mahp Michigan Association of Health Plans

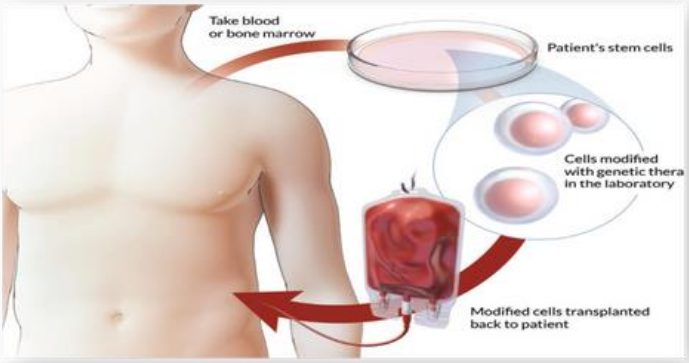
Your Source for Health Care Information

WHAT ARE GENE MODIFICATION PROCEDURES?

Gene and cellular therapies are medical procedures that alter the DNA makeup of an individual. Typically, blood or bone marrow is withdrawn from an individual; their cell structures are manipulated in a laboratory, and new modified cells are injected and transplanted back into the individual.

Gene modifications replace a missing or damaged gene or add genes to immune cells to help them combat diseases. Because physicians can't perform such gene modifications by hand, these procedures involve scientists in a laboratory who alter your genes with viruses. While a virus as we know it today enters your body to cause harm, scientists have found ways to use certain parts of viruses for other means.

Gene modification procedures are similar to an organ transplant, which involve multiple stages and require active participation from physicians, specialists, and scientists.



Gene modifications have unlimited possibilities for medical advancements, but there is still a lot of unknown medical efficacy surrounding these procedures. Concerns about the procedures' impact on immune systems, mutations, and unknown long-term effects related to reproduction are still being studied. In 2023, the FDA opened a new investigation on 22 cases of new cancers emerging in individuals following gene modification treatments.

COSTS OF GENE MODIFICATION PROCEDURES?

The FDA approved the first gene modification procedure (CAR-T) in 2017 to treat acute lymphoblastic leukemia. Before this, gene modification procedures were only used in experimental clinical trials. Since 2017, the number of applications for new gene modification procedures has flooded the FDA. The number of FDA fast-tracked approved applications is expected to grow to more than 100 in the next year. More than 2,000 new gene modifications are already being developed for potential application. According to The Institute for Clinical and Economic Review, cell and gene modification procedures cost between $1 million and $2 million per treatment.

DRUG NAME	MANUFACTURER	INDICATION	COST
Luxturna (voretigene neparvovec-rzyl)	Spark	Inherited retinal disease	$850,000/ for both eyes
Kymriah (tisagenlecleucel)	Novartis	Acute lymphocytic leukemia Diffuse large B-cell lymphoma	$475,000 $373,000
Yescarta (axicabtagene ciloleucel)	Kite	Large B-cell lymphoma and Follicular lymphoma	$373,000
Zolgensma (onasemnogene abeparvovec-xioi)	AveXis	Spinal muscular atrophy	$2.125 million
Tecartus (brexucabtagene autoleucel)	Kite	Mantle cell lymphoma	$373,000
Breyanzi (lisocabtagene maraleucel)	BMS	Large B-cell lymphoma	$410,300
Abecma (idecabtagene vicleucel)	BMS and bluebird bio	Multiple myeloma	$419,500

FDA'S FAST TRACK PROCESS FOR GENE MODIFICATIONS

The FDA has recently laid out its welcome mat for new and emerging drugs and medical procedures by creating a **"fast-track" accelerated FDA approval process**, which does not have the same rigorous guidelines that ensure the drug, or medical procedure provides clinical benefits, thus creating uncertainty about long-term efficacy. Instead, the FDA grants conditional approvals based on interim data and requires additional studies to confirm clinical benefits later. As a result, the FDA has withdrawn approval for roughly 20% of drug and medical procedures specific to cancer treatment, which have been subsequently proven to have no clinical benefit. Furthermore, the fast-track FDA approval process does not undergo a cost-effective analysis. That means the government doesn't set the price nor analyze whether the drug or medical procedure is worth the price paid. As such, insurers must diligently monitor a drug or medical procedure's clinical outcomes, value, and costs to our healthcare system.

STANDARD APPROVAL PROCESS vs. ACCELERATED APPROVAL PROCESS

STANDARD APPROVAL PROCESS

This is the commonly used FDA approval process for prescription drugs that focuses on efficacy, health impact, outcomes, and safety.

CLINICAL BENEFIT REQUIREMENT

- Traditional approval necessitates **demonstrating clinical benefit** before granting approval.
- Drugs must provide **evidence of effectiveness** based on measurable outcomes.

MEASURES OF EFFECTIVENESS

- Two clinical trials required to directly assess the drug's impact on patients' health outcomes.
- The FDA expects that the drug maker will submit results from two well-designed clinical trials, to be sure that the findings from the first trial are not the result of chance or bias.
- In certain cases, especially if the disease is rare and multiple trials may not be feasible, convincing evidence from one clinical trial may be enough.
- Evidence that the drug will benefit the target population should outweigh any risks and uncertainties.

ACCELERATED APPROVAL PROCESS

This approval process seeks to balance urgency with safety by allowing patients quicker access to potentially life-saving treatments. Risks include uncertainties about long-term efficacy and safety for such treatments.

CLINICAL BENEFIT REQUIREMENT

- The FDA grants conditional approval based on **interim data** and surrogate endpoints.
- Accelerated approval often involves **single-arm clinical trials** without a control group.

MEASURES OF EFFECTIVENESS

- Manufacturers must conduct **additional studies** to confirm clinical benefit.

HEALTH PLANS PRIORITIZE EFFICACY

Health plans are required by their accreditation standards to use an internal Pharmacy and Therapeutics (P&T) committee, which is comprised of primary care and specialty physicians, pharmacists, and other professionals in the healthcare field. These committees are specifically charged with evaluating FDA-approved medications to determine a drug's eligibility for a health plan's formulary or preferred drug list. P&T committees are even more important when dealing with FDA treatments approved through the FDA's accelerated approval process.

To ensure the safe and effective use of such treatments, the P&T committee determines utilization management strategies for each medication reviewed. P&T committees meet regularly to review new therapies and additions to therapeutic classes of drugs. P&T reviews include the following focus and priorities:

- Medical and clinical literature including clinical trials and treatment guidelines, comparative effectiveness reports, pharmacoeconomic studies and outcomes data;
- FDA-approved prescribing information and related FDA information including safety data;
- Relevant information on use of medications by patients and experience with specific medications;
- Current therapeutic use and access guidelines and the need for revised or new guidelines;
- Economic data, such as total health care costs, including drug costs;
- Health care provider recommendations.

Content from the Formulary Concept Series, Academy of Managed Care Pharmacy 7/18/19

How are Gene Modification Procedures Managed in Medicaid and Medicare?

MEDICAID: Under the Michigan Medicaid program, cellular and gene modification procedures are "carved out" (paid for separately by the state) from Medicaid Health Plan (MHP) coverage. In other words, these **procedures are excluded from coverage** by managed care plans **and are instead billed as a fee-for-service** (FFS) benefit for all FFS and MHP enrollees. There are currently eight gene modifications that are covered under the Michigan Medicaid program: Yescarta, Kymriah, Tecartus, Breyanzi, Abecma, Carvykti, Zynteglo, and Zolgensma. All eight of these gene modification procedures **require prior authorization** by MDHHS for coverage.

In summary, under Michigan's Medicaid program, **gene modification procedures are so expensive that the state cannot afford to cover them under managed care, as capitation rates would be exorbitantly high, and managed care plans would face extreme financial risk.**

MEDICARE: Medicare is significantly even more limited in its coverage for gene modification procedures than Medicaid. Currently, Medicare provides coverage for chimeric antigen receptor (CAR) T-cell gene modification procedures. Medicare will only cover CAR T-cell procedures when they are provided in a health care facility that complies with the FDA's risk evaluation and mitigation strategies (REMS), and the treatment must be used for an FDA-approved indication as directed by the FDA's label.