Insightsfeature

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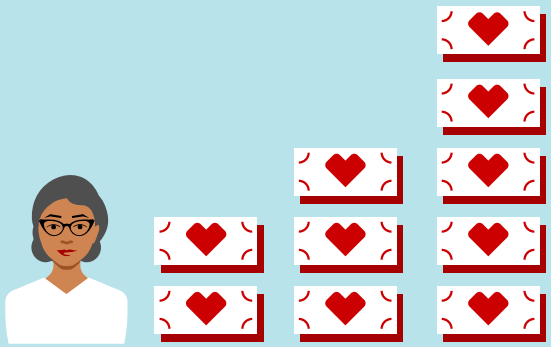
Two New Treatments for Sickle Cell Disease

Research Into Gene Therapies Could Bring More Options

CVSHealth®

About 100,000 Americans have sickle cell disease (SCD).[1]

The condition is caused by a mutation in the beta globin (*HBB*) gene which provides instructions to make part of hemoglobin, the protein in red blood cells that carries oxygen.[2,3] The mutation causes the hemoglobin in the blood to distort in shape and results in red blood cells taking on a sickle shape. Until recently, approved pharmacologic treatments for SCD included hydroxyurea (Siklos and Droxia) and Endari (l-glutamine).[4]



$1M

average total lifetime health care costs for a patient with sickle cell disease.[6]

About 90 percent of people with SCD in the U.S. live to adulthood, but nearly all experience acute painful episodes, called vaso-occlusive crises (VOCs), when sickled red blood cells block small blood vessels.[5] The sickled shape also causes abnormal destruction of red blood cells, resulting in anemia, or low red blood cell count. The average sickle cell disease patient is estimated to face nearly $1 million in total lifetime health care costs with annual costs of more than $30,000 for adults.[6]

The U.S. Food and Drug Administration (FDA) recently approved two new treatments for SCD that could expand treatment options for patients. Research is also ongoing for gene therapies that could provide an alternative to bone marrow transplant — currently the only available cure for SCD.

Adakveo (crizanlizumab)

The FDA approved Adakveo (crizanlizumab), a monoclonal antibody developed by Novartis, on November 15, 2019.[7] Adakveo aims to reduce the frequency of VOCs, which are painful, can lead to life-threatening conditions, and are a major cause of additional costs such as hospitalization.[8] The drug is initially administered as bi-weekly treatments for a month. Following that, it is taken as an intravenous infusion every four weeks, and is intended as an alternative, or add on, to hydroxyurea for the estimated 50,000 patients aged 16 and older who have VOCs despite optimized treatment regimens.

~3X more patients had no VOCs when being treated by Adakveo compared to the control group.

In a pivotal trial, patients receiving Adakveo had about half as many VOCs leading to health care visits compared to the control group receiving placebo, regardless of whether they received hydroxyurea. They also had a longer time before their first VOC, and the percentage of patients who had no VOCs during treatment was triple the rate for patients receiving placebo — 37.5 percent compared to 12.2 percent.

Dosage depends on the patient's weight. Depending on the dosage needed, Adakveo will cost between $7,000 and $9,500 per month and will be covered under the medical benefit.[9]

Oxbryta (voxelotor)

The FDA approved Oxbryta (voxelotor), developed by Global Blood Therapeutics, 10 days after Adakveo, on November 25, 2019. Roughly one quarter of patients with SCD experience a stroke by the age of 45.[10] Oxbryta could help reduce strokes by increasing hemoglobin levels.[11] The drug is approved for the treatment of sickle cell disease in patients aged 12 and older — about 80,000 patients in the U.S. — and is administered daily as an oral treatment. Oxbryta's expedited approval was conditional on the manufacturer completing a follow-up study to confirm clinical benefit.

In a phase III trial, hemoglobin levels increased by more than one gram per deciliter in 51 percent of patients receiving high-dose voxelotor, compared with 7 percent of those on placebo.[12] The Oxbryta group also showed fewer signs of hemolysis — destruction of red blood cells.

The list price for Oxbryta is $10,417 a month and it will be covered under the pharmacy benefit.[9] The Institute for Clinical and Economic Review (ICER) is expected to publish a draft review of the drug in late January.

Ensuring Appropriate Use

With new therapies coming to market, it is important to ensure appropriate use to help plan sponsors balance member access and cost. We have developed clinical criteria for sickle cell treatments to help clients manage this category.

- Endari currently is approved for members, aged five years or older, with sickle cell disease if they have either tried and failed hydroxyurea or have a contraindication to it, or for concurrent use with hydroxyurea.
- Adakveo is approved to help reduce frequency of VOCs among members aged 16 years and older with sickle cell disease and prior vasooclusive crises.
- Oxbryta treatment is approved for members 12 years of age and older with sickle cell disease and a pretreatment hemoglobin level of 10.5 g/dL or less.

Gene Therapy for SCD

Currently the only cure for SCD is a bone marrow transplant. However, finding a bone marrow match can be challenging, and the treatment is complex, requiring the patient's own marrow to be eliminated with chemotherapy.

Researchers are now looking for potential gene therapies to help cure SCD.[13] There are different approaches, all involving genetically altering the patient's own hematopoietic stem cells, and the use of the gene editing technique known as CRISPR (clustered regularly interspaced short palindromic repeats). Hematopoietic stem cells — the precursors of all blood cells found in bone marrow — divide and specialize to produce different types of blood cells, including red blood cells.

The first approach is to harvest the patient's stem cells, replace the faulty *HBB* gene with a healthy copy in the lab, and transplant the cells back into the patient using a viral vector.[14]

The hope is that the cells with the corrected copy of the gene would repopulate the bone marrow and produce healthy red blood cells. In October 2019, researchers at the National Institutes of Health announced that they had developed a new and improved viral vector that was up to 10 times more efficient at incorporating corrective genes into marrow stem cells than conventional vectors currently in use.[15] The vector also had a carrying capacity up to six times higher. This could make gene therapy for SCD more effective and available to more patients.

Another approach to gene therapy uses the CRISPR gene-editing technique to boost the production of fetal hemoglobin by genetically altering another gene in hematopoietic stem cells.

Fetal hemoglobin — a form of hemoglobin produced by babies from about seven months before birth to about six months after birth — represses sickling of cells in patients with sickle cell anemia, but most people only produce a tiny amount of it after infancy.

However, some patients with SCD — those not badly affected by symptoms — have genetic variations that enable them to produce fetal hemoglobin into adulthood. Fetal hemoglobin binds more strongly to oxygen. By using a highly specific enzyme to remove one of the genes that stops production of fetal hemoglobin, scientists aim to boost the production of fetal hemoglobin in adult patients with SCD. Researchers aim to increase production of fetal hemoglobin in stem cells by using a highly specific enzyme to cut the cell's DNA in the section containing one of the genes that suppress production of fetal hemoglobin.

Among the companies working to develop gene therapies for SCD are Bluebird Bio, Sangamo Therapeutics, and Vertex and CRISPR Therapeutics, who recently announced a deal for the development of up to six gene therapies, including potential candidates for SCD.[16,17] If and when such treatments are approved, how the medical community receives them, and therefore their utilization, remains to be seen.

It is clear the pipeline for SCD treatments continues to evolve. This is likely to offer patients more options and perhaps even greater potential for a cure. For payors, the key consideration will be effectively balancing what are likely to be high — and rising — price tags with appropriate access.

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