# GENE AND CELL THERAPIES


## Abstract

*Rapid advances in medical science's understanding of the human genome have led to the recent development of novel gene-based therapeutic strategies. Only a short time ago, such approaches would have been considered technically difficult or impossible to carry out. While not yet common or widely used, new gene and cell therapies are being developed and approved for use today at an increasing rate and are demonstrating promise for diseases that otherwise have had few options for treatment or were deemed incurable. This Brief Report will define gene and cell therapies and provide some insights into these rapidly developing and impactful technologies.*


## What Are Gene and Cell Therapies?

According to the U.S. Food & Drug Administration (FDA), human gene and cell therapies seek to modify or manipulate the expression of a gene or to alter the biological properties of living cells for therapeutic use. Gene and cell therapies fall into two main categories: replacement or inactivation of a disease-causing gene; or introduction of a new or modified gene.[1] Cell therapy products include cellular immunotherapies, cancer vaccines, and other types of autologous and allogeneic cells for certain indications, including hematopoietic stem cells and adult and embryonic stem cells.[2]

## How Are Gene and Cell Therapies Delivered?

The several techniques and mechanisms for delivery of these new therapies can generally be categorized as either *ex vivo*, where the gene and/or cell modification is performed on cells removed from a person's body and the cells then transplanted back into the body, or *in vivo*, where the gene or cell modification is delivered either intravenously or conveyed directly to the affected tissue or organ in the body.[4] New genetic material can be transported to cells via engineered nanoparticles or adeno-associated virus vectors. The latter method can be problematic, as up to 50% of people have pre-existing immunity to these adenoviruses which excludes them from treatment. Research to circumvent this issue continues.[5]

Oligonucleotide therapies, which use synthesized nucleic acid polymers to treat or manage a wide range of diseases, are considered gene therapies for the purposes of this article but are often considered a separate treatment category in the medical literature.

## What Diseases Have Approved Gene and Cell Therapies?

Several gene and cell therapies, including oligonucleotide therapies, have been approved for use, but this differs depending on the country. The U.S. FDA, for example, has approved gene and cell therapies for several diseases,[3, 9] including:

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- Spinal muscular atrophy
- Duchenne muscular dystrophy
- Diffuse large B-cell lymphoma
- Mantle cell lymphoma
- Acute lymphoblastic leukemia (ALL)
- Unresectable melanoma
- Hormone refractory prostate cancer
- RPE65 mutation-associated retinal dystrophy
- Neovascular age-related macular degeneration
- Hereditary ATTR amyloidosis
- Cartilage defects of the knee
- Cytomegalovirus (CMV) retinitis
- Homozygous familial hypercholesterolemia (HoFH)
- Acute hepatic porphyria (AHP)

Many additional diseases are being studied for possible applicability of gene-based therapies. Much success has thus far been achieved, especially for hemoglobinopathies such as sickle cell disease and beta thalassemia. Notably, a gene therapy treatment for beta thalassemia was approved in 2019 in the European Union and its application is currently under review in the U.S.,[7] and studies are ongoing to assess the potential of using gene therapy to prevent HIV from infecting T-cells.[5]

**Gene and cell therapies fall into two main categories.**

Regulators are, however, proceeding with some caution: although U.S. approval had been expected last year for the novel gene therapy Roctavian for hemophilia A, the FDA is requesting to see at least two years of follow up data from the manufacturer's Phase 3 trial before proceeding.[8]

## Insurance Implications

Advances in gene and cell therapies have been extraordinary, and in many cases, life-changing. However, insurers have several potential challenges when assessing the risk of using these new therapies. Considering that more than 900 gene therapies are currently in development and more will be approved, they will be more frequently encountered in patient histories both during underwriting and claims adjudication. Also, as many of these therapies are so new, their long-term efficacy is still unknown. In addition, certain gene therapies require toxic conditioning regimens prior to administration of the actual therapy, imparting additional risk.

The overall safety profile of gene and cell therapies will need to be monitored closely since unlike other clinical studies, gene therapy studies are often performed on very small cohorts of patients. One pharmaceutical company recently halted the clinical trial for its gene therapy for sickle cell disease after receiving reports that a few patients had been subsequently diagnosed with

myelodysplastic syndrome and leukemia, although direct cause and effect are still being investigated.[10]

Finally, the cost of gene and cell therapies can be incredibly high, which may present a barrier for patient access as well as concern for insurers providing medical coverage. For example, one gene therapy for an inherited form of blindness costs U.S. $425,000 per eye and one for a type of spinal muscular atrophy costs U.S. $2.1 million in total.

**Insurers have several potential challenges when assessing the risk of using these new therapies.**

## Conclusion

Multiple next-generation gene and cell therapy technologies are advancing quickly, and will ultimately improve the specificity, accuracy, efficiency, and applicability to different classes of disease. The rapid pace of these advances will dramatically broaden the scope of human disease to which these approaches can be applied.

Indeed, many of these treatments address previously incurable diseases and could offer great hope to those suffering from them. While the benefits are very promising, much remains to be learned with regard to long-term efficacy, outcomes, and safety. Insurers will need to keep up to date with this technology and monitor the impact on mortality and morbidity as well as costs, especially to those providing health cover. RF

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