TUFTS Health Plan

Gene Therapy: Making Life-changing Treatments Affordable

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Genes: They're the blueprints for the chemical processes that keep our bodies' cells alive and functioning. But when genes are defective, they can cause diseases or medical conditions ranging from muscular dystrophy to sickle cell anemia to progressive blindness. Gene therapy is an emerging therapy for treating or preventing disease by altering the genetic instructions within an individual's cells.

The implications of gene therapy are enormous and exciting, with the potential to change the lives of people with conditions previously considered incurable. At the same time, these therapies are extremely costly. While curing a complex medical condition may, indeed, reduce lifetime medical costs, gene therapies require a huge initial outlay of money—in some cases millions of dollars for a single procedure.

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With more than 900 cell and gene therapies in clinical trials, the Food and Drug Administration (FDA) expects to approve 10 to 20 gene and cell therapies per year by 2025, **and annual sales of gene therapies are expected to reach more than $8.6 billion in the U.S. by 2024.**[1] It's crucial for health plans and employers to understand novel therapies, who they benefit, and the strategies for containing costs.

[1] Source: "Novel Therapies: What you need to know" - Tufts Health Plan

How Gene Therapy Works

For decades, scientists have been working on ways to modify genes or replace faulty genes with healthy ones to treat, cure or prevent diseases or medical conditions. Progress has accelerated in recent years, and multiple viable techniques and applications for gene therapy have emerged.

There are currently two main approaches to gene therapy: in vivo (meaning in the body) and ex vivo (outside the body).

Ex vivo gene therapy

In ex vivo gene therapy, cells with the faulty or missing genes are extracted from the patient's blood, usually in a hospital or other clinical setting. They're then re-engineered in a laboratory, where scientists remove the faulty genes and replace them with healthy ones.

There are numerous techniques for conducting this re-engineering, the most well-known of which is CRISPR technology. This technique allows researchers to "edit" DNA sequences and modify gene functions, using a protein called Cas9. Cas9 can selectively cut DNA sequences that contain a problematic gene or mutation and replace them with healthy gene sequences. After the cells are re-engineered, they're infused back into the patient. As these cells multiply, the new gene is distributed throughout the patient's system.

Ex vivo gene therapies are complex to administer and highly personalized. They often require long hospital stays in advance of cell extraction, and also carry the potential for serious and life-threatening complications. As a result, total cost of care for administration for ex vivo treatments is likely to be considerable.

At present, approved ex vivo therapies are available only at select treatment centers. But as new therapies and technologies are approved, more patients will likely have access to these types of treatments.

In vivo gene therapy

In the in vivo approach, a healthy gene is transferred directly to cells inside the patient's body. Usually this is done by inserting the healthy gene into a vector (vehicle) that can deliver it to cells, administered to the patient via an injection or infusion. One of the most commonly used types of vectors in in vivo gene therapy is adeno-associated viruses (AAV). Viruses have a natural ability to deliver genetic material into cells. Once they've been modified to remove their ability to cause disease, they can then carry therapeutic genes directly into human cells.

In vivo gene therapies are currently being used to mitigate vision loss in patients with a type of progressive blindness called Retinitis Pigmentosa (RP) and to treat patients with Spinal Muscular Atrophy (SMA).

Applications of Gene Therapy, Current and Future

In addition to the handful of gene therapies currently in use, multiple others are now in development or in clinical trials. These include therapies for hemophilia, sickle cell anemia and Hepatitis B.

Cancer is another emerging application for gene therapy, with approaches including genetically-engineered viruses that kill cancer cells, gene transfer to alter the abnormal functioning of cancer cells, and immunotherapy (including CAR T-cell therapy), which helps the immune system better find and kill tumor cells. This last approach has received FDA approval for use in certain groups of patients and is expected to receive additional approvals soon.

A gene therapy technique is even being leveraged in the development of an experiment vaccine for COVID-19. The vaccine, called AAVCOVID, uses a gene-transfer technology that's already approved by the FDA for treating inherited blindness (Luxturna) and spinal muscular dystrophy (Zolgensma). This new vaccine delivers a fragment of genetic code from the coronavirus into the harmless virus (AAV), which would normally deliver a gene therapy. Instead of delivering a gene therapy, however, the AAV will deliver instructions for making the so-called 'spike' protein that sits on the surface of the coronavirus. Exposing the body to this protein should teach the immune system to recognize and fight off future infections of COVID-19.

The Balancing Act of Risks, Costs and Benefits

For all the potential of gene therapy, the high cost of the technique presents a significant stumbling block. Prices for a single treatment can be as high as $2 million—and that's in one fell swoop, as opposed to spread out over the course of months or years. Employers are grappling with how to offer coverage for gene therapies without bankrupting their health plans or having to significantly increase premium costs for everyone. Health plans, meanwhile, are struggling with the best approach to covering therapies.

> **Health plans must carefully evaluate which treatments offer the greatest potential benefit for patients, and then balance those factors with cost and risk considerations.**

The challenge of coverage for gene therapy is complicated by the fact there are still many unknowns when it comes to the risks, side effects and long-term efficacy of treatments. As with any treatment, gene therapies may be more effective for some patients than others. Health plans must carefully evaluate which treatments offer the greatest potential benefit for patients, and then balance those factors with cost and risk considerations.

At Tufts Health Plan, we're actively monitoring the evolving gene therapy landscape, staying out in front when it comes to assessing and evaluating high-cost therapies. That means monitoring the novel therapy pipeline, meeting with manufacturers and soliciting input from key opinion leaders, and informing and engaging key internal and external stakeholders. It also means building financial impact models and reviewing milestones as therapies near approval.

Once novel therapies are approved by the FDA, we evaluate them on a case-by-case basis, using a multi-departmental approach.

The process includes:

- Developing medical necessity guidelines
- Evaluating options for where therapy can take place
- Engaging provider and pharmacy contracting to negotiate discounts
- Monitoring supplemental approvals, which allow a company to make changes to an already approved therapy

Throughout the process, the needs and concerns of employers remain front and center. It's our goal to balance the life-changing potential of gene therapy for members with the financial risks and realities for employers.

At Tufts Health Plan, we're excited about the promise of gene therapy to transform human health for the better. You can count on us to keep you informed and keep your needs at the forefront as we make more novel therapies available to our members. Have questions?

Contact us today: **tuftshealthplan.com/contact-us/employers**

TUFTS Health Plan

ABOUT TUFTS HEALTH PLAN

At Tufts Health Plan, we strive to set the standard for outstanding quality health care, service and value. Founded in 1979, Tufts Health Plan is nationally recognized for its commitment to providing innovative, high-quality health care coverage. The plan offers members and employers an array of health management programs, which support evidence-based approaches to health and wellness.

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