MILLIMAN WHITE PAPER

The uncertainties and benefits of gene and cell therapies: A payer's dilemma

Is an alternate payment arrangement the answer?

E. Anne Jackson, FSA, MAAA
Jessica Naber, FSA, MAAA

Milliman

When it comes to innovative therapies, sharing the risks may be key.

Gene therapies, CAR T-cell therapies, and other innovative (and potentially curative) therapies are beginning to enter the market, and are making waves with their record-setting prices. These therapies are curing, extending life, or providing increased quality of life to patients who—in many cases—had exhausted all other options. From the patient's perspective, there may be no question that the drug is worth it. But from the payer's perspective, there are risks and benefits that should be considered.

This paper explores the following:

- What are sources of uncertainty regarding gene and cell therapies?
- What will affect appropriate solutions for mitigating these risks?
- What are potential solutions? Is an alternate payment arrangement (APA) necessary?

What are sources of uncertainty?

There are only a handful of gene and cell therapies approved for use in the United States today, and they are currently indicated for rare diseases. For this reason, the U.S. healthcare market has been able to bear the cost of these drugs because the need for them occurs on such an infrequent basis. However, there are a large number of these therapies currently in development worldwide. According to the Alliance for Regenerative Medicine's Q3 2018 data report, there are 561 phase II and 81 phase III clinical trials underway globally for gene therapies, gene-modified cell therapies, and cell therapies.[1] The aggregate effect of these therapies entering the market impacts both small and large insurers, and will increase the need for viable solutions to mitigate their risks and uncertainties.

Some gene and cell therapies differ from most traditional treatments in that they have limited administration periods—as short as a single procedure or injection—but have the potential for ongoing clinical benefits. There are four key uncertainties related to these therapies from the payer's perspective: initial performance, durability and efficacy, cost offsets, and price. Understanding these risks will influence how a payer perceives the value of the therapy. Will the drug work when it is administered, and how will that be measured? If it does work initially, will it continue to work long-term? What will the cost be, and will the member have continued or additional residual costs, even after treatment?

Because gene and cell therapies are a fairly new paradigm of treatment, there is considerable uncertainty around their efficacy and long-term durability. For therapies that are indicated for rare diseases, clinical trials rely on very small patient populations to determine whether they are effective. Additionally, the expectation for many of these therapies will be that they last for a lifetime, but because clinical trials are conducted over a few years, it is difficult to prove that the therapy will continue to work beyond the clinical trial timeframe.

From the financial perspective, the drug itself is likely to have a substantial price tag, but there are additional financial risks. For example, some therapies can be administered with a single injection in an outpatient setting, while others may require an autologous bone marrow transplant and many days in the hospital. After the therapy has been administered, there are also questions around long-term cost offsets. Treated patients may be brought to full health, or they could continue to incur significant expenses due to comorbidities or residual costs. Last, but not least, payers may be concerned about paying for these high-cost treatments and being unable to accrue the benefits if the member were to leave. Patient turnover is a considerable risk from the payer's perspective.

What will affect appropriate solutions for mitigating these risks?

Ideally, patients and providers should have access to these therapies if they are appropriate for care. Payers and pharmaceutical manufacturers can work together to enable this access. The appropriate solution depends on the characteristics of

[1] Alliance for Regenerative Medicine. Q3 2018 Data Report. Retrieved January 31, 2019, from https://alliancerm.org/publication/q3-2018-data-report/.

the treated members, disease state, and therapy. In this context, the risk includes both the budget impact associated with the treated patient population as well as the risk that the cost of the therapy is not consistent with the value received. The following are considerations that affect how an innovative contract or APA may be structured:

- **Size of treatable population.** If only one or two indicated patients exist in the payer's population, the administrative burden of entering into an innovative contract may outweigh the benefit, unless there is the ability to aggregate across multiple indicated populations and therapies.
- **Identifying indicated members.** For a chronic condition, a payer may be aware of an indicated (prevalent) population based on diagnosis codes or utilization. For an acute condition, patients may not be identified until treatment is necessary. Additionally, many rare diseases do not have specific ICD-10 diagnosis codes, and even those that do have a diagnosis code may not have the necessary level of detail (e.g., severity classifications). The ability to identify a treatable member early could allow contracting discussions to occur months or years in advance of a patient's need for the therapy. Otherwise, discussions may not occur until the point that a patient requires treatment.
- **Demand and uptake.** For chronic conditions, there may be a bolus of patients in the initial years after a therapy is approved that may level out after the prevalent population is treated. In contrast, an acute condition is more likely to have a consistent demand pattern year-over-year. Additionally, if there are other effective treatments available or in the pipeline, patients may prefer a traditional therapy over gene or cell therapies.
- **Site and intensity of treatment.** Outcomes or value-based contracting between a payer and manufacturer may be appropriate for mitigating the risk of the drug's performance. However, the manufacturer cannot take on the risk (i.e., reimburse the payer) for other medical costs related to the professional and facility costs of administration without potentially violating the Anti-Kickback Statute (AKS).[2] For example, if an autologous bone marrow transplant is required, the manufacturer may guarantee no payment for the drug if it is ineffective, but the payer would still be responsible for the transplant, hospital stay, and all associated medical costs.
- **Measuring success and durability.** After treatment is administered, is there a clear marker for success or failure? A defined marker of success, such as a specific lab result, can make contracting more straightforward, versus if success is determined by something more ambiguous like a cognitive screening or patient-reported results. For long-term contracting, the ability to track, monitor, and/or continue testing the treated patient for success or failure may be difficult to execute because it relies upon the patient to comply, and becomes especially difficult if the patient leaves the payer.

Beyond the characteristics related to the indicated population and therapy, innovative contracting could also be subject to government pricing rules, such as Medicaid Best Price. Under this policy, manufacturers are required to offer the drug to Medicaid at the lowest price available in the market (with a few exceptions), after accounting for rebates and other discounts. In the context of an innovative contract or installment payment arrangement, this could have major implications to a manufacturer. For example, if payment is contingent on the success of the therapy, the manufacturer would be required to offer the drug to Medicaid at the lowest price in the market—which could be equal to the price when the drug fails—even if the drug was effective for the Medicaid beneficiary.

What are potential solutions?

For traditional therapies, the clinical benefit usually aligns closely with the administration of the therapy, such that ongoing treatment is necessary to maintain the desired level of health. Gene and cell therapies differ from most traditional therapies because they have limited administration periods but have the potential for ongoing clinical benefits. The current U.S. healthcare system is structured to cover costs at the time the service is incurred. In the case of gene and cell therapies, this creates a mismatch between the payment of the therapy up-front at time of administration versus the long-term realization of clinical benefits. The uncertainties related to these therapies and their associated price tags has initiated much research and interest in APAs. These types of arrangements disrupt the status quo, which may have legal, accounting, and financial ramifications.

Figure 1 outlines three potential risks associated with gene and cell therapies, the necessary conditions to measure or assess the risk, potential solutions, and key barriers to implementation or residual risk. The potential solutions are displayed as non-APA (i.e., a solution that borrows from currently available processes or resources), and as APA (i.e., a solution that requires a novel action that disrupts the status quo).

[2] Anti-Kickback Statute, 42 U.S.C. § 1320a-7b(b).

FIGURE 1: RISKS AND POTENTIAL SOLUTIONS

	INITIAL PERFORMANCE	DURABILITY/EFFICACY	PATIENT TURNOVER
Necessary conditions	▪ Available objective metric to measure success ▪ Short time to measurement	▪ Available objective metric to measure success ▪ Expectation for sustained performance of therapy	▪ Identification of patients with the indicated condition ▪ Expectation of turnover for these patients
Potential non-APA solution	▪ Manufacturer incorporates this risk into price of drug. ▪ Example: if clinical trials show drug is initially effective 80% of the time, price the drug with a 20% discount	▪ Manufacturer incorporates this risk into price of drug. ▪ Example: If clinical trials indicate drug is effective for the length of the trials (e.g., four years) but has an expectation of lifetime durability, price the drug based on proven length of efficacy with price adjustments as more experience is accrued	▪ Insurance policy for the price of the therapy if the patient were to leave the payer. ▪ Example: Payer purchases insurance for a set number of years to cover the risk that a patient leaves (voluntarily or involuntarily) ▪ Note: An insurance policy like this may be vulnerable to fraud or perverse incentives
Potential APA solution	▪ Conditional payment: Payment is required only after initial success is determined. ▪ Example: If clinical trials show drug is initially effective 80% of the time, the payer will pay full price 80% of the time and nothing 20% of the time	▪ Installment payments or refund: Payment is required, but only if ongoing success is determined. ▪ Example: Payment is made annually, but ceases if the drug is no longer effective ▪ Example: Payment is made up-front, but manufacturer agrees to pay back a portion of the drug cost (i.e., a rebate) in the future if the drug is no longer effective	▪ Reciprocity agreements or pooling mechanisms. ▪ Example: In a reciprocity agreement, follow-on payers agree to "pay back" a portion of the expected future cost benefits to the original payer (see the "Health Currency" model in our Society of Actuaries research report)[3] ▪ Example: Claims for patients with a specific condition are pooled together across payers. Payers are responsible for a premium to fund the pool. May be similar to carve-out insurance or high risk pools.
Residual risks and barriers to implementation	▪ Costs of administering the treatment (and other medical costs) are not mitigated ▪ Could introduce Medicaid Best Price issues	▪ Legal and accounting concerns affect the ability to administer the APA contract ▪ APA relies upon willingness of patient to continue tracking and testing over time ▪ Death or disenrollment of patient—who is responsible for continued payments?	▪ Legal and accounting concerns affect the ability to administer ▪ APA requires a large amount of buy-in across payers and payer channels (Medicare, Medicaid, commercial, etc.) ▪ May require legislative action or an aggregator to manage and administer the contractual agreements

The potential solutions in Figure 1 are not exhaustive, and each solution has positives and negatives. Some solutions may add considerable administrative burden to payers and partnering entities, which may make them infeasible. There is no single solution that can mitigate every risk or uncertainty related to gene and cell therapies. For this reason, the solution may need to be tailored to address the specific concerns of the payer. If we approach the problem by considering each source of risk to the payer and manufacturer, we may find that this provides greater clarity around an appropriate solution, whether it is an APA or something simpler.

CONTACT

E. Anne Jackson
anne.jackson@milliman.com

Jessica Naber
jessica.naber@milliman.com

Milliman

[3] Buckle, J., Jackson, A., Naber, J., & Serre, D. (October 2018). Evaluating Payment Models for High-Cost Curative Therapies. Society of Actuaries. Retrieved January 31, 2019, from https://www.soa.org/Files/resources/research-report/2018/evaluating-payment-models.pdf (PDF download).