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Accessing Cell and Gene Therapies

Insights on Coverage, Reimbursement and Emerging Models

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Introduction

Over the past five years, cell and gene therapies have increasingly moved from the R&D pipeline to the health care setting, putting lifesaving treatments for certain cancers and genetic diseases within patients' reach. Over ten cell and gene therapies have been approved by the FDA in the past five years[1] and over 500 gene-based therapies are in clinical development[2] as of 2023. Based on current pipeline and product success rates, the FDA anticipates approving 10–20 a year by 2025,[3] with spending expected to reach $25 billion annually over the next ten years.[4]

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With the emergence of these transformative treatments, payers are facing a practical reality of paying for them, with list prices ranging from $400,000 to $3.5 million per course of treatment. Payers are looking for predictable financing solutions for these large often one-time payments and for proof of therapeutic efficacy via value-focused payment approaches.

Cell and Gene Therapy Today

Cell and gene therapies seek to modify genetic material in order to treat an inherited or acquired disease. Preparing and administering cell and gene therapies is a complex and expensive process. Cell therapy aims to infuse whole cells into a patient's body to replace or repair damaged tissues and may involve blood transfusion or transplantation of stem cells to create bone marrow. Gene therapy aims to modify a mutated gene or introduce a new copy of a gene; different types of gene therapy include gene addition, silencing, reprogramming or elimination.[5]

Payers are looking for predictable financing solutions to support patient access to these lifesaving treatments.

Once a therapy gains FDA approval, a patient's journey typically involves (1) an assessment of eligibility, risks and benefits of a particular therapy, (2) insurance coverage authorization, (3) preparation of any personalized gene therapy, (4) treatment, potentially as an inpatient or outpatient procedure, and (5) a follow-up recovery period.

Various cell and gene therapies have gained market approval over the past five years (see Exhibit 1), creating the need for state Medicaid agencies and commercial payers to find financing solutions to cover therapy costs that have currently reached as high as $3.5 million per course of treatment.

Exhibit 1. FDA-Approved Cell and Gene Therapies 2017–2023[6]

Product Name	Disease	Year First Approved	Company
Elevidys	Duchenne muscular dystrophy	2023	Sarepta Therapeutics
Adstiladrin	Bladder cancer	2022	Ferring Pharmaceuticals
Hemgenix	Hemophilia B	2022	CSL Behring
Carvykti	Multiple myeloma	2022	Janssen Biotech
Skysona	Early cerebral adrenoleukodystrophy (CALD)	2022	Bluebird Bio
Abecma	Multiple myeloma	2021	Bristol Myers Squibb
Breyanzi	Diffuse large B-cell lymphoma; follicular lymphoma	2021	Bristol Myers Squibb
Tecartus	Mantle cell lymphoma; acute lymphocytic leukemia	2020	Kite Pharma (Gilead)
Zynteglo	Transfusion-dependent beta thalassemia	2022	Bluebird Bio
Zolgensma	Spinal muscular atrophy	2019	Novartis
Kymriah	Acute lymphocytic leukemia; diffuse large B-cell lymphoma; follicular lymphoma	2017	Novartis
Yescarta	Large B-cell lymphoma	2017	Kite Pharma (Gilead)
Luxturna	Leber's congenital amaurosis; retinitis pigmentosa	2017	Spark Therapeutics (Roche)

Medicaid Coverage

State Medicaid programs are required to cover all FDA-approved drugs if the drug manufacturer has signed a federal Medicaid rebate agreement.[7] In practice, states sometimes delay coverage of newly approved drugs, and cell and gene therapies are almost always subject to prior authorization given their price point. There is significant variability in whether or how states cover cell and gene therapies. For instance, some states limit eligibility to more narrow clinical trial criteria rather than relying on the FDA label.[8] Reimbursement and access are further complicated by out-of-state (OOS) dynamics, since many patients will need to travel to another state to get cell and gene therapies. OOS providers are often paid at a lower rate and may lack supplemental funding available to in-state providers; they also have to enroll in every state Medicaid program to which they provide services, further reducing incentives to provide OOS care. Additionally, limited Medicaid coverage of travel benefits may make such travel cost-prohibitive for patients.

Most Medicaid programs use a diagnosis-related group (DRG) system to reimburse hospitals for inpatient services, where a hospital receives a bundled payment for both the services provided and any drugs administered. Since the costs of cell and gene therapy to hospitals may be significantly higher than such reimbursement, such reimbursement structure could disincentivize hospitals from offering cell and gene therapies to patients. To ensure adequate reimbursement to hospitals and patient access to cell and gene therapies, some state Medicaid agencies implement separate payment policies, where a cell preparation or a drug itself is paid separately from inpatient drug administration. Often the reimbursement rate is close to the hospital's acquisition cost for the drugs.

Over ten states have published policies indicating they make separate payments for at least some cell and gene therapies. These states represent nearly half of all Medicaid enrollees. States that have developed separate payment policies for cell and gene therapies are more likely to cover these therapies, resulting in greater access by beneficiaries.

Another emerging approach to balancing costs and patient access is value-based arrangements, where performance-based contracts are linked to targets around efficacy and durability of patient response. Fifteen states[9] have established Medicaid pharmacy supplemental rebate agreements that provide them with legal authority to enter into value-based payment (VBP) arrangements. As of February, two states—Massachusetts and Arizona—have applied this authority to implementing cell and gene therapy specific VBP arrangements.[10]

Several states are using reinsurance programs to manage cell and gene therapy costs. These programs are intended to provide protection to Medicaid managed care organizations (MCOs), which, depending on their size, can face financial troubles if they pay a higher-than-expected number of cell and gene therapy claims. Some states mandate that MCOs obtain reinsurance coverage for specific therapies through private reinsurers. Other states provide reinsurance protection themselves by, for example, withholding a portion of the capitation payment to the MCO as the reinsurance premium and then paying to the MCO all or a portion of cell and gene therapy claims. Other states have gone further, carving out certain cell and gene therapies from the managed care benefit entirely.

State Medicaid agencies use separate payment policies, VBP arrangements and reinsurance programs to manage cell/gene therapy costs and patient access.

State calculus for offering separate payments for cell and gene therapies may change in the future given a proposed rule issued by Centers for Medicare and Medicaid Services (CMS) in May 2023,[11] which could trigger rebate liability from the drug manufacturer to the state for drugs that are reimbursed as part of a bundled payment. Currently, a drug provided as part of a bundled payment is not considered a "covered outpatient drug" (COD) and as such is exempt from rebates.[12] The CMS rule proposes that a drug provided as part of a bundled payment would be eligible for rebates, making separate payment options potentially less attractive to states than they are now.

The same rule proposes another cost control mechanism—a new "drug price verification survey," which would collect cost, utilization and pricing data for high-priced therapies (cell and gene therapies were specifically called out as an area of focus). Alternatively, manufacturers can provide higher supplemental rebates in exchange for being exempt from the survey and its time-consuming transparency data requirements.

Another proposed federal initiative is the Cell and Gene Therapy Access Model, in which CMS would coordinate and administer outcomes-based agreements with participating manufacturers for certain cell and gene therapies on behalf of state Medicaid agencies.[13] These agreements could be in the form of outcomes-based payments, rebates or annuities, where continued payment is based on durability of benefit. This model may initially be targeted to a specific therapy (e.g., sickle cell disease), and further details will be released in 2024/2025, with implementation expected in 2026. The proposal is a step toward "federalizing" the cell and gene therapy benefit, with states ceding some control over rebate negotiations in exchange for less administrative burden in managing these drugs.

On the federal level, CMS has proposed Cell and Gene Therapy Model, in which CMS would coordinate outcomes-based agreements with drug manufacturers for cell and gene therapies on behalf of states.

Medicare Coverage

Medicare covers services that are "reasonable and necessary for the diagnosis or treatment of an illness or injury,"[14] with most coverage policies decided by local Medicare Administrative Contractors (MACs), some determined on the national level (national coverage determinations), and some determined on a case-by-case basis.

Medicare is somewhat behind Medicaid in its flexibility to cover and reimburse high-price transformative therapies. Medicare may pay additional funds to a hospital for a newly launched high-price therapy via New Technology Add-On Payments (NTAP) or outlier payments in the case of inpatient therapies or pass-through payments in the case of outpatient payments. Medicare has also established a new DRG for chimeric antigen receptor (CAR) T-cell and other immunotherapies. The Medicare program, however, has not experimented with VBP arrangements or separate payments for therapies provided in the inpatient setting. In the case of CAR T therapies, it took over three years to establish a new DRG, given the need to accumulate sufficient data and the timing of the rulemaking cycle. Cell and gene therapy would likely face similar hurdles, with patient access potentially limited in the meantime.

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In its August 2022 Inpatient Prospective Payment System (IPPS) rule,[15] CMS indicated that it would consider a new DRG for cell and gene therapies in future rulemaking but is not yet ready to make structural reimbursement changes to accommodate cell and gene therapies. In the meantime, including new therapies in an existing DRG presents a challenge, given some therapies have list prices above $2 million while the CAR T DRG base payment rate is approximately $300,000.

In February 2023, the Center for Medicare and Medicaid Innovation issued a report describing the innovation models it has selected for testing based on affordability, accessibility and feasibility of implementation.[16] As opposed to an outcomes-based access model suggested for Medicaid, CMS suggests a bundled payment approach for Medicare—a model that would replace fee-for-service billing during cell/gene therapy care episodes. The proposal appears aimed at controlling costs provided to a Medicare beneficiary post receipt of the cell and gene therapy and does not focus on the question of how to balance affordability with the need for access.

Commercial Coverage

In commercial coverage, there are no federal requirements for plans to cover specific drugs, although plans in the individual and small group market are required to cover essential health benefits (EHBs) that set minimum standards for prescription drug coverage.[17] With the emergence of cell and gene therapies, plans and employers are looking for ways to enable access for their beneficiaries while managing high upfront costs. Given the legal flexibility to define the benefit package provided under large group health plans, some employers have considered excluding coverage of cell and gene therapies from their benefit packages entirely, although that approach does not appear to be widespread.

Obtaining reinsurance for cell and gene therapies is critical for commercial payers. Since general reinsurance policies may exclude cell and gene therapies, secondary reinsurance policies have been established specifically for these therapies. For example, Cigna/Express Scripts, United Healthcare/Optum and Aetna/CVS all offer cell and gene therapy reinsurance programs, which allow self-insured plan sponsors to pay a fixed per member per month fee, in exchange for transferring claim risk for cell and gene therapies.

> Commercial payers generally use secondary reinsurance policies and stop loss products to manage cell and gene therapy costs.

Similar to reinsurance products, United Healthcare and Optum offer to self-insured plans a stop-loss product, called Gene Therapy Risk Protection, for several gene therapies (e.g., Luxturna, Zolgensma, Lenti-D and NSR-REP1[18])—this product provides claim protection once a deductible is met. The program includes prior authorization and utilization management, risk analytics and other support.

VBP arrangements for pharmaceuticals are getting off the ground, but as with Medicaid, progress has been in part limited by Medicaid rules, requiring drug manufacturers to provide "best price" to state Medicaid agencies. In 2022, a CMS rule that allows manufacturers to report separate pricing in the context of value-based arrangements (multiple "best prices") opened the door to such arrangements in the commercial market. Under that rule, if a manufacturer enters into a VBP arrangement with a commercial payer, as long as

it offers a similar arrangement with the same pricing to state Medicaid programs, it can report multiple VBP and non-VBP best prices.[19] But manufacturers have not yet embraced such arrangements; as of the end of 2022, no such arrangements had been reported to states.

Nevertheless, some commercial payers have experimented with VBP arrangements, even if those have not focused on cell and gene therapies. As of 2021, approximately half of commercial payers are estimated to have entered into an outcomes-based contract, with the majority of those indicating two to five outcomes-based contracts.[20] Challenges include required investments into infrastructure as well as operational hurdles, such as patients staying on average 3–4 years with the same insurer (e.g., deciding which insurer receives the rebate if outcomes are not met may be problematic).

Looking Ahead

Anticipating a growing cell and gene therapy market, payers are increasingly thinking about using innovative cost management strategies. According to the 2022 national Magellan Rx Medical Pharmacy Report, gene therapies represent a top concern for half of the surveyed payers.[21]

Similarly, state Medicaid agencies reported in a recent survey that addressing the costs of cell and gene therapies is a key priority, with separate payments and the use of the National Medicaid Pooling Initiative for supplemental rebates among state strategies.[22]

Cell and gene therapies offer life-changing opportunities for patients suffering from blood cancers, genetic diseases and rare diseases. Protecting patient access, managing costs and linking payments to quality will be top of mind for payers as they adopt new cell and gene therapy payment models going forward.

[1] Cell and gene therapies approved by the FDA over the past three years include Elevidys for Duchenne muscular dystrophy, Adstiladrin for bladder cancer, Skysona for neurological dysfunction with active cerebral adrenoleukodystrophy, Zynteglo for beta-thalassemia, Hemgenix for hemophilia B, and Breyanzi and Carvykti for blood cancers/disorders, among others. The first three therapies—Kymriah, Luxturna and Yescarta—were approved by the FDA in 2017.

[2] ASGCT & Citeline. (2023). *Gene, Cell, & RNA Therapy Landscape*. ASGCT. https://asgct.org/global/documents/asgct-citeline-q1-2023-report.aspx

[3] Gottlieb, S. (2019, January 15). *Statement from FDA Commissioner Scott Gottlieb, M.D., and Peter Marks, M.D., Ph.D., director of the Center for Biologics Evaluation and Research on new policies to advance development of safe and effective cell and gene therapies*. U.S. Food and Drug Administration. https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-peter-marks-md-phd-director-center-biologics

[4] Becerra, X. (2023, February 14). *A Report in Response to the Executive Order on Lowering Prescription Drug Costs for Americans*. Centers for Medicare & Medicaid Services. https://innovation.cms.gov/data-and-reports/2023/eo-rx-drug-cost-response-report

[5] American Society of Gene + Cell Therapy. (n.d.). *Gene & Cell Therapy FAQs*. ASGCT. https://asgct.org/education/more-resources/gene-and-cell-therapy-faqs

[6] U.S. Food and Drug Administration. (2023, May 19). *Approved Cellular and Gene Therapy Products*. FDA. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products and see Endnote 2.

[7] The Medicaid Drug Rebate Program (MDRP), authorized by Section 1927 of the Social Security Act, requires drug manufacturers to enter into a National Drug Rebate Agreement with HHS in exchange for state Medicaid coverage of most of the manufacturer's drugs. It includes CMS, state Medicaid agencies and ~780 drug manufacturers. For more information, see https://www.medicaid.gov/medicaid/prescription-drugs/medicaid-drug-rebate-program/index.html.

[8] In its 2022 state and national MCO survey of coverage policies for cell and gene therapies, the American Society of Gene and Cell Therapy (ASGCT) identified coverage and access barriers related to Luxturna, Zolgensma and Kymriah. For more information, see https://doi.org/10.1016/j.ymthe.2022.08.009.

[9] AL, AZ, AR, CO, LA, MA, MI, NC, OH, OK, TN, TX, WA, NY and PA.

[10] See Endnote 4.

[11] Centers for Medicare & Medicaid Services. (2023, May 26). *Medicaid Program; Misclassification of Drugs, Program Administration and Program Integrity Updates Under the Medicaid Drug Rebate Program*. Federal Register. https://www.federalregister.gov/documents/2023/05/26/2023-10934/medicaid-program-misclassification-of-drugs-program-administration-and-program-integrity-updates

[12] CMS proposes that a drug provided as part of a bundled payment could be a COD eligible for rebates "if the drug and the itemized cost of the drug are separately identified on the claim." This is a significant change from current practice, where drugs paid for under DRGs and other bundled payments generally are exempt from rebates. CMS appears to be saying that so long as a claim references the provision of a drug and there is a charge for that drug on that claim (whether that charge is for $1 or for $10 million), that is enough to trigger rebate liability. For more information, see the Manatt on Health Analysis from May 30, 2023 titled "CMS Proposes Drug Price 'Verification' in Medicaid Rule."

[13] See Endnote 4.

[14] Centers for Medicare & Medicaid Services. (n.d.). *Medicare Coverage Determination Process*. CMS. https://www.cms.gov/Medicare/Coverage/DeterminationProcess

[15] Centers for Medicare & Medicaid Services. (2022, August 10). *Medicare Program; Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long-Term Care Hospital Prospective Payment System and Policy Changes and Fiscal Year 2023 Rates; Quality Programs and Medicare Promoting Interoperability Program Requirements for Eligible Hospitals and Critical Access Hospitals; Costs Incurred for Qualified and Non-Qualified Deferred Compensation Plans; and Changes to Hospital and Critical Access Hospital Conditions of Participation*. Federal Register. https://www.govinfo.gov/content/pkg/FR-2022-08-10/pdf/2022-16472.pdf

[16] See Endnote 4.

[17] For prescription drugs included in the EHB, cost-sharing is capped by a plan's maximum annual limit on cost-sharing. For those drugs or plans not subject to EHB (e.g., large group or self-insured plans) patients' out-of-pocket costs for cell and gene therapies may be prohibitive.

[18] UnitedHealthcare (2021, March 9). *Gene Therapy Risk Protection may help cover therapies and manage financial risk*. UHC. https://www.uhc.com/broker-consultant/news-strategies/resources/gene-therapy-risk-protection-may-help-cover-therapies-and-manage-financial-risk

[19] Centers for Medicare & Medicaid Services. (2022, March 23). *Technical Guidance – Value-Based Purchasing (VBP) Arrangements for Drug Therapies using Multiple Best Prices*. CMS. https://www.medicaid.gov/prescription-drugs/downloads/mfr-rel-116-vbp.pdf

[20] McCarthy, K., Cricchi, L., Shvets, E., Santiesteban, D. (2021, November 4). *Avalere Survey: Over Half of Health Plans Use Outcomes-Based Contracts*. Avalere. https://avalere.com/insights/avalere-survey-over-half-of-health-plans-use-outcomes-based-contracts

[21] The national report covers 152 million lives across 40 payers that include Medicaid state agencies, Medicare and commercial payers. For more information, see https://www1.magellanrx.com/documents/2022/12/medical-pharmacy-trend-report-2022.pdf.

[22] Hinton, E., Guth, M., Raphael, J., Haldar, S., Rudowitz, R., Gifford, K., Lashbrook, A., Nardone, M., Wimmer, M. (2022, October). *How the Pandemic Continues to Shape Medicaid Priorities: Results from an Annual Medicaid Budget Survey for State Fiscal Years 2022 and 2023*. KFF. https://files.kff.org/attachment/REPORT-How-the-Pandemic-Continues-to-Shape-Medicaid-Priorities-Results-from-an-Annual-Medicaid-Budget-Survey-for-State-Fiscal-Years-2022-and-2023.pdf

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