PATIENTS RISING NOW

Guide for Commenting on ICER's Draft Evidence Report on

Treatments for Hypertrophic Cardiomyopathy

On August 18, 2021, ICER released its draft evidence report, "Mavacamten for Hypertrophic Cardiomyopathy: Effectiveness and Value." This guide provides a framework for considering what aspects of the new hypertrophic cardiomyopathy treatment are important to patients and their families, and how to consider presenting those perspectives. This guide specifically provides insights about how to read and respond to ICER's "draft evidence report," as well as how to request a slot to make comments during ICER's public meeting.

Key Dates

August 18, 2021:	Draft Evidence Report released
September 15, 2021:	Written comments due by 5:00pm ET; deadline to submit request to speak at Public Meeting
October 7, 2021:	Updated Evidence Report released
October 22, 2021:	Public Meeting conducted by ICER's California Technology Assessment Forum (CTAF)
November 16, 2021:	Final Evidence Report and Public Meeting Summary released

Background & How to Participate

The Institute for Clinical and Economic Review (ICER) is a private entity that uses its own analytical process and "value framework" to assess potential new treatments for a variety of diseases. These assessments often occur before FDA approval, and may result in conclusions that could harm patients by limiting access to new and innovative treatments. You can learn more about ICER here.

There are two primary ways advocates and other stakeholders can give input:

1. **Submit written comments on the draft report.**
2. **Request a slot to make oral comments during ICER's October 22nd meeting.**

Submitting written comments on the draft report

Written comments must be submitted to publiccomments@icer.org as a Word document in 12-point Times New Roman font, and are limited to 5 pages, not including references or appendices. The deadline to submit written comments is 5:00pm ET on September 15, 2021.

Requesting a slot to make oral comments

ICER's Public Meeting on its revised report and discussion by one of its advisory committees is scheduled to occur virtually on October 22nd. The meeting will have a short period available for public comments. To request a slot to make public comments, an email needs to be sent to publiccomments@icer.org with the person's name, title, and organization. The deadline to make a request to speak is 5:00pm ET on September 15, 2021. Oral comments are limited to no more than five minutes per speaker.

NOTE: Not all requests to make public comments are granted. According to ICER: "We sort through all the requests to make an oral public comment at the meeting. Because we only have a limited time for oral comments at the public meeting, we can only allow a few stakeholders to share their perspective."

Key Points to Consider for Written or Oral Comments

Clinical Effectiveness

- ICER's review of hypertrophic cardiomyopathy is focused on mavacamten, a potential medicine that is still pending FDA review. The FDA is expected to make a decision on this treatment by January 28, 2022.

- Mavacamten is a potential new treatment for hypertrophic cardiomyopathy that acts at the cellular level in the heart muscle. It is taken orally once a day.

- ICER's review is based on limited data – primarily from one Phase 3 trial with 251 people, (123 receiving mavacamten and 128 who received placebo).

- The results of the Phase 3 trial were very good, with improvements seen in clinical status (e.g., 37% of the people receiving mavacamten improved their blood oxygen levels and did not have worsening heart failure compared to 17% who received placebo). And more importantly, of the 194 who completed the health status questionnaire, on average there was significant improvement in all parameters over the 30 weeks of the trial, and those improvements disappeared

when they stopped receiving mavacamten. (See slides in Appendix A from this presentation at the American College of Cardiology May 2021 meeting.)

- Despite those positive results, ICER focuses on the limited data – and the fact that the Phase 3 clinical trial only lasted for 30 weeks. (This is a common theme for ICER, i.e., it conducts its review before FDA approval, and is critical about the lack of long-term data.)

Recommendation: Advocates for better treatments for hypertrophic cardiomyopathy should consider making the following points in their written or oral comments:

- Not only has mavacamten been found to provide clinical benefits, but it improves patients' quality of life and overall wellbeing.

- While the Phase 3 trial only had data for 30 weeks, the trend was for ongoing benefits, and there is an "extension" study enrolling people who had been in the Phase 2 and Phase 3 trials of mavacamten. This trial will provide additional long-term information – particularly adverse effects – about the use of mavacamten for treating hypertrophic cardiomyopathy, which will help clinicians and patients understand how to best use this potential new medicine in real-world situations. ICER should recognize this trial, and be prepared to update its findings with new data – or delay releasing its report until the FDA approves mavacamten and more long-term and real-world data is available.

- While mavacamten is not a "home run" cure for hypertrophic cardiomyopathy, on average it benefited a significant percentage of people in the clinical trials. It is a significant step forward that clinicians and researchers can build upon – hopefully with future treatments that work even better and for more people with hypertrophic cardiomyopathy. Thus, the value of mavacamten as a bridge to better treatments in the future is very important for patients and their families, and ICER should not dismiss or discount that value to patients and families as part of its evaluation.

- Discuss how hypertrophic cardiomyopathy affects the daily lives and productivity of people and their families.

- One of the critically important aspects of the benefits and value of mavacamten is that for some people with hypertrophic cardiomyopathy they will be able to avoid

having heart surgery or other procedures for hypertrophic cardiomyopathy. Taking a pill is clearly less invasive and does not carry the same significant risk of death as the invasive procedures – according to ICER's research, those risks are 1 in 40 for surgical myomectomy, and 1 in 75 for septal reduction therapies.

- While mavacamten may not benefit every patient with hypertrophic cardiomyopathy, it certainly will provide another important option for patients and their clinicians to consider. Joint decision-making by patients and their clinicians to develop a treatment plan that is best for the individual patient is critical for quality healthcare that fits the particular situations of specific patients. ICER's homogenized population-wide assessments may make sense for insurance companies and academics, but ICER also needs to recognize the rights and priorities of individuals in the real world where people live and receive actual clinical care.

Cost Effectiveness

- ICER's economic modeling and analysis has at its core the concept of Quality Adjusted Life Years (QALYs), which have been widely criticized when used for decisions about payment, coverage and rationing of care – particularly because QALYs can discriminate against people with chronic conditions and disabilities, since QALY calculations assume that people with less than perfect health have diminished quality of life.

- When presenting a report about a potential treatment that has not been approved by the FDA, as part of the cost effectiveness modeling, ICER includes a "placeholder price" – since ICER needs that to determine the cost-per-QALY, which is the fundamental final number that ICER uses to determine "value" as well as to determine what it believes is a "fair price." (ICER will typically highlight its "fair price" in it press releases and other materials, and the difference between what it has determined to be a "fair price" and the "placeholder price" – or later the actual list price of a treatment once it is approved by the FDA.) For mavacamten, ICER is using a "placeholder price" of $75,000 per year based upon a financial analyst's estimate that was included in a May 2020 news report about the early release of clinical trial information (i.e., before publication in a peer-reviewed journal, which occurred in September).

- In the case of mavacamten, ICER's draft report concludes that mavacamten provides little or no cost-effectiveness benefit. Specifically, it seems that it will

conclude it only increases QALYs by about 0.6 to 0.8 over standard care or an older medicine, and that mavacamten improves QALYs less than surgery, even though ICER notes that about 1 out of every 40 people who undergo heart surgery with myectomy for their hypertrophic cardiomyopathy die from the surgery, with 1 out of 75 who undergo septal reduction dying from that procedure. (Those risks of death accounts for the reduction in total life years for those individuals in ICER's assessment.) See below Table 4.3 from ICER's Draft Evidence Report.

Table 4.3. Results for the Base Case for Each of the Treatments

Treatment	Total Drug Cost	Total Cost	QALYs	Life Years	NYHA I Years	evLY
Mavacamten*	$1,258,000†	$1,568,000	13.51	16.58	12.64	13.51
Standard Treatment	$12,600	$434,000	12.54	16.58	4.94	12.54
Disopyramide*	$116,000	$509,000	12.82	16.58	6.96	12.82
Septal Ablation*	$67,700	$297,000	13.71	16.37	18.49	13.71
Myectomy*	$135,000	$364,000	13.75	16.40	18.53	13.75

evLY: equal-value of life years, N/A: not applicable, NYHA: New York Heart Association, QALY: quality-adjusted life year

*Each of these treatments includes use of standard first-line therapy.

†Cost estimates for mavacamten were based on a placeholder price of $75,000 per year.

- In developing its economic model for cost effectiveness, ICER makes many wide-ranging assumptions that also fail to consider how treatments will improve over time – including the possibility of new treatments that are in development. For example, another compound for treating hypertrophic cardiomyopathy is in development by a company called Cytokinetics. Preliminary reports are very promising – and this treatment could potentially help more patients than mavacamten.

Recommendation: Advocates for better treatments for hypertrophic cardiomyopathy should consider making the following points in their written or oral comments:

- Question ICER's use of QALYs as a fundamental basis for its cost effectiveness evaluation, and refute the concept that someone with a chronic health condition has a reduced quality of life since the concept of "perfect health" is fictional – everyone has health issues and challenges.

- Question the source or relevance of the "placeholder price" that ICER has chosen, particularly since it is from financial analysts, which may be biased to drive up stock prices, or because it is from a source that is more than 12 months old and based upon information from before the results of Phase 3 trials were available for review.

- Present the patient perspective that while list prices may have relevance for public policy, what is important for patients to know is what they have to pay for treatments they need, i.e., co-payments and other forms of cost-sharing based upon their specific health insurance plans.

- Insurance companies should not establish very high co-payments, or erect access barriers such as prior authorization or similar restrictions to access because of costs, but should help facilitate access to new beneficial medicines.

- Raise questions about the assumptions and underlying uncertainties that ICER itself notes in its report. Those assumptions and uncertainties might include limited data because the drug has not been approved so there is essentially no "real world" experience with the medicine, and there may be patients who were excluded from the clinical trials that could benefit from mavacamten.

Budget Impact

- One of the more controversial aspects of ICER's reports looking at potential new treatments is their development of a fictional "budget impact" that assumes the U.S. healthcare system is a monolithic single payer entity. ICER's budget impact process asserts that in any year, all new medicines shouldn't receive more than a certain amount of money in total – regardless of how much they benefit patients. In addition, because this "budget impact" calculation encompasses all medicines that could be introduced in a year and allocates the same dollar amount to each medicine based upon a formula that uses how many new treatments the FDA had approved in recent years, ICER's model provides a feedback loop that if adhered to would be a disincentive for developing new treatments, i.e., if many more new treatments were approved, then in future years, ICER's budget limit for each new medicine would be lower.

- In doing its budget impact assessment, ICER does not consider other treatment options that have been developed or are in development, such as devices or

surgical interventions.

- If ICER's "budget impact" concept seems bizarre or confusing, that's because it is both bizarre and confusing.

Recommendation: Advocates for better treatments for hypertrophic cardiomyopathy should consider making the following points in their written or oral comments:

- Similar to the fictional cost-effectiveness analysis, ICER's budget impact assessment does not represent patients' perspectives. Rather, real people are concerned about what they have to pay for the treatments they need. In contrast, ICER's "budget impact" assessments and "fair price" provide rationale for insurance companies to deny coverage and erect access barriers. In particular, the budget impact "assessment" may be used by government healthcare programs like the Department of Veterans' Affairs (VA), Medicare, and state Medicaid programs to create barriers or extend administrative delays for making new medicines available.

- Criticize ICER for presenting fictional, somewhat arbitrary numbers based on so many assumptions that they are essentially meaningless. Advocates should express concern that ICER's faulty numbers will be used by insurance companies to justify denying patients access to medicines that could improve their health and lives.

Additional Thoughts and Perspectives

- Provide your personal perspectives and insights as someone with hypertrophic cardiomyopathy or as a family member or friend of someone with hypertrophic cardiomyopathy about the importance of having more and better treatments.

Conclusions

- Summarize and restate your thoughts and provide overall recommendations for what ICER should do – or not do – particularly related to the harm that ICER's conclusions could cause by limiting access to this potential new treatment for hypertrophic cardiomyopathy by empowering health insurance companies and government programs to deny payment or create barriers for patients receiving the treatments their physicians recommend.

Additional Resources

- "A plain language summary of the EXPLORER-HCM study: mavacamten for obstructive hypertrophic cardiomyopathy" – link here.

- American College of Cardiology Presentation Slides: "Health Status Benefits of Mavacamten in Patients with Symptomatic Obstructive Hypertrophic Cardiomyopathy: Results from the Explorer-HCM Randomized Clinical Trial" – link here. (See slides in Appendix A)

- ICER's "Mavacamten for Hypertrophic Cardiomyopathy: Revised Scope Background and Scope," May 22, 2021 – link here.

- ICER's "Mavacamten for Hypertrophic Cardiomyopathy: Effectiveness and Value," Model Analysis Plan, July 6, 2021 – link here.