

Pharmacy trend **ALERT**

What's trending?

Gene therapy is a rapidly growing form of breakthrough therapy that has transformed the treatment of many serious or fatal conditions for which there were previously no or very few treatment options. The U.S. Food and Drug Administration (FDA) issued its first approval of a gene therapy in 2017. Since then, 16 more have been approved and dozens more are on the horizon. Most gene therapy treatments only need to be administered once. They work by modifying a person's genes to treat or cure a medical condition.

Many current gene therapies treat rare conditions. In the case of sickle cell disease, there are two new “headline-grabbing” gene therapy treatments available. Each gene therapy uses a slightly different technology, but both appear to stop the sickling of cells and prevent complications of sickle cell like tiredness, pain and restricted blood flow to organs. Other gene therapies under development are focused on treating conditions that result in a significant cost to the health care system, such as cancer, joint degradation or heart failure.

How does gene therapy work?

Gene therapy is a technique that modifies a person's genes to treat or cure a disease. Gene therapies can work by several mechanisms:

- Replacing a disease-causing gene with a healthy copy of the gene
- Inactivating a disease-causing gene that is not functioning properly
- Introducing a new or modified gene into the body to help treat a disease

Source: FDA



A few considerations

There are several factors to consider with these complex therapies.

Gene therapies offer potential opportunities in treatment and potential cures for rare and life-threatening conditions, but they come with a steep price tag.

Many of these therapies target rare conditions. The number of potential candidates is usually in the thousands for most therapies, though one slated for release later this year could be a treatment option for around two million people.

Gene therapies also require highly specialized handling, care and administration, as well as careful patient monitoring. These treatments are offered at a limited number of hospitals or treatment centers throughout the country.

While gene therapies offer tremendous promise for those living with rare and life-threatening conditions, the one-time treatment cost can pose a financial burden to payers.

As a plan sponsor, it's important to consider the cost offset of the chronic, long-term therapies members will no longer need to utilize. In most cases, assuming the therapy remains effective, it becomes the most cost-effective solution over time.

Wellmark has adopted an innovative strategy to utilize appropriate cost management opportunities, including rebates, value-based contracting and stop-loss insurance.



The Wellmark Pharmacy and Therapeutics (P&T) Committee

The pharmacy world is a constantly changing landscape as new drugs and treatments become available.

A team of local doctors and pharmacists reviews new and existing drugs and selects medications for the Wellmark Drug List based on safety and efficacy. While they don't weigh-in on benefit design, they do evaluate drugs on how their effectiveness compares to similar drugs used to treat the same condition, which helps determine their tier.

The P&T committee considers such things as:

- Need for a new drug therapy
- Effectiveness
- Costs
- Medical necessity

The goal is always to use unbiased, third-party research and clinical data along with committee members' collective expertise to select drugs that reduce overall health care costs without sacrificing effectiveness.





CURRENTLY APPROVED GENE THERAPIES

These therapies are FDA-approved and available on the market today.

Drug name	Luxturna® (voretigene neparvovec)
Indication	Treatment of confirmed biallelic RPE65 mutation-associated retinal dystrophy
Clinical considerations	Currently, there are no other approved pharmacologic treatment options. For an individual to receive therapy, genetic testing is needed to confirm diagnosis, and the treatment must be administered at an ocular gene therapy treatment center.
Key cost considerations*	\$850,000 (\$425,000 per eye)

Drug name	Zolgensma® (onasemnogene abeparvovec)
Indication	Treatment of patients <2 years of age with spinal muscular atrophy (SMA)
Clinical considerations	Alternative treatment options include Spinraza® and Evrysdi®, both of which require ongoing administration. Genetic testing is required, and there are currently weight-limit restrictions at the time of administration.
Key cost considerations*	The cost of therapy is approximately \$2.13M. It is important to consider cost offset related to ongoing alternative therapies: • Spinraza – \$765k for first year & \$380k for subsequent years • Evrysdi – \$357k/year

Drug name	Zynteglo™ (betibeglogene autotemcel)
Indication	Treatment of adults and pediatric patients with transfusion-dependent beta thalassemia (TDT)
Clinical considerations	Clinical considerations: It is expected this therapy will be reserved for individuals with a severe case of the disease that cannot be managed with transfusions and chelation therapy (with or without Reblozyl®). If TDT is left untreated, 85 percent of individuals will die by age 5.
Key cost considerations*	The estimated cost is approximately \$2.8M. IPD Analytics estimates alternative treatment options for TDT: • Transfusion (\$22K/year) + Iron chelation therapy (\$75K/year): \$97K/year • Reblozyl: \$186K/year

Drug name	Skysona™ (elivaldogene autotemcel)
Indication	Treatment of male patients 4 to 17 years of age with early, active cerebral adrenoleukodystrophy (CALD)
Clinical considerations	The alternative treatment option is allogeneic hematopoietic stem cell transplantation (HCST), which has reported five-year survival rates of 56 percent and 75 percent. Only about 30 percent of patients can find a matched sibling donor according to Bluebird Bio. Currently, most young males with CALD die within five to 10 years of the onset of neurologic symptoms, unless they receive HSCT early in the disease process when symptoms have not progressed.
Key cost considerations*	The estimated cost is \$3M.

Drug name	Hemgenix® (etranacogene dezaparvovec)
Indication	Hemophilia B
Clinical considerations	Eligibility will be limited to adult patients with moderate to severe hemophilia B based on clinical trial population. Alternative treatment options include prophylactic FIX (factor IX) products.
Key cost considerations*	The estimated cost is \$3.5M. It is important to consider cost offset related to decreased use of other prophylactic therapies, as the average cost of those prophylactic therapies in eligible members is estimated to be approximately \$668k per year.

Drug name	Elevidys (delandistrogene - moxeparvovec-rokl)
Indication	Duchenne muscular dystrophy (DMD)
Clinical considerations	DMD affects approximately one in 3,500 live male births worldwide. The 2016 practice guidelines from the AAN for corticosteroid treatment of DMD recommend prednisone therapy to improve strength and pulmonary function. Emflaza® (deflazacort) is an alternative option to corticosteroids. No treatment guidelines currently address the place of Elevidys or the exon-skipping therapies in overall therapy.
Key cost considerations*	\$3.2M

Drug name	Roctavian™ (valoctocogene roxaparvovec)
Indication	Hemophilia A
Clinical considerations	The prevalence of hemophilia A is estimated to be approximately 17.1 cases per 100,000 male individuals for all severities and accounts for up to 85 percent of all hemophilia cases. Roctavian is the first FDA-approved gene therapy for hemophilia A in the United States and is administered as a single dose versus the currently available clotting factor concentrates, which are typically administered twice to four times weekly.
Key cost considerations*	\$2.9M

Drug name	Casgevy [®] (exagamlogene autotemcel)
Indication	Sickle cell disease (SCD)
Clinical considerations	Prior to FDA approval of the potentially curative gene therapy agents Casgevy (exagamlogene autotemcel) and Lyfgenia [™] (lovotibeglogene autotemcel), hematopoietic stem cell transplantation (HSCT) was the only curative therapy for SCD. Due to the risks associated with the procedure and the need for a matched donor, not all patients are candidates for HSCT. Blood transfusions are used to treat and prevent SCD complications.
Key cost considerations*	\$2.2M

Drug name	Lyfgenia [™] (lovotibeglogene autotemcel)
Indication	Sickle cell disease
Clinical considerations	Prior to FDA approval of the potentially curative gene therapy agents Casgevy (exagamlogene autotemcel) and Lyfgenia (lovotibeglogene autotemcel), hematopoietic stem cell transplantation (HSCT) was the only curative therapy for SCD. Due to the risks associated with the procedure and the need for a matched donor, not all patients are candidates for HSCT. Blood transfusions are used to treat and prevent SCD complications.
Key cost considerations*	\$3.1M

Drug name	Lenmeldy [™] (atidarsagene autotemcel)
Indication	Metachromatic leukodystrophy (MLD)
Clinical considerations	The prevalence of MLD ranges from one in 40,000 to one in 160,000 births worldwide. There are no standard guidelines for the treatment of MLD, and treatment mainly relies on symptomatic supportive care to address neurocognitive disturbances, neuropsychiatric disturbances, seizures, dystonias, spasticity, feeding problems and constipation. HSCT is a promising treatment option, but most patients will eventually decline and experience progressive loss of motor function.
Key cost considerations*	\$4.25M

Drug name	Beqvez [™] (fidanacogene elaparvovec-dzkt)
Indication	Hemophilia B
Clinical considerations	Hemophilia B occurs in approximately one in 15,000 to one in 30,000 live male births. Approximately one-third to one-half have severe disease. Severe hemophilia is almost exclusively a disease of males, although females can be affected in some rare cases.
Key cost considerations*	\$3.5M



GENE THERAPIES IN THE PIPELINE

These highly-anticipated therapies are expected to come to market within the next year.

Drug name	Upstaza™ (eladocagene exuparvovec)
Indication	Aromatic L-amino acid decarboxylase (AADC) deficiency
Clinical considerations	There is no cure and no currently approved therapies for AADC deficiency in the U.S.
Key cost considerations*	The estimated price is \$3M or more wholesale acquisition cost (WAC) for a one-time treatment. This estimate is based on the rarity of disease and lack of treatment options.

Drug name	fordadistrogene movaparvovec
Indication	Duchenne muscular dystrophy (DMD)
Clinical considerations	This therapy is intended to deliver its mini dystrophin-encoding gene to muscle tissue for the targeted production of the mini dystrophin protein.
Key cost considerations*	The estimated price is \$2-\$3M for a one-time treatment (likely to be closer to \$3M).

Drug name	prademagene zamikeracel (EB-101)
Indication	Recessive dystrophic epidermolysis bullosa (RDEB)
Clinical considerations	EB-101 will compete with Krystal Biotech's Vyjuvek® (beremagene geperpavec), an FDA-approved topically applied gene therapy for treating open wounds in patients with RDEB.
Key cost considerations*	The estimated price is \$1-\$2M WAC per treatment. The cost per treatment and the total cost per patient will likely vary depending on the size and number of open wounds.

Drug name	pariglasgene brecaparvovec (DTX401)
Indication	Glycogen storage disease type 1a (GSD1a; von Gierke disease)
Clinical considerations	Current treatment is supportive and includes frequent cornstarch feeds to maintain glucose levels, which are often inadequate in preventing hypoglycemia
Key cost considerations*	The estimated price is between \$1.5-\$2.5M for one-time treatment.

Drug name	RP-L102
Indication	Fanconi anemia (FA)
Clinical considerations	FA is a rare, autosomal recessive disease that leads to bone marrow failure; it is the most common inherited form of aplastic anemia. The current standard of care treatment for FA is allogeneic hematopoietic stem cell transplantation (HSCT), which is associated with significant toxicities and complications. About 80 percent of patients with FA will require a transplant within the first decade of their life.
Key cost considerations*	The estimated price is \$2-\$3M per one-time treatment.

Drug name	RP-L201
Indication	Primary immunodeficiency
Clinical considerations	Leukocyte adhesion deficiency type 1 (LAD-1) is caused by mutations in the ITGB2 gene encoding for the beta-2 integrin component CD18. CD18 is a key protein that facilitates leukocyte adhesion and extravasation from blood vessels to combat infections.
Key cost considerations*	The estimated price is \$2-\$3M per one-time treatment.

*Cost of therapy only includes the ingredient cost of the gene therapy and not the potential additional costs of care that may result from therapy (admissions, follow-ups, etc.).



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