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USC Graduate Student Team Analyzes ICER Assessments to Assist a Pharmaceutical Manufacturer in Pipeline Development and Strategy



Graduate Student Team: Ivy Bien, PharmD, MS, Jennifer Chen, PharmD, MS, Nanxi Huang, PharmD, MS, Nikitha Kolapalli, PharmD, MS, Ziqian Wang, MS, Binglun Wu, MS

Faculty Advisor: Daniel Tomaszewski, PharmD, PhD

In the fall of 2020, a team of University of Southern California (USC) Healthcare Decision Analysis masters degree students conducted an independent strategic assessment of published Institute for Clinical and Economic Review (ICER) evaluations as third-party observers. Knowledgeable in both the clinical and business aspects of healthcare, this graduate student team was tasked to assess various perspectives on the role of ICER in pipeline management, market access planning, and overall company engagement in the ICER review process.

Background

The ICER is well known for its cost effectiveness assessments of healthcare technologies.[1] The institute attempts to provide an independent review to answer the primary question of whether new treatment options being offered in the United States (primarily pharmaceutical products) provide cost effective care compared to existing alternatives. ICER currently serves as the key source for HTA reviews within the U.S.; however, the reviews are not completed on all new health technologies and their findings are non-binding and separate from any FDA approval or public or private coverage determination.

The impact and value of ICER studies have been debated since the creation of the organization itself. Due to the non-binding nature of their findings, lack of universal review of new technologies, and free-market pricing in the U.S., healthcare decision makers have limited reliance on the findings of an ICER study. This has also led pharmaceutical manufacturers to question the degree of engaging ICER and the practical value of the findings of its reviews.[2]

At the same time ICER has worked to expand its role in healthcare decision making, so has the recognition of many biopharmaceutical and medical technology manufacturers for the need to embrace the field of Health Economic and Outcome Research (HEOR). HEOR is often referred to as the connection between medical affairs, market access, and commercial teams. The role of HEOR has become a vital component of health technology market access efforts. As companies develop innovative, next generation treatments, product viability must also be ensured. Market access efforts are focused on developing a value proposition to compel payers to provide appropriate access and reimbursement for these agents. The HEOR team and strategies developed using HEOR concepts help to establish this value story and demonstrate the cost-effectiveness of novel health technologies.[3]

Biopharmaceutical and medical technology firms continue to expand efforts in developing a product's value proposition that incorporates cost-effectiveness analyses and the perspective of ICER reviews. One consideration is how companies can leverage previous ICER evaluations to help ensure a successful launch of future health technologies. Previously completed ICER assessments can provide manufacturers a glimpse into the key data driving the final conclusions of the assessment. This can allow manufacturers to use these findings during the design of clinical development strategies, for example, using the ICER findings to establish key clinical data to collect, inform the length of registrational and post-marketing studies, and target additional data collection where appropriate. In addition, ICER results can help companies prioritize assets, shape future pricing and forecasting, and work more effectively with payers embracing the cost-effective view on health technology assessment.

The Project

Focused on cystic fibrosis and cardiovascular disease for a U.S.-based pharmaceutical company, the team identified ICER strengths and weaknesses with respect to clinical development and stakeholder involvement. Key findings included:

- ICER is widely acknowledged as a U.S. authority in health technology assessment (HTA) but has less influence compared to HTA bodies in other countries.
- ICER is gradually taking on a more important role in payers' coverage decision-making, with payers increasingly reporting the use of ICER findings or alternative cost-effectiveness data to help support health technology reviews and coverage decisions.
- The role and importance of the pharmaceutical manufacturer to support or engage with ICER as assessment is conducted remains unclear and has perceived risks and benefits.

Based on these general findings, the team recommended that pharmaceutical companies focus on:

- Developing a robust clinical development plan that would provide data to support a positive review from ICER.
- Ensure clinical trial and overall clinical data collection is sufficient to support an assessment in the desired target populations.
- Clearly stratify patient sub-populations within any clinical evidence generation plan to support robust statistical assessment.

Findings associated with the company engaging ICER during an assessment related to the company's pipeline products

- Consider utilizing ICER's input periods and contributing to draft documents during the manufacturer input windows to help frame the clinical findings.
- Develop a publication strategy, including the consideration of conducting preliminary cost-effectiveness analyses to establish key model considerations and assumptions to help frame the ICER review.
- Expedite the publishing of key clinical data and economic models that could improve product standing during the ICER assessment.

Cystic Fibrosis Focused Findings [4]

ICER strengths:

- The use of the Quality Adjusted Life Year (QALY) as the primary clinical outcome of interest helps ensure the inclusion of both extension of life and improvement in the quality of life as drivers for the impact estimate of future health technologies.
- ICER conducts a structured review of available data when conducting the assessment, which gives pharmaceutical companies the opportunity to drive the clinical assessment based on published studies supporting quality of care outcomes.
- The addition of even value Life Years Gained (evLYG) measurement was viewed as a unique opportunity to establish value that includes a demonstration of extension of life for CF patients if the study is not powered to establish quality of life effects.[5]
- The significant engagement of advocacy groups, direct patient engagement, and overall opportunity for stakeholders to engage throughout the ICER assessment to ensure real-world stories of a product impact are included.

ICER Weaknesses:

- The assessments completed to date focus on the need for costly long-term, large-scale clinical trials, which is a significant challenge in the development of new CF therapies.
- There appears to be an extremely limited engagement of specialist and practitioners overall that care for Cystic Fibrosis patients.
- The inflexibility of the ICER model does place significant burden on pharmaceutical manufacturers to fit into Cost Effectiveness Analysis model, which may not be supported by clinical trial strategies to date.
- The previously conducted ICER assessment did not provide a robust enough description of cost assumptions and the role of pricing strategies to evaluate the impact competitive contracting efforts would have on final findings.

How can a company use these findings to improve future product strategy in Cystic Fibrosis?

- Focus studies on the health technology assessor's target population, including those that best match the anticipated place in the treatment algorithm, and include combination approaches and relapsed/refractory populations.
- Prioritize data collection in both planned clinical trials and post-marketing studies to help establish the impact the new CF treatment has on both QALYs and evLYG.

In general, the CF assessment suggested these steps:

- Consider submitting relevant data to ICER during the manufacturer feedback periods and participate in open input periods/public comments.
- Interact with patient advocacy groups and partner with practicing CF specialists and overall provider groups to encourage additional support during public input periods.
- Develop cost effectiveness and budget impact models and publish findings prior to the initiation of the ICER review to ensure the alternative model will be available for review by ICER.
- Consider additional exploratory endpoints for future studies with longer follow-up periods.

- Focus on drug design and drug administration methods and evidence generation that supports administration in an outpatient setting, preferably as self-administered in the patient's home.

Impact of ICER on payers:

- Payers are currently using ICER as an additional, independent review of clinical evidence and economic models to help support internal Pharmacy & Therapeutic (P&T) committee reviews.
- Payers also report value in being able to review ICER indirect comparison of a treatment's ability to impact QALYs, evLYG, and ability to achieve cost-effectiveness as specific willingness to pay thresholds.

Cardiovascular (CV) Disease Focused Findings [6]

The review of new treatments for cardiovascular disease includes the challenge of a relatively large number of existing treatment options, with many being available as low-cost generic alternatives. The current treatment landscape itself was generally thought to create significant challenges for investment and return for future pipeline products that may not be able to compete on price alone. Due to this constraint, the overall perception is the ICER assessment is likely to have increased impact on healthcare decision makers.

ICER strengths:

- ICER reported a broad use of clinical data to drive its findings, including the use of both clinical trial endpoints of the 3-point Major Adverse Cardiac Events (MACE) as a primary endpoint and 5-point MACE as a secondary endpoint.
- ICER also reported previous use of patient population stratification, to conduct a review with a focus on a specific subset population based on clinical trial evidence, risk stratification, or a product's anticipated place in therapy.

ICER weaknesses:

- The role of patient experience and patient engagement during the completion of prior ICER assessments was not well described or transparent compared to other ICER reports.
- The final reports previously provided made it difficult to ensure that ICER is including all appropriate risk reductions of CV events when conducting the assessment of innovative treatments.
- Prior reviews did not appear to include the impact of altering the intensity of statin therapy and the role that may have on patient outcomes and quality of life.
- The prior assessments appear to be missing direct engagement and feedback from primary care providers, who are key care providers in CV disease.

How can a company use these findings to improve future product strategy in cardiovascular disease?

- Preemptively prepare for ICER's evaluation of new products by reviewing ICER's primary clinical criteria used for their literature search and review of clinical evidence as it directly relates to cardiovascular disease.
- Understand ICER's Evidence Rating Matrix.

- Develop clinical data evidence generation focused on establishing changes to patient reported quality of life based on the ability to reduce the burden of statin therapy.
- Ensure trial design, e.g. cohort size and length of studies, support the ability of the innovative treatment option to impact QALYs-gained over the well-established, low-cost standard of care in the treatment of cardiovascular disease.

Impact of ICER on payers:

- Payers are demanding long-term data, including key clinical outcomes that directly demonstrate the cost-effectiveness of the new health technology.
- The need to include evaluation in combination or as an alternative to OTC Omega-3.
- Payers reported the importance of subpopulation stratification to support their ability to evaluate future treatments for specific patient populations based on comparative efficacy, level of risk, comorbid conditions, or other patient-specific clinical considerations.

1. <https://icer.org/our-approach/methods-process/>
2. <https://www.xcenda.com/insights/htaq-winter-2020-icer-payer-decision-making>
3. <https://www.medicalaffairsspecialist.org/blog/value-of-heor>
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