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Managing the challenges of paying for gene therapy: strategies for market action and policy reform in the United States

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Gene therapies delivered through a single administration have revolutionized treatment possibilities for many patients living with serious or fatal conditions such as spinal muscular atrophy, hemophilia and sickle cell disease. However, shadowing the excitement about the transformational potential of many gene therapies has been widespread concern about the combination of uncertainty in the durability of their benefits over the long term and the short-term financial shock of high prices. As the healthcare payment ecosystem prepares for the growing number of gene therapies entering the market, three key interconnected challenges must be addressed: determining a fair price, managing clinical uncertainty and managing short-term budget impacts. This paper identifies specific policy reforms and market-based tools to help the US health system address these challenges to achieve more equitable and affordable access for patients to the growing number of gene therapies expected to be approved in the coming years.

Tweetable abstract: New policy analysis from ICER and NEWDIGS analyzes the challenges and potential policy options for paying for gene therapies.

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Gene therapies delivered through a single administration have revolutionized treatment possibilities for many patients living with serious or fatal conditions such as spinal muscular atrophy, hemophilia and sickle cell disease [1]. However, shadowing the excitement about the transformational potential of many gene therapies has been widespread concern about the combination of uncertainty in the durability of their benefits over the long term and the short-term financial shock of high prices, which are now cresting above $3 million dollars [2].

Although the aggregate costs of gene therapies at these prices have not proven yet to be unmanageable to large payers given the small number of patients currently treated, growth in the approval of gene therapies for larger populations is on the horizon. All told, 85 new gene therapies across more than 12 therapeutic areas are expected to receive regulatory approval by 2032, with an estimated ten-year list price spend of $35 to $40 billion [3]. The pipeline of gene therapies and their anticipated costs raise concerns that gene therapies will create budget pressures and consequent constraints on access even for larger payers. Smaller employers, state Medicaid departments, and regional health plans may find providing access financially impossible without some modification in pricing or payment methods [4–8].

As the healthcare payment ecosystem prepares for the growing number of gene therapies entering the market, three key interconnected challenges must be addressed: determining a fair price, managing clinical uncertainty and managing short-term budget impacts. Given the potential impact of these therapies on human lives, novel solutions to these challenges must be considered to achieve the right balance of providing incentives for innovation while ensuring equitable and affordable access for health systems and for patients.

The goal of this paper is to explore the range of emerging market approaches and possible policy reforms that may help the broader US health system meet this goal. We analyze the relative advantages and potential unintended consequences for each option, along with an exploration of unique opportunities for combination or layered

approaches. None of the tools or policy reforms we discuss are 'silver bullets' that can singlehandedly solve all the barriers and tensions inherent in the current healthcare insurance and payment landscape. Still, we seek to present policymakers and industry leaders with insights and lessons learned from experts and market experience to date that will help all stakeholders be part of an innovative future of gene therapy pricing, coverage, payment and access.

Methods

To inform this work, we performed a targeted literature review and drew upon the body of work on gene therapy issues from the Institute for Clinical and Economic Review (ICER) and NEWDIGS FoCUS (Financing and Reimbursement of Cures in the US) Project [9]. Our targeted literature review included keyword and hand searches for peer-reviewed and gray literature to understand the impact that payment challenges have on payer affordability and the downstream impact on patient access.

Additionally, we performed interviews using a structured discussion guide (available upon request) to collect input from twenty-two experts from payer organizations, large and small biopharmaceutical manufacturers, patient advocacy groups, providers and ancillary vendors offering or providing necessary execution support for potential solutions. From this background work, we developed a set of market actions and policy reforms reflecting possible solutions, or enablers to solutions, from the key challenges identified. These market actions and policy reforms were the basis of formal discussion and further revision during a 2-day policy summit in December 2023 with senior policy leaders from 33 patient, purchaser, employer, payer and life science companies. A final white paper was posted in April 2024.

Determining a fair price

The main thrust of this analysis is to explore innovative insurance and payment mechanisms to help address the challenges facing health systems seeking to reap the opportunities presented by gene therapy. But pricing is an inextricable element in any model to improve access and affordability. Whether the price for a cell or gene therapy is paid as a single fee at the time of administration or is paid through some form of installment payment agreement, determining a 'fair' price remains a foundational step in managing uncertainty while providing incentives aligning the cost of new treatments with their benefits to patients.

Strategy 1: reduce pricing to reflect uncertainty

There are several technical methods that could be applied to cost–effectiveness modeling to produce lower pricing recommendations in the context of enhanced uncertainty [10]. The simplest approach would be to set a lower cost–effectiveness threshold. For example, if established parameters for value-based pricing range from $100,000 to $150,000 per quality-adjusted life year (QALY) or equal value of life year gained (evLYG), the lower threshold alone could be used when determining a fair value-based price for gene therapies that lack data on outcomes beyond a certain time point (for example 5 years).

A second approach would use the same range or threshold for all treatments but would calculate a scenario for gene therapies using conservative assumptions about the duration of benefit beyond that shown in clinical trials. For example, a formal conservative scenario could assume that the benefit of treatment ends or begins to decline rapidly at the time horizon of existing data, thereby producing a lower value-based price range. cost–effectiveness analysis could also be done to calculate the value-based prices needed to meet established cost–effectiveness thresholds with an assumed duration of benefit ending at different time points. For consistency, however, when longer-term data are lacking, policymakers might want to consider setting a formal conservative time horizon for assumed benefit in all cost–effectiveness analyses at no more than 5 years.

Any method for modulating initial pricing to address uncertainty would serve to share financial risk between plan sponsors and manufacturers. Conceptually, lower prices at launch should be paired with price increase (or decrease) mechanisms later in the life cycle of the treatment should evidence demonstrate longer (or shorter) durability of benefits than initially assumed. It must also be considered whether establishing a framework using lower cost–effectiveness thresholds for gene therapies would shift incentives for investment away from one-time treatments toward chronic treatments. Patients and the healthcare system are likely to benefit more from effective one-time treatments, so unintended consequences of structural approaches to discounting the calculated value of value-based pricing for these treatments should be carefully deliberated.

Strategy 2: integrate considerations of special ethical priorities into value-based pricing

Whether qualitative approaches or cost–effectiveness analyses are used to help evaluate fair pricing levels for new interventions, policymakers must have some mechanism to integrate considerations of special ethical priorities into evaluations of evidence to guide a broader judgment of value. The most common ethical priorities considered by HTA groups and insurers relate to treatments for conditions that are particularly severe, that extend life near the end of life, and/or that involve children. Most of these considerations will be factors in conditions treated by gene therapies, highlighting the challenging interplay of evidence and values in setting priorities and pricing levels for these treatments.

Quantitative methods for varying value-based pricing according to the relative severity of the condition are being used by a few HTA agencies, notably those in the UK, Norway, Sweden and The Netherlands. Still, no established best practice exists and each agency uses a different method. Without a consensus regarding quantitative methods to guide the integration of special ethical priorities into value-based price determination, HTA programs have emphasized the vital role that public deliberation can play in achieving this goal. Although the public deliberation methods of HTA programs vary widely, there is a common attempt to have some structured discussion related to ethical priorities that might influence thinking on fair pricing. ICER's methods for public deliberation have served as one model in which assessment reports have structured sections related to the 'benefits beyond health' and 'special ethical priorities' relevant for treatments. The special ethical priorities considered include health equity and unmet need (i.e., severity). Guided deliberation on these elements during ICER public meetings culminates in voting on specific issues by independent appraisal committees. This approach seeks to make integrating special ethical priorities into pricing as tangible and routine as possible without reducing the process to an algorithmic quantitative approach that would raise substantial concerns among many stakeholders. However, the major risk of relying on a deliberative process remains. Deliberation will prove less consistent and lack the concrete power to affect value-based pricing considerations in the way that quantitative methods could.

Strategy 3: calculate value-based prices with 'shared savings'

ICER has introduced the concept of a 'shared savings' approach for calculating value-based price benchmarks for one-time gene therapies. In this shared savings approach, health gains are valued in a traditional manner, but the value of cost offsets assumed from successful treatment are not assigned entirely to the manufacturer (in the price of the treatment). Instead, the value of cost offsets is split between the manufacturer and the health system [10,11]. This approach is controversial because it decreases the calculated value-based price of a one-time gene therapy, but its philosophical justification arises from the idea that society should be able to share in the long-term cost savings from one-time treatments, especially when those cost savings are substantial and often based on eliminating future treatments that have not been priced at cost-effective levels.

There is no empirical way to determine the most appropriate division of potential cost savings when calculating a value-based price under a shared savings scenario. Through a formal methods development program with extensive input from industry, plan sponsors and other stakeholders, ICER developed two methods for performing a shared savings scenario: a method in which 50% of the lifetime health system cost offsets from a new treatment are 'assigned' to the health system instead of being assigned entirely to the new treatment, and a cost-offset cap method in which the health system cost offsets generated by a new treatment are capped at $150,000 per year but are otherwise assigned entirely to the new treatment.

The potential downside of adopting a shared savings approach to value-based pricing centers on the risk that it may be viewed as seriously undervaluing cures that help reduce healthcare costs, thereby reducing incentives for innovators to tackle the most expensive conditions. In addition, selecting a 50% share in cost savings is arbitrary. Criteria could be developed to guide whether innovators get a larger or smaller proportion of cost-offset savings, but ultimately the selection of a 'fair' sharing of this component of the value of a one-time therapy would be subjective.

A summary of the advantages and disadvantages of each potential strategy is shown in Table 1.

Managing clinical uncertainty

All drugs have some level of uncertainty at the time of launch regarding their long-term safety and effectiveness, but as noted above, for multiple reasons, gene therapies enter practice with more limited data and unique levels of uncertainty regarding the durability of their beneficial effects. Paying millions of dollars all at once at the time of administration magnifies the concerns that payers have about whether they will receive a reasonable clinical value for their investment.

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Table 1. Tools to determine a fair price.

Tool	Distinctive advantages	Distinctive barriers/disadvantages
Reduce pricing to reflect uncertainty	Plan sponsor simplicity. Would share financial risk between plan sponsors and manufacturers. A mechanism for price increases when more evidence is generated on durability would incentive post-launch studies. Would not require additional data collection/reporting infrastructure.	No governmental program in the US for regulating launch price and different arbiters of value produce disagreement on calculations of fair pricing. May shift manufacturer incentives for investments away from gene therapies and toward chronic therapies. Reduced pricing + mandated discounts for Medicaid and 340B might jeopardize small manufacturer financial stability.
Integrate special ethical priorities into value-based pricing	Can build upon current international experience. Accounts for difficult-to-quantify benefits of treatments for specific patient populations who have disproportionate unmet need and health inequity.	No government HTA body in the US reduces consensus on methods for integrating these elements into value-based pricing.
Calculate value-based pricing with 'shared savings'	May promote equity in savings calculations for those conditions that are severe but do not have established treatments available/are low cost without gene therapy but have a significant impact on quality of life.	No empiric way to determine the appropriate allocation of potential cost savings to value-based price. Unintended consequences for patients and society if incentives shifted away from treatments to tackle the most expensive conditions.

Payers we spoke with expressed more concern about the uncertainty in clinical durability than safety. In part, this was because side effects or longer-term risks of gene therapy have been relatively minor among the treatments approved so far. The other reason that the uncertain durability of effect has troubled payers is that they feel that the high prices being set by manufacturers are being justified implicitly, if not explicitly, by assuming that the durability of effect will be complete and everlasting.

It is certainly true that substantial uncertainty regarding longer-term clinical effectiveness is not unique to gene therapies. Payers and policy analysts have noted similar challenges with the rising number of drugs approved through the accelerated approval pathway [12]. In our discussions with payers, we often heard that sustained benefit over 5 years was the minimum duration that could justify the one-time prices being seen in the market. Since gene therapies are unlikely to enter practice with robust evidence on outcomes at 5 years, the potential payment solutions all represent some form of value-based contract that links the generation and assessment of real-world outcomes to some modulation of the total price paid for the treatment.

Value-based contracts fall broadly into three categories: milestone-based rebates, warranties and performance-based installment payments (sometimes referred to as an annuity). Note that we use 'value-based' as the overarching term for contracts in which some aspect of payment is linked to clinical outcomes. Market experience with these tools is still in the early stages, with mixed implementation success to date.

All versions of value-based contracts face several common barriers, some of which may be addressed by market or policy changes. First, patients treated with gene therapies may change insurers during the term of any payment contract, greatly complicating efforts to track outcomes and link them to additional rebates, a warranty, or performance-based installment payments. Additionally, members may move between private and public payers over time, increasing the difficulty in structuring longer-term value-based agreements.

A second common barrier to value-based contracts is a lack of agreement between payers and manufacturers on meaningful and practical outcomes to use as the dispositive elements of any contract. Without a third party involved in determining the outcomes for a value-based contract, the terms are subject to the relative negotiating power of payers and the manufacturer.

A third barrier, Medicaid Best Price (MBP) provisions, applies to all value-based contracts except warranties [13,14]. Under regulations for the Medicaid Drug Rebate Program (MDRP), Medicaid is to be provided with net prices comparable to or lower than the lowest price received by any other payer in the commercial market (i.e., Medicaid is guaranteed to receive the 'best' price). Deep rebates triggered by milestone-based rebate contracts would, therefore, in principle, be included in calculating the MBP and be available to the Medicaid programs in all 50 states.

A fourth common barrier to value-based contracts is a lack of data infrastructure and personnel with skills adequate for the clinical analytics needed to track outcomes [15]. Determining the extent to which performance thresholds have been met requires patient outcomes tracking that is timely (often quarterly), accurate, low cost and auditable among other characteristics. To date, the use of practical, low-cost claims data has been preferred in most cases despite the desire of most payers for more detailed clinical (medical record) or patient quality of life (patient-reported outcome) data.

Lastly, developing and implementing any value-based contract requires time and effort, not only at the outset of the contract but over multiple years. Payers have been largely willing to explore these types of contracts, but all payers acknowledge that the internal effort and expertise required have proven very challenging. The appetite for more value-based contracts varies across payers, and the rising number of new gene therapies expected over the coming years may burden payer resources and dampen interest even further.

Nonetheless, value-based contracts have gained a foothold in the market and have the potential to help manage the combination of high prices and clinical uncertainty that is central to the tensions surrounding gene therapy.

Strategy 1: upfront payment with milestone-based rebates

A milestone-based rebate contract involves upfront payment with some percentage or absolute rebate amount, up to a full 100% rebate, returned if the gene therapy does not meet performance expectations. For example, Lyfgenia™ (lovotibeglogene autotemcel), bluebird bio's gene therapy for sickle cell disease, launched in December 2023 with an option for payers to select a milestone-based rebate contract that offers a rebate for patients who are hospitalized for a vaso-occlusive event within the first 3 years after administration [16]. These contracts can cover a single patient or a group of patients, and any rebate received may be fully retained by the first-line payer (such as a pharmacy benefit manager) or shared with downstream risk carriers, such as self-insured employers and their stop loss carriers.

Payers usually leverage their internal resources to administer milestone-based rebate contracts, although smaller payers may outsource some of these functions to the administrative services organization arm of a larger insurer or engage the services of one of the existing market solution providers [17]. Market solution providers consider pharmaceutical companies, self-insured employers, health plans, Medicare and Medicaid as potential customers. They can be paid either by the payer or the pharmaceutical company on behalf of the payer and offer services such as negotiation of performance-based contracts, contract administration and data capture (clinical and patient-reported outcomes). These market solutions providers are slowly growing in importance as the number of gene therapies increases.

Milestone-based rebate contracts are most appropriate for therapies for which clinical uncertainty can be addressed with outcomes seen over a relatively brief period. These contracts are also best suited for payers with the infrastructure (or willing to contract with a third party) to track patients and assess outcomes. Longer-term milestone-based rebate contracts are possible [18], but we consistently heard from payers that most are only willing to extend a performance-based contract length to 2 years due to member turnover and the administrative burden of outcomes tracking.

Strategy 2: upfront payment with warranty

A warranty provides reimbursement for future payer expenses incurred (either demonstrated or estimated) in the event the covered therapy does not meet a manufacturer's promise of a specific magnitude or duration of benefit. For example, Roctavian™ launched with an outcomes-based warranty offered to all US insurers, which will reimburse payers on a pro-rated basis over the first 4 years from the time of dosing if the patient loses response – up to 100% of wholesale acquisition [18].

Warranties may be self-administered by the manufacturer as a performance-based rebate agreement or may be administered by a third party as an insurance-based instrument with premiums paid by the manufacturer [19]. Like consumer product warranties such as automobile extended warranties, warranty payments in gene therapy contracts represent covered damages as opposed to a payment associated with the price of the therapy.

The primary advantage of third-party administered warranties over milestone-based rebate contracts is that only the manufacturer premiums to the warranty program are considered rebates under MBP regulations, not the warranty payments themselves that are triggered if treatment fails and some or all of the upfront payment is returned. However, public information on the use and impact of warranty contracts is limited. There are some new insurance efforts and other partnerships that have been launched to aid manufacturers in providing warranties to payers, including Medicare and Medicaid [20–22].

Strategy 3: performance-based installment payments

A performance-based installment payment arrangement helps payers manage clinical uncertainty associated with therapy by spreading payments over time and linking these payments to positive performance targets. This strategy helps address short-term budget impact concerns as well as manage the clinical uncertainty about the duration of benefit. This approach might include an up-front payment of some portion of the product price and a commitment

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Table 2. Strategies to manage clinical uncertainty.

Tool	Distinctive advantages	Distinctive barriers/disadvantages
Upfront payment with milestone-based rebate	Simpler to design and administer than value-based installments.	The payer remains responsible for the upfront full cost of the gene therapy Difficult to agree on meaningful and practical outcome measures. May be difficult to agree on a meaningful amount of money at risk. Single patient's net price after rebate may impact Medicaid Best Price for all Medicaid programs.
Upfront payment with warranty	Allowable by Medicare and Medicaid. Does not impact Medicaid Best Price in most circumstances. Reduced administrative burden on plan sponsors.	The plan sponsor is responsible for the upfront full cost of the gene therapy. Warranty amount for incurred healthcare expenses due to treatment failure may not account for much of the initial price.
Performance-based installment payments	Spreads payments over time with future payments contingent on the therapy meeting performance thresholds.	Payments over time problematic from a payer accounting perspective and for secondary insurance. Member turnover – the original payer is responsible for the full cost even if the patient leaves the plan and benefit can no longer be tracked. State Medicaid programs may be prohibited from multi-year contracts. May not be compatible with self-insured employer stop loss contracts.

to further payments every year for a defined number of years, with 'out-year' payments triggered as desired outcomes are achieved.

The use of performance-based installment payments with future payments contingent on the therapy meeting performance thresholds is still limited due to the practical difficulties plan sponsors encounter [23]. One disadvantage of these arrangements is that they raise accounting complexities. Some payers operating under accrual accounting may need to recognize future payments upfront or have reserves to cover them. Medicaid plans operating under cash accounting would recognize only the current year's payment, though single-year budgeting rules may hamper them. The FoCUS Project has identified potential finance solutions for these challenges, but each organization would need to engage with its technical experts to identify the best solution for its circumstances [24].

Some payers may have other challenges with paying for gene therapy in installments over multiple years. For example, many states prohibit multi-year Medicaid contracts. Additionally, a one-year stop loss contract may not be compatible with performance-based installment payments. Payers should also be sensitive to the risk that breaking a single payment into multiple installments may trigger multiple co-insurance cost-sharing requirements for patients, increasing their financial burden.

A summary of the distinctive advantages and disadvantages of each tool is shown in Table 2. Note that the challenges common to all value-based contracts are not included for brevity but should be considered by payers considering value-based contract options.

Managing short-term budget impact

Managing the short-term budget impact of gene therapy is a problem for many small payers, especially self-insured employers or other plan sponsors with <10,000 employees. For these payers, an unpredictable $1–3 million treatment may be such a large percentage of their annual health costs that an upfront payment would be financially destabilizing. The actuarial nightmare of such a 'lightning strike' cost has led some plan sponsors to exclude coverage for all gene therapies [25]. Even larger payers, however, may experience cost and income statement volatility from statistical variation in patient numbers in rare conditions and cost surges from new gene therapy approvals in larger indications. Performance-based installment payments and any other mechanism to pay through installments can help manage the short-term budget impact of gene therapies. Still, challenges in launching those contracts mean that additional strategies are needed that can work for both small and larger payers. Most current strategies employ pooling across larger and larger populations to spread the costs and smooth the impact of high one-time gene therapy payments. Current and potential strategies are discussed below.

Strategy 1: stop loss & reinsurance

Stop loss insurance protects self-insured plan sponsors or payers administering full-risk benefits against unexpected catastrophic healthcare costs [26,27]. Reinsurance functions similarly to stop loss but is offered to smaller payers who administer full-risk benefit designs. As helpful as stop-loss policies can be, they are severely limited in addressing the insurance dilemma of patients with easily predictable future costs of gene therapy. Stop-loss carriers often exclude any payment for conditions known to be eligible for gene therapy. Thus, costs for conditions such as sickle cell disease or hemophilia are usually not covered by stop-loss policies, shifting the costs for gene therapy for these

individuals back to the plan sponsor. In some cases, the stop loss carrier may not fully exclude payment but will use other mechanisms, such as raising the deductible for known high-risk members or entire conditions, increasing the stop loss premium, or both [28]. A common scenario is the exclusion of known future high-cost conditions, a practice known as 'lasering'. Stop-loss contract terms also routinely include elements that do not fit well with some value-based contracts. Stop loss is typically administered annually, requiring claims to be incurred and paid within the contract year or at least paid within a specified 'run out' period. This structure does not accommodate value-based agreements that use installment payments over time.

Strategy 2: gene therapy subscription models

Gene therapy subscription models seek to aggregate vast pools of covered lives and 'carve out' coverage for gene therapies so that smaller plan sponsors and payers can join and pay a relatively small per-member per month (PMPM) fee to gain coverage for any needed gene therapy treatments. These programs, also known as gene therapy 'financial protection programs', are now offered by many large payers with a vertically integrated pharmacy benefit manager, including Aetna/CVS (Gene Therapy Stop Loss), Cigna/Evernorth (Embarc® Benefit Protection) and United Healthcare/Optum (Optum Gene Therapy Risk Protection) [17]. Since these gene therapy subscription models provide 'unlimited' access to gene therapies for a single fee, they have also sometimes been called 'Netflix models' [29]. Currently, subscription or similar models are only offered to risk-bearing (primary) payers by intermediaries such as PBMs and not directly by manufacturers. For manufacturers, offering subscription models may be challenging because the safe harbors for payment discounts and rebates under Physician Self-Referral rules (the Stark Law) and Anti-Kickback Statutes may not apply. Further, volume fluctuations in subscription models impact Medicaid rebate and Average Sales Price calculations, which can affect provider reimbursement as well as possibly trigger excess price increase (inflation) rebates.

Strategy 3: federal gene therapy coverage benefit

A strategy not in place today but one that garnered considerable support in our stakeholder discussions is a federal 'carve-out' benefit for gene therapy. It is possible that, despite the private insurance market's attempts to manage the tension between cost and access to gene therapies, the actuarial problem of both predictable and unpredictable prices at this level will not lead to private insurance models that can provide adequate, affordable access. Thus, much like Medicare was extended to cover all patients needing renal dialysis, a federal benefit for gene therapy could be created to cover the costs for all patients deemed eligible for this type of treatment. With a federal program, lasering and other barriers to access would be eliminated.

To avoid too broad a scope of coverage, the benefit might be limited to potentially curative gene therapies, only the one-time costs of the gene therapy might be covered and a new separate federal benefit might be limited initially to state Medicaid programs. In January 2024, the Centers for Medicare and Medicaid Innovation (CMMI) announced the launch of their new Cell and Gene Therapy Access Model [30]. This voluntary pilot program allows states to opt into a CMS-led outcomes-based agreement for cell and gene therapies, consolidating purchasing power for these products across state Medicaid programs and providing technical and funding support to states. Currently, the program is focused only on expanding access to gene therapies for sickle cell disease but might serve as a model that could be expanded to include all gene therapies or be designed to allow coverage eligibility for patients with any form of primary health insurance. This type of federal gene therapy carve-out could be financed by general tax revenues or by per capita payer fees. The mechanics could range from full federal operation, including product and provider contracting, to federal funding with reimbursement schedules (as is done with coverage for renal dialysis), to private sector implementation with competing entities, as is done in Medicare Advantage and Medicare Part D benefits.

There are several important implementation issues that would arise with any federal gene therapy benefit program. Federal coverage would likely raise the need for some centralized process for review of clinical effectiveness and perhaps cost–effectiveness as well to address program costs.

A summary of the advantages and disadvantages of each strategy to manage the short-term budget impact of gene therapies is shown in Table 3.

Combining strategies to address gene therapy payment challenges

A single strategy cannot currently address the full complement of gene therapy payment challenges for all payers [31]. Different market segments face the challenges outlined in this paper to different degrees. Thus, some strategies are

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Table 3. Tools to address the short-term budget impact of gene therapies.

Tool	Distinctive advantages	Distinctive barriers/disadvantages
Stop loss and reinsurance	Protects against very high claims and unpredictable costs. Established and well-understood by plan sponsors.	Policies subject to gene therapy exclusion 'lasering' for known gene therapy candidates, high-cost members, conditions, and/or products. Annual premiums may be volatile based on prior year claims experience.
Gene therapy subscription model	Fixed per member per month fee, which is similar to other pharmacy benefit manager/insurance programs. May include some additional patient services.	May limit gene therapies included and exclude certain patients depending on enrollment date. Limited market traction to date with reports of high premiums and too few gene therapies included.
Federal gene therapy coverage benefit	Single pool provides scale and broader cost-sharing. Creates universal access that prevents private market risk of lasering or of some employers opting out of coverage entirely. May support price negotiation/setting that achieves lower prices in return for guaranteed broad access. May provide alternative funding tools such as mandatory fees or tax funds.	If federally operated may lead to inefficiency, inadequate patient appeal, or misuse of single buyer power that could raise administrative costs, reduce patient access, or provide inadequate innovation incentives, and, like Medicare Part D, may inhibit integrated medical and therapeutic management.

better suited to some markets than others. Whether within a single market or across markets, differences among diseases, products and payer types require a set of strategies that can be customized and possibly combined to meet the challenges of each specific situation. During stakeholder interviews, one consistent theme that emerged was that there was no perfect model based on a single strategy, so efforts to experiment with new strategies or to link others together are needed.

Stacking strategies

One option payers can consider is to 'stack' two or more separate strategies. For example, a plan sponsor can purchase reinsurance to mitigate the high-cost budget impact of any gene therapy and then, for specific therapies, negotiate a standard rebate to gain a fair price while seeking a value-based or warranty agreement from a manufacturer to mitigate the clinical performance risk. In this example, each strategy entails its own contract, but in combination, the plan sponsor has addressed the three core challenges of paying for gene therapies.

State Medicaid programs could combine existing mandatory rebates with value-based milestone rebates and reinsurance. This might allow states disproportionately impacted by certain diseases, such as sickle cell disease, to balance their budgets and provide patient access.

Many such stacking combinations can be envisioned, with payers and manufacturers having the flexibility to customize each strategy or ignore certain strategies as needed. For example, large national insurers have sufficient patient pool sizes that they do not need reinsurance.

Integrating strategies into a new offering

Integrating two or more tools into a new solution, sometimes called 'layering', may allow for efficiencies for all parties.

- Traditional and milestone rebates are already offered together today by manufacturers who combine a milestone-based rebate with a reduced upfront discount in a single contract.
- Value-based gene therapy subscription models that integrate a warranty or other value-based contract with a subscription model could be offered by national insurers/PBMs to smaller health plans and self-insured plan sponsors. Current subscription models may implicitly do this if the payer negotiates multiple value-based contracts with manufacturers and uses the estimated payouts to reduce the gene therapy subscription premium for all participating employers. There may be advantages to a more explicit pass through of performance rebates for plan sponsors who incur increased costs for members for whom a particular gene therapy does not perform well.
- Value-based contracts integrated with processes to determine fair pricing could be considered an offering by private gene therapy subscription offerings or could be developed for piloting by CMMI in its gene therapy coverage model. The premise is that accelerated and broad access through a private or governmental model would be offered to gene therapy manufacturers based on their agreeing to have the initial upfront payment fit within transparent fair pricing guidelines and for rebates or warranties also to be included in a broader value-

based contract. This combination and integration of three different strategies would face significant challenges, potentially including changes to ERISA regulations to require self-insured plan sponsors to cover gene therapies, naming acceptable sources of independent pricing benchmarks and procedures for negotiating the outcomes, time horizons and amount of money at risk in the value-based contract.

Value-based milestone contracts with a volume cap or modifier could be developed between manufacturers and PBMs to manage clinical uncertainty while using a volume target to manage short-term budget impact concerns by sharing some or all financial risk of greater utilization with the manufacturer. Volume targets can be used to cap total costs for a payer or to create a laddered approach to rebates that increase with utilization beyond certain targets.

Multi-year stop loss policies with pass-through warranties could integrate stop loss insurance with a pass-through warranty that reimburses smaller health plans and plan sponsors when clinical effectiveness or durability measures are unmet. This type of integrated product would not only protect against lighting strikes to plan sponsor budgets. It would also reimburse plan sponsors for at least part of their portion paid by the claim fund, and possibly help offset potential premium increases for stop loss policies as gene therapy claims increase. It would also enable stop loss carriers to better manage gene therapy costs through multi-year engagement with clients and enable them to directly contract with manufacturers and even clinical providers.

Policy reforms & market actions to enable payment innovation for gene therapies

Policy reforms and broader actions within the private market are needed to support innovative models for payment for gene therapies. Among those considered most important in our conversations with payers, manufacturers and patient advocacy groups are the following.

State Medicaid programs should enhance their capabilities to enter value-based purchasing arrangements

More than half of states have not sought approval from CMS to enter directly into value-based payment (VBP) arrangements [32]. State Medicaid programs should also build organizational capacity in personnel skilled in designing outcomes-based contracts, design procedures for working with manufacturers, and invest in needed computer and medical record systems to track outcomes. States should also actively consider joining the emerging Centers for Medicare and Medicaid Innovation (CMMI) model for gene therapy coverage and payment to benefit from centralized expertise and resources.

CMS should clarify the Medicaid prescription drug rebate program regulations to allow innovative payment methods to be tested & improved upon

CMS Proposed Rule CMS-2482-P takes an important step in addressing calculation barriers to the broader adoption of milestone-based rebate contracts. However, further clarification is needed regarding the specific mechanics and interpretations. For example, one manufacturer we spoke to noted that they needed guidance on how to enter their warranty model into the MDRP data system, and CMS was very responsive. CMS has emphasized flexibility to accommodate the many emerging payment innovation variations. Unfortunately, the lack of established practices (regulatory 'case law') also leads to uncertainty regarding the degree to which customization of the terms for a commercial customer triggers a distinctly reportable value-based purchasing agreement, the extent of accommodation that will be given to a state Medicaid program to enable implementation of a performance-based contract and the specific mechanics for reflecting terms and reporting in the MDRP computer systems. Additional explicit examples and a more public corpus of acceptable practices from CMS are needed to reduce uncertainties and spur payment innovation.

CMS should update the average sales price calculation in Medicare part B to match the MBP multiple-best prices approach

The Average Manufacturer Price (AMP) calculation and the Medicare Part B Average Sales Price (ASP) calculation were identical until the Multiple Best Prices refinement was introduced, which excluded value-based performance arrangement transactions from AMP calculations. By continuing to include these transactions in the calculation of the ASP, CMS has introduced volatility that can disincentivize provider prescribing due to reimbursement often being tied to ASP. Re-aligning ASP calculations to AMP would eliminate these disincentives.

10.57264/cer-2024-0118

CMS & the HHS office for civil rights should clarify HIPAA regulations to ensure appropriate data access for all entities engaged in value-based agreements

Clarification is needed so developers, prior payers, data intermediaries and others can access required outcomes and other data needed for payment adjudication. Additional rulemaking would also be helpful to clarify the criteria for being a Business Associate who has the right to see patient data without needing a separate legal agreement. These clarifications would help address the uncertainties that magnify the member turnover barrier of value-based rebate contracts.

Congress should revise the ERISA law governing self-insured plan sponsors to require them to cover gene therapies when medically necessary, just as fully insured commercial plans must do under both federal & state laws

The resulting increased risks, and perhaps costs, to smaller self-insured plans would likely encourage them to rejoin the larger pools operated by traditional insurers. This would eliminate 'lightning strike' risks, improve coverage for patients and reduce volatility for traditional insurers through greater scale. Premiums for the small plans may exceed their prior total health spending if the traditional insurer economies of scale do not offset (or are not passed through) to employers.

CMS should reduce private payer risk by including patients undergoing treatment with gene therapies in risk-adjustment programs such as those used in Medicare Advantage, some state Medicaid plans, & Affordable Care Act exchanges

Subsidies received by plans are adjusted based on patient characteristics that significantly influence spending. Risk adjustment distributes payments according to the risk of enrollees.

Congress should modify the Medicaid Drug Rebate Program (MDRP), the physician self-referral law, & the Anti-Kickback Statute to enable developer-offered subscription models

The MDRP requires manufacturers to report a unit price on each contract from which a 'best price' may then be calculated and used to set the Medicaid drug rebate amount for the product. With gene therapies, volatile product volumes under a fixed subscription price will naturally lead to unpredictable unit price volatility, and this uncertainty disincentivizes developers from offering or agreeing to subscription models. Reforming MDRP to eliminate unit price reporting or exempt subscription models from the unit pricing rule would foster greater acceptance of subscription models. Similarly, expanding the safe harbor provisions in the Physician Self-Referral law (commonly known as the Stark law) and anti-trust regulations to include subscription models is needed.

Conclusion

Gene therapies have the potential to transform thousands of lives, but only if all stakeholders find feasible and economically sustainable ways to price these therapies and pay for them. The need to find new market and policy solutions will only grow as increasing numbers of gene therapies are approved, including those for larger populations, such as sickle cell disease.

This paper is intended to call for thoughtful consideration of both market actions and policy reforms. Our analysis has sought to emphasize that although each specific action or reform has the potential to address one of the major challenges presented by gene therapies, there is no single solution, no 'magic bullet' that addresses the full complement of gene therapy payment challenges for all payers [31]. Different market segments face challenges in different degrees. Thus, some strategies are better suited to some markets than others. Whether within a single market or across markets, differences among diseases, products and payer types require a set of strategies that can be customized and possibly combined through stacking or layering various options to meet the challenges of each specific situation.

What, therefore, is the best way forward? Key policy reforms will be needed to buttress and facilitate any market-based effort. We encourage market leaders to advocate for these policy reforms and to take early action to pilot test models, including combination approaches. Unmet patient needs and the tremendous scientific advances underpinning the new era of gene therapy will not wait. Gene therapies were still just on the horizon 7 years ago. Today, they represent among the most transformative advances in our healthcare system. Starting today, we need innovative pricing and payment options to ensure that those advances reach all individuals who can benefit while strengthening the overall sustainability of our healthcare system. The time for action is now.

Summary points

- Gene therapies delivered through a single administration have revolutionized treatment possibilities for many patients living with serious or fatal conditions such as spinal muscular atrophy, hemophilia and sickle cell disease.
- However, shadowing the excitement about the transformational potential of many gene therapies has been widespread concern about the combination of uncertainty in the durability of their benefits over the long term and the short-term financial shock of high prices.
- The pipeline of gene therapies and their anticipated costs raise concerns that gene therapies will create budget pressures and consequent constraints on access even for larger payers and smaller employers, state Medicaid departments and regional health plans may find providing access financially impossible without some modification in pricing or payment methods.
- As the healthcare payment ecosystem prepares for the growing number of gene therapies entering the market, three key interconnected challenges must be addressed: determining a fair price, managing clinical uncertainty and managing short-term budget impacts.
- The authors identify specific policy reforms and market-based tools to help the US health system address these challenges to achieve more equitable and affordable access for patients to the growing number of gene therapies expected to be approved in the coming years.
- Options such as value-based pricing, value-based outcomes contracts, warranties, subscription insurance models, installment payment arrangements and a federal carve-out benefit program are explored.
- For each option, the authors analyze the relative advantages and potential unintended consequences, along with suggestions for implementation and an exploration of unique opportunities for combination or layered approaches.
- None of the tools or policy reforms discussed are 'silver bullets' that can singlehandedly solve all the barriers and tensions inherent in the current healthcare insurance and payment landscape.
- Still, the authors seek to present policymakers and industry leaders with insights and lessons learned from experts and market experience to date that will help all stakeholders be part of an innovative future of gene therapy pricing, coverage, payment and access.

Author contributions

All authors were responsible for the conception and design of this project. All authors participated in the drafting and review of this manuscript and are responsible for its contents.

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The full ICER White Paper, which includes an examination of the current payment landscape and how the costs of gene therapies impact different payer types, as well as an analysis of the limitations of stop loss insurance and reinsurance to protect payers against potentially catastrophic costs, is available on the ICER website at https://icer.org/assessment/managing-the-challenges-of-paying-for-gene-therapy-2024/.

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No assertion, judgment, or recommendation included in this manuscript should be viewed as representing the opinion of any participant or their company. ICER and NEWDIGS are ultimately responsible for the final content.

Competing interest disclosure

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