What is Sickle Cell Disease?

Sickle cell disease (SCD) is a disorder passed down through families that causes red blood cells to take on a "sickle" or crescent shape. These abnormal red blood cells deliver less oxygen to different parts of the body, causing a range of symptoms and complications.

Sickle cell disease affects approximately 100,000 Americans, most of whom are of African descent. Historically, SCD has been overlooked and underfunded, with a lack of awareness of SCD in broader communities. Racism and discrimination can make getting appropriate care very difficult for patients.

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Sickle Cell Disease 2023

Impact on Sickle Cell Warriors
What ICER Learned from the Community

- Social isolation from limitations to physical activity, travel, or being in cold weather
- Inadequate pain management, lack of specialists, lack of adult care providers
- Anemia, blood clots, stroke, neuro-cognitive impairment
- Huge impact on caregivers
- Difficulty maintaining employment, needing to avoid marriage or having children, issues with fertility
- A condition with physical, emotional, and mental toll
- Racial bias, stigma, lack of societal awareness of disease
- Anxiety, depression, hopelessness
- Chronic daily pain, acute pain, vaso-occlusive pain
- Huge impact on caregivers

Treatments of Focus in ICER's Review

**GENE THERAPY** | **HOW IT WORKS** | **CLINICAL TRIAL***
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1. **Lovo-cel** (bluebird bio) | Increases levels of functional adult hemoglobin | HGB-206
   - 36 patients
   - Ages 12 to 50 yrs
   - Followed for 2+ yrs
2. **Exa-cel** (Vertex Pharmaceuticals & CRISPR Therapeutics) | Uses CRISPR technology to increase levels of fetal hemoglobin | CLIMB-121
   - 35 patients
   - Ages 12 to 35 yrs
   - Followed for 2+ yrs

Both lovo-cel and exa-cel are gene therapies that patients only take once. Chemotherapy and bone marrow transplant are part of the treatment with gene therapy.

*These trials excluded patients who were eligible for a stem cell transplant.

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Both therapies had serious adverse events in the trials, such as blood cancer (lovo-cel only) and death (both trials). These events were mainly linked to the bone marrow transplant required before receiving the gene therapies. The long-term risks of these gene therapies in the real world are still uncertain. Patient input helped inform ICER’s understanding about the broader safety of these therapies.

Safety of Lovo-Cel and Exa-Cel

What Did Clinical Trials Show?

Both Lovo-cel & Exa-cel

- REDUCED painful crises
- REDUCED hospitalizations
- INCREASED total hemoglobin levels

These represent some, but not all outcomes that were measured in the clinical trials. In addition, these clinical trials only show short-term benefits.

What We Still Don't Know

- How well the gene therapies work outside of clinical trials
- How often the therapies really work (only studied in small number of people so far)
- How the therapies will work in children under 12 years old
- How the therapies affect other chronic complications of SCD, such as organ damage
- How lovo-cel and exa-cel compare to each other
- How the therapies work for patients in the long-term

ICER's report findings are NOT recommendations that support the use of these gene therapies. Patients and families should always talk with their doctors to make shared decisions about treatment for sickle cell disease.
How Did ICER Calculate a Fair Price?

Using economic modeling, we calculated the cost effectiveness of lovo-cel and exa-cel based on how well they reduced acute and chronic complications, compared to standard of care. See below for what types of information ICER considered to calculate a fair price range for the two gene therapies.

Factors Included in ICER's Economic Analysis

Population
This analysis included adolescents and adults with severe SCD who were not eligible to get a stem cell transplant.

Complications of SCD

Benefits & Risks of Treatment

Age

Patient-Reported Level of Health

# of Pain Crises*

Medical Costs

Productivity & Unpaid Work Costs

Size of bubbles does not show level of importance for the analysis.

*Patient input helped ICER better understand the average # of pain crises to use for our analysis.

Fair Price Range for Lovo-Cel and Exa-Cel

A fair price is how much a treatment should cost based on how well it works for patients. Our economic analysis concluded that the fair-price range for lovo-cel and exa-cel is between $1.35 and $2.05 million. This price is for a one-time treatment.

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The Policy Roundtable at the ICER public meeting informed several policy recommendations for pricing, access, guidelines, and future research in SCD. A few key recommendations are summarized below.

1. **Patient groups have a powerful voice to create significant pressure for fair pricing and appropriate insurance coverage across all parts of the health system.**

   Working with insurance plans and clinical societies, patient organizations can help lead the work to improve access to treatments and hold drug makers accountable to fair pricing.

2. **Insurance plans should 1) design coverage policies that can support travel for patients and their families to receive therapy, and 2) provide insurance coverage for fertility preservation.**

   Since lovo-cel and exa-cel will only be available in specialized medical centers, sickle cell warriors should have fair opportunity to access these gene therapies without issues with how far they live or how much money they make. In addition, we heard from both warriors and clinical experts that fertility preservation is an important consideration when managing SCD. Insurance plans should cover fertility preservation along with coverage for gene therapies.

3. **The FDA, drug makers, and clinical researchers should be consistent in how they measure patient-important outcomes for sickle cell disease.**

   The FDA should require drug makers to use the same definition for outcomes (such as vaso-occlusive crises) in order to allow researchers and the patient community to directly compare therapies. Outcomes captured in clinical trials should reflect all important aspects of living with sickle cell disease, including mental health outcomes that were highlighted by sickle cell warriors as often overlooked.
All stakeholders have a responsibility to ensure equitable and optimal patient access to gene therapies for SCD.

Steps should be taken by all stakeholders to ensure that all sickle cell warriors have access to multidisciplinary care that takes a broad view of the needs of patients and their families for services such as mental health and social support.

Impact of Patient Engagement

Community input allowed ICER to better understand the average number of pain crises that sickle cell warriors experience in the real world. As a result, ICER revised this number in our economic model.

ICER gained valuable insights from the patient community about the impacts of living with SCD, and the hopes of patients and their families about new treatments.

Patient and caregiver testimony at the public meeting about the benefits of treatment for the whole family helped shape ICER’s recommendations for policy makers to provide equitable access to treatments.

The Institute for Clinical and Economic Review (ICER) is an independent nonprofit organization that does research on how well new treatments work and what a fair price should be. Patients and families should always talk with their doctor to make shared decisions about the best treatment option for them.