innovative Rx STRATEGIES™

Pharmacy Benefits Briefing

Gene and Cell Therapies

What plan sponsors need to know to strike a balance between care and cost

Do You Have a Pharmacy Game Plan?

As the cost of pharmacy benefits continues to escalate, employers must be strategic in finding a balance between providing care for their members and protecting their bottom lines.

As expensive gene and cell therapies continue to come to market, it's vital that employers are aware of the clinical landscape.

This brief outlines what employers need to know today about current and future gene and cell therapies.

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Introduction

Innovations in medical treatments have brought forward a potentially life altering and lifesaving class of therapies. Gene and cell therapies came to market in 2010 and, almost 15 years later, innovation is only picking up speed.

With record setting advancements come record setting prices — these therapies often top $1M along with additional supportive care costs. Indications for these therapies have been limited to rare and ultra-rare conditions, but the pipeline is deep and will extend into more common conditions.

What are Gene and Cell Therapies?

Gene and cell therapies both involve the potential to impact genetic and acquired diseases. The U.S. Food and Drug Administration (FDA) Center for Biologics Evaluation and Research approves gene and cell therapies. A complete list of approved therapies is updated regularly by the FDA and can be found on their website.

There are some differences between the two therapy categories:

Gene Therapy is the use of genetic material in the treatment or prevention of disease; it involves the transfer of genetic material into the body. Transfer is completed with a carrier or vector and involves the uptake of the gene into the cells of the individual being treated. There are currently five different ways these therapies work including adding a gene, correcting a gene, silencing a gene, reprogramming a gene and elimination of a cell. Some gene therapies also utilize cell therapy for treatment.

Cell Therapy involves transferring live cells into a patient. The cells are either from the patient themself or a donor. Some cells are used without modification, such as in blood transfusions and stem cell transplants. Newer, advanced therapies involve reprogrammed cells. One such advancement is **T-Cell therapy,** which uses the patient's own immune cells to express a receptor on their surface in a way that recognizes the antigen on the surface of cancer cells.

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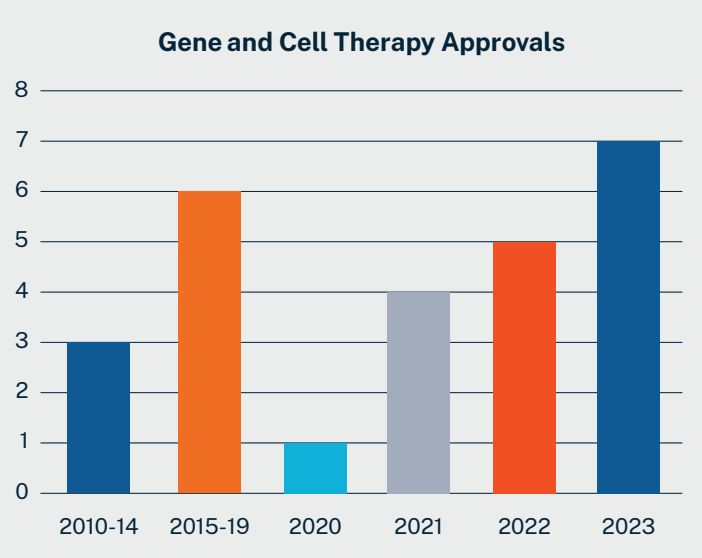
History and Recent Innovation

While earlier approvals exist, impact has grown significantly in the last decade due to new treatments. Luxturna®, a gene therapy, was approved in 2017 for inherited retinal disease — at a cost of $425,000 per eye. In the same year, the first two T-cell therapies for blood cancers were approved with Kymriah® and Yescarta®, both priced around $450,000 per treatment. In 2019, the first multi-million-dollar gene therapy, Zolgensma®, was approved for patients with spinal muscular atrophy at a cost of $2.3M.

Innovation within this category is not slowing down. At the end of 2023, the FDA gene and cell list contained 26 non-cord-based gene and/or cell therapies. While the initial years of innovation brought a few therapies to market per year, 2023 saw a new record with seven therapies approved including therapies for sickle cell disease and hemophilia. According to some predictions, 2024 will be another record-setting year.



In addition to the increasing volume of therapies released, recent years have seen new advancements. In 2023, Casgevy™ was approved for sickle cell disease and approved again in 2024 for beta thalassemia. Casgevy™ is the first gene therapy to utilize **CRISPR-based therapy**, a type of genome editing. While development of the first CRISPR-based therapy took over a decade, it is predicted that this innovation could potentially be used in over 6,000 disease states. The beginning of 2024 has already brought the first **CAR-T therapy** for a solid tumor with Amtagvi™, which is approved for types of advanced melanoma. Before this approval, all CAR-T therapies were for blood-based cancers.

Cost of Innovation

Most gene therapies have come to market with multi-million-dollar price tags. But it is important to note that these prices only encompass the actual therapy. Preparations for gene and CAR-T therapy sometimes include chemotherapy and supportive care with and after therapy, which can add upwards of $1M to the cost of treatment. While most CAR-T therapies have a cost around $450,000 to $500,000 per treatment, the total cost exceeds $1M per patient.

In March of 2024, a new record for the cost of gene therapy has been set with the approval of Lenmeldy™. Approved for the treatment of metachromatic leukodystrophy, it will launch with a price of $4.25M. The chart on the next page lists the 10 most expensive gene therapies on the market today, but we can expect the list to grow with new approvals.

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Most Costly Gene and Cell Therapies			
Therapy	**Approval**	**Indication**	**Cost**
Casgevy™	2023 2024	Sickle Cell Disease Beta Thalassemia	$2.2M
Zolgensma®	2019	Spinal Muscular Atrophy	$2.3M
Rethymic®	2021	Congenital Athymia	$2.7M
Zynteglo™	2022	Beta Thalassemia	$2.8M
Roctavian™	2023	Hemophilia A	$2.9M
Skysona®	2022	Cerebral Adreno-leukodystrophy	$3.0M
Lyfgenia™	2023	Sickle Cell Disease	$3.1M
Elevidys	2023	Duchenne Muscular Dystrophy	$3.2M
Hemgenix®	2022	Hemophilia B	$3.5M
Beqvez™	2024	Hemophilia B	$3.5M
Lenmeldy™	2024	Metachromatic Leukodystrophy	$4.25M

Remaining Questions

While the price tags on these therapies are shocking, many of the disease states these therapies target cost millions of dollars to treat over the course of many years. If the gene or cell therapy successfully treats its target condition, it can result in cost savings for the health care system.

For plan sponsors, this is a tricky line to walk. If the member who receives therapy remains on the plan for years, these therapies could lead to cost savings.

For example, one year of medication treatment for hemophilia often costs over $1M, not including the cost of care for complications. The correlating gene therapy for hemophilia, Roctavian™, is priced at $2.9M. Within the first few years of treatment, it is possible to see savings. However, if a member leaves the plan after receiving therapy, their future plan sponsor would reap the cost-saving benefits of the therapy.

Another consideration is the durability of these therapies. Not all patients will respond or will experience a complete remission. Using the same example of hemophilia, results showed that 90 out of 112 patients responded to Roctavian™. While bleeding rate decreased in the remaining patients, it did not go to zero. In these cases, continued high cost with previous treatments and complications may remain. For those that do respond the question remains how long these therapies will last. The durability issue has arisen in a variety of gene therapies, including Zolgensma®. In this case some patients had to go back to their previous treatment method, Spinraza®, a few years after their gene therapy treatment. Spinraza® comes at a price tag of over $400,000 per year.

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Strategies for Management

With the high prices and potential risks of gene therapies, plan sponsors are looking for ways to protect their costs while also providing potential life-changing care for their members. There currently is no perfect solution, but a few options do exist.

STOP LOSS AND REINSURANCE

Stop loss shields self-funded employers from large catastrophic claims. With the introduction of more high-cost gene and cell therapies, the protection from stop loss on these high-cost claims may become less reliable. Stop loss vendors often are aware of patients who may benefit from gene therapy, having flagged their high cost of care. With this knowledge, stop loss providers are preemptively increasing lasers on patients with these disease states to protect themselves from the higher one-time costs of any future gene or cell therapy use.

Stop loss providers may also exclude or lower coverage available for any gene and cell therapies. For example, the provider could choose to provide coverage for just 50% of the cost of the gene therapy above the specific deductible. In addition, if a gene therapy does hit a plan and the stop loss provider does cover it, there is concern over the ability for a plan sponsor to obtain stop loss coverage in future years at a reasonable cost.

GENE THERAPY SOLUTIONS

Third party vendors have come to the market offering new solutions for coverage for these agents. For a fee, typically per member per month (PMPM), the vendor provides some coverage for gene therapies. However, these solutions often include very detailed exclusion criteria leaving plan sponsors on the hook. The most common exclusion is members who were on plan before the start of the policy, or in some cases members who were born before the start of the policy. In addition, some of these solutions cover a limited number of gene therapies — leaving plan sponsors unprotected for therapies not on their list.

TOUGH DECISIONS

Ultimately, for some smaller plan sponsors, the cost of a gene therapy may lead to financial collapse for their organization. These organizations have had to make the tough decision of excluding gene and cell therapies from their plans. The risk to employers (if stop loss does not pick up the cost) of not being able to offer health benefits or facing organizational collapse is simply too great.

WORK WITH MANUFACTURERS

Some manufacturers have identified the cost of these therapies as a barrier to use and are coming to the table with solutions. One example is an outcomes-based contract which some manufacturers are offering to all patients. For example, the manufacturer of Zynteglo™ is offering to reimburse up to 80% of the cost if the patient fails to achieve and maintain transfusion independence for up to two years. Other manufacturers may be open to individually negotiating outcomes-based contracts or payment plans for their therapies.

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Pipeline

With the potential for dozens of FDA approvals in the coming years, gene and cell therapies remain a top industry trend to monitor. So far in 2024, three agents have received approval, three agents have anticipated FDA approval dates and additional agent approvals are anticipated.

2024 Gene and Cell Therapy Approvals		
Therapy	**Indication**	**Watch Date**
Amtagvi™	Melanoma (CAR-T)	Approved 1/16/24
Lenmeldy™	Metachromatic Leukodystrophy	Approved 3/18/24
Beqvez™	Hemophilia B	Approved 4/26/24
Kresladi™	Leukocyte Adhesion Deficiency	Pending 6/30/24
AUT01	Acute Lymphocytic Leukemia (CAR-T)	Pending 11/16/24
EB-101	Epidermolysis Bullosa	Pending 2024

The gene and cell therapy pipeline is full of potential approvals for rare diseases including choroideremia, Duchenne muscular dystrophy and Wilson's disease. It also includes treatments for multiple cancers including prostate, non-small cell lung cancer and multiple myeloma.

Future innovation in the pipeline includes multiple therapies in late phase studies for non-rare, non-cancer indications. Some examples in this space include human immunodeficiency virus (HIV), coronary artery disease, Parkinson's disease and diabetic complications including foot ulcers and retinopathy.

As gene and cell therapies move into more common disease states, the population eligible for these groundbreaking innovations will expand exponentially. This expansion into larger populations is anticipated to bring much lower pricing for these new agents.

In addition to new therapies in the pipeline, current therapies are being studied for new indications. Recent small-scale studies have shown positive results with CAR-T therapy for autoimmune conditions. Positive results were published in early 2024 for 15 patients treated with CAR-T for either lupus, scleroderma or idiopathic inflammatory myositis.

How We Can Help

With rapidly escalating innovation in a category with potentially plan-busting price tags, working with the right pharmacy benefits consultant is critical to mitigate risk and strike a balance between plan member care and pharmacy cost.

Our team monitors market trends, the drug development pipeline and the latest clinical evidence to ensure our clients receive the support and professional recommendations needed to make the best decisions possible for their plans.

If you don't have a pharmacy consultant to help you navigate the gene and cell therapy landscape, please reach out and any one of our pharmacists would be happy to assist. Contact us at info@innovativerxstrategies.com or (847) 943-3151.