



February 2, 2020
Institute for Clinical and Economic Review
Two Liberty Square
Boston, MA 02109

RE: Draft Evidence Report for the Treatment of Sickle Cell Disease

Dear Dr. Pearson,

Sick Cells is pleased to have the opportunity to engage with the Institute for Clinical and Economic Review (ICER) during their review of treatments for sickle cell disease (SCD). Sick Cells has been heavily involved in this review as a key stakeholder and, because of our high engagement, identified the large constraints of this report. We urge ICER to suspend the review at this time, as this review is premature and inappropriate. The lack of published quality of life and real-world data for these new treatments severely limits ICER's ability to measure the benefit of them. Moreover, the process simply did not allow enough time to adequately and robustly review a disease as complex as sickle cell disease. SCD is too serious and the impact is too large for this vulnerable population to be denied access to therapies because this value assessment was conducted with an inadequate evidence base.

If ICER decides to move forward with the timeline, we have included recommendations for ICER to consider in the final report:

1. Introduction

- a. The authors discuss how patients' baseline health and usual care vary considerably. Thank you for calling this out. Please discuss the implications this has on the analysis included in the report. The comparator is listed as "optimal usual care" however it is not clear how ICER reached a definition of usual care given this variation.
- b. More information is needed in the background section regarding current treatments. Please discuss which patients the medications are recommended for, as the eligibility may be limited. Additionally, provide details regarding the undesirable side effects of each treatment.
- c. Table 1.1 Please provide greater detail on WAC and cost per year.
- d. Include definition for "optimal usual care" utilized as a comparator.
- e. Include identification of data measures and data sources utilized for each outcome. For example, quality of life is listed as an acute outcome, however the quantitative vs. qualitative quality of life improvement is an ongoing tension between the patient perspective and the health economics perspective. Please provide greater detail on the definition and measurements used to capture quality of life as an acute outcome.



- f. Please provide citations for how ICER has defined chronic and acute health conditions.
2. Patient Perspectives
 - a. We acknowledge and thank the organization for seeking input from patients and patient advocacy organizations to gather the patient perspective on this devastating disease. Please provide specifics on how this information contributes to other sections of the report, including the base-case model. It is not clear how this section has impacted the specifics of the report.
 - b. We recommend discussing your methods for capturing the patient perspective. Include citation statements where appropriate. For example, the quotes should be attributed to individuals.
 - c. We appreciate the documentation of racism faced by this community, however, the connection of lack of resources and patient experience to racism is unclear. Please provide citations.
 - d. The “one size fits all” policy for acute pain management is not necessarily a hospital issue. Many states have passed laws on the number of days opioids can be prescribed for acute, opioid naive patients.
 3. Summary of Coverage Policies and Clinical Guidelines
 - a. The authors mention reviewing insurance policies from specific states. It is unclear why these states were selected. The majority of patients with SCD live in other geographic areas not covered by these state-specific insurance policies.
 4. Comparative Clinical Effectiveness
 - a. We appreciate the attention to the limitations of RCT inclusion criteria, including the lack of representation from pediatric populations. Please discuss how this impacts ICER’s ability to accurately measure benefit for the defined population of patients two years of age and older with sickle cell disease.
 - b. In the conclusion section of each treatment, please footnote the data source for quality of life. Please provide details on the measures and methods used to collect quality of life data, noting if any other sources or real-world data was considered.
 5. Long-Term Cost Effectiveness
 - a. We recommend for ICER to develop an equity-sensitive framework for diseases that face increased discrimination and stigma, like sickle cell disease. Anticipated equity effects of this review require adaptation of the usual review processes.
 - b. Quality-adjusted life years fails to capture a wide variety of other benefits such as person’s return to economic productivity, school performance, and ability to function as a caregiver for SCD patients. We recommend using a modified equity-sensitive framework to include these factors in the base case analysis.
 - c. ICER extracted data from Medicare and Commercial claims, however Medicaid is a more common payment source among SCD patients. We recommend utilizing Medicaid data for a more accurate representation of the population.



- d. Prevalence estimates reported by Shah et al. 2019 are based on July 01, 2009 and 31 Dec 2012 data. It is unclear how accurately these prevalence estimates reflect the current period with regards to the acute chest syndrome, stroke, and pulmonary hypertension. Similarly, Van Tuijn et al. 2010 uses dated data to estimate the prevalence. We recommend using updated data sources for these prevalence estimates.
- e. We have identified several concerns related to utility values used in the report:
 - i. Several utility values used in this report are cited from U.K. studies, such as Anie et al., 2012. These utility measurements are inappropriate to be utilized in this assessment, given the differences between health care, health care systems, and the impacts of race and ethnicity in the UK and the US. Complex historical and sociological processes influence the relationships between pain, hospital care, coping responses, and overall quality of life. Given the role of patient utility as a key determinant of value in this model, this is a major concern and limitation. ICER inadequately addresses this uncertainty in the draft report.
 - ii. ICER model input 0.7 utility for uncomplicated SCD patients; however, the Anie utility function is 0.81. Please explain the rationale for using the 0.7 utility function.
 - iii. Anie et al., 2012, estimates “SCD without pain” one week after hospital discharge. These measurements do not accurately reflect the optimal physical, mental, and social functioning associated with SCD patients without pain. Please include utility measures that can more accurately represent the experience of patients without pain.
 - iv. Additionally, Anie et al., 2012, estimates the utility function of patients upon hospital admission from pain crisis. In reality, patients often manage pain in outpatient settings, emergency rooms, or at home. Patients may only be admitted for extreme pain crises. Please include utility measures that can more accurately represent the experience of patients with acute pain crises.
 - v. ICER should assess if utility functions can be derived from the Sick Cells “My Life with Sickle Cell Disease” survey data.
- f. We have identified several concerns related to cost estimates:
 - i. SCD patients experience multidimensional pain, including emotional stress and mood changes. It is unclear if multidimensional pain and the severities of each pain type are accounted for in cost estimates.
 - ii. ICER should review the indirect costs obtained from the Sick Cells survey and consider if the data are appropriate for including in the model.
 - iii. ICER used average cost from Market Scan (non-representative for SCD patients given the use of Medicare and Commercial claims) instead of



individual cost data. Majority of the SCD patients have complicated treatment history and typically have comorbidities; treatment is tailored to each patient. So, without accounting for other factors such as indirect costs, the calculated average treatment cost does not reflect the true patient costs.

- g. ICER should include scenario analysis to assess drug price changes when patent protected drugs expire.
 - h. ICER should consider using Cost Effective Analysis or try using some value of medical innovation beyond QALY. At this moment QALY is missing the value of innovation.
 - i. ICER's scenario analysis shows that discount rate has major impact on patient cost. Changing the discount rate to 1.5% will increase the drug price by more than 20%, meaning the model is considerably impacted by the discount rate change. Provide justification for the discount rate included in this analysis.
 - j. ICER reports "Patients with SCD on optimal usual care are predicted to live to 45 years old, which when discounted at 3% per year equates to approximately 15 additional life-years, 8 additional evLYG, and 8 additional QALYs." Is this distribution similar in other populations? Please explain in more detail and add relevant citations.
 - k. Table 5.36: The table shows the Medicare population reports higher prevalence of pHTN, HF, and CKD for ages 18-45 as compared to the prevalence of age 46 and over predicted by model. Please explain how the model accounts for these differences.
 - l. Baseline prevalence rate over-reported such as pHTN: The model assumes a high prevalence of organ damage at young age. Please justify the rationale for the high prevalence for organ damage.
 - m. ICER is potentially over estimating mortality. Patients have mortality risk assigned to each comorbidity thus potentially double counts the mortality risk. ICER should consider methods used by Krueger et al. 2013.
6. Potential Other Benefits and Contextual Considerations
- a. ICER mentions the impact of racism and bias but does not say how the model accounts for these factors.
 - b. Are the contextual considerations in section 6.2 reflected in ICER's decisions on effectiveness of the medications? Please discuss the use of the information in this paragraph.
7. Value-Based Price Benchmarks
- a. No comments
8. Potential Budget Impact
- a. No comments



Thank you for your consideration of these suggestions.

Sincerely,
Ashley Valentine, MRes
President and CEO