)	Pediatric and young adult patients with a form of acute lymphoblastic leukemia . ¹⁵³
LAVIV (Azficel-T)	Autologous cellular product (cell therapy)	Improvement of the appearance of moderate to severe nasolabial fold wrinkles in adults. ¹⁵⁴
LUXTURNA (voretigene neparvovec-rzyl)	Adeno-associated virus vector-based gene therapy	Children and adults with confirmed RPE65 mutation-associated retinal dystrophy , which leads to vision loss and sometimes complete blindness. ¹⁵⁴
MACI (autologous cultured chondrocytes on a porcine collagen membrane)	Autologous cellularized scaffold product (cell therapy)	Repair of symptomatic, full-thickness cartilage defects in the knees of adult patients. ¹⁵⁵
PROVENGE (sipuleucel-T)	Autologous cellular immunotherapy (cell therapy)	Prostate cancer in patients with asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) cases. ¹⁵⁶
TECARTUS (brexucabtagene autoleucel)	Cell-based gene therapy (chimeric antigen receptor (CAR)-T cell therapy)	Mantle cell lymphoma (MCL) in patients who have not responded to or relapsed after other types of therapies. ¹⁵⁷
YESCARTA (axicabtagene ciloleucel)	Cell-based gene therapy (CAR-T cell therapy)	Certain types of large B-cell lymphoma in patients who have not responded to or have relapsed after at least two other types of treatment. ¹⁵⁸
ZOLGENSMA (onasemnogene abeparvovec-xioi)	Adeno-associated virus vector-based gene therapy	Spinal muscular atrophy (SMA) in patients less than 2 years of age. ¹⁵⁹

SOURCES

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- ²The Margolis Center for Health Policy at Duke University and the Massachusetts Institute of Technology's (MIT's) NEW Drug Development Paradigms (NEWDIGS) program have both worked on collaborative efforts in cell and gene therapy coverage and payment. Their works are cited throughout this paper.
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