BMS Response to ICER’s Call for Improvements to its Value Assessment Framework

BMS has taken on some of the most challenging health problems of our time and welcomes the opportunity to participate in ICER’s national call for suggestions on how to improve its value assessment framework. BMS’ pipeline is a reflection of the desire to cause the same transformation in cancer care as our research contributed to the transformation of HIV to a manageable chronic disease. As a leader in immuno-oncology research and innovation, we have delivered on the challenge of fighting cancer and developing lifesaving therapies. An evidence-driven approach to measuring treatment value is critical as we tackle the most challenging diseases of highest unmet need, but the science is progressing rapidly.

BMS will support the development of best practices in value assessment, but we disagree on the ICER framework’s focus on cost-containment and care rationing as well as on many methodological details of how innovative and transformational treatments are currently being evaluated. We believe that value in healthcare should be measured in the longer, healthier lives of patients. We are aligned with society’s desire to make major advances in cancer, which Americans overwhelmingly support. However, by failing to account for disease and patient complexity, while also narrowly focusing on a single component of healthcare spend, ICER’s value framework sidesteps an opportunity for appropriate assessment of value. BMS believes in and works to promote a comprehensive and current approach to value that incorporates key elements: a real-world approach, patient priorities, total health system value over a multi-year timeline, multi-stakeholder input and the most up-to-date clinical science.

We have reviewed ICER’s list of the highest priority areas for potential revision and believe the ICER value framework could be improved in the following ways:

- Include more robust clinical expertise into the evaluation design
- Remove the budget impact threshold analysis
- Increase transparency and reproducibility of methodology and processes
- Improve care value methodology
- Incorporate stakeholder critiques into methodology and processes
- Define value from patient perspective, including recognition of the heterogeneity of treatment effects

We discuss each of these recommendations in greater detail in the following sections. Finally, we outline a more comprehensive approach to value assessment that defines value from the patient perspective and looks at the full range of patient experience with care.

Include more robust clinical expertise into the evaluation design

ICER’s value assessment framework sidesteps an opportunity for a meaningful assessment of value by failing to account for the complexity of disease and patient experience. The goal of a cost-effectiveness analysis is to identify high value treatments for a specific patient population.
To do so, extensive clinical expertise is needed to identify the population of interest, relevant treatments and key outcomes among other factors. Thus, it is imperative that ICER better incorporate clinical expertise into its value framework design and evaluations. In addition, a 21st century approach of value assessments should assess patient values in the real-world from resources, such as patient reported outcomes (PROs). ICER utilizes a model similar to the National Institute for Health and Care Excellence (NICE) which was launched in 1999. However, since NICE’s inception, the healthcare community has seen major technological advances in clinical data-gathering that truly reflect the patient experience.

1. Clinical panel should represent a diverse group of disease area experts.

To achieve the goal of including robust clinical expertise, ICER’s voting panel should be well-rounded and include members with diverse areas of expertise. In particular, clinical panel members should have strong expertise in the therapy or disease area being evaluated, and ICER should ensure these members attend and participate in the meetings. Non-clinical experts should be briefed by clinical experts prior to the voting process to ensure all panel members have a strong understanding of the key clinical questions. Not only should clinical experts be used to inform the broader voting panel, but ICER should also involve clinical experts on its panel to provide input early on when the project scoping documents and protocols are developed. Clinical experts could even be required to sign off on the patient population and clinical question of interest before the project announcement and draft scope are released. For example, in the NSCLC therapy review announcement, the listed drugs were used to treat entirely disparate patient populations. The input of NSCLC experts early in the review process likely would have prevented this oversight.

In addition to better incorporating clinical expertise into its voting panel process, ICER should also better incorporate clinical expertise from the broader provider community. ICER’s new open input period is useful, but it is unclear if comments from the clinical community and other stakeholders will be used to inform the model. For ICER’s rheumatoid arthritis review, for example, the due date for the open comment period was the same day as the release of the draft scoping document, which clearly did not leave sufficient time for ICER to carefully review and then incorporate clinical comments. As another example, ICER initially proposed to combine treatments for rheumatoid arthritis and psoriatic arthritis, however, these disease areas have different outcomes of interest.

2. Assessments should be timely and recognize the evolution of the value of medicines over time. In the future, ICER should update its results and reports when new data or information is available. This will allow ICER’s reports to reflect real-world practices and utilization patterns. For instance, new phase III trial evidence on daratumumab was released after ICER’s final report on multiple myeloma. Therefore, ICER should update its review of multiple myeloma therapies to reflect this new evidence. Specific areas of concern include:

   Remove the budget impact threshold analysis

ICER’s budget impact framework arbitrarily establishes budget caps for societal expenditures on medical innovations and fundamentally ignores the value of innovation in healthcare and the value of care provided to individual patients.

1. Deters innovation and access in areas of high unmet need. Setting budget criteria instead will deter innovators from developing therapies that could benefit a broader patient population. Nevertheless, treatments that provide significant benefits to a large number of patients are exactly the treatments most desired by society. It is fundamentally flawed to assume patients subjected to a cancer of high incidence or
prevalence are worth 'less' than patients who have a rarer form of cancer. Applying this threshold to past innovations, such as statins and anti-retrovirals, would have limited access to these drugs at the time they were introduced to the market.\textsuperscript{11,12} Further, the short-term nature of the budget impact analysis ignores not only any health benefits to patients, but also ignores how improved patient outcomes can reduce medical costs in both the short and long run.

2. **Sets an arbitrary threshold for one component of healthcare spending.** We believe the budget impact threshold ICER selected is highly arbitrary. First, the threshold focuses narrowly on one component of healthcare costs, with emphasis on medicines. The ICER budget cap limits allowable spending growth amount per new medicines. In essence, this practice implies that spending on new medicines should be frozen based on current patterns of care. Second, we believe that the ICER budget cap is based on flawed estimation of GDP growth, a highly volatile number of newly approved medicines each year, and an unrealistic adoption rate. There is no clear economic reason why drug spending should be limited to an excess cost growth of 1\% (i.e., GDP + 1\%). ICER states that this threshold is “embodied” in current federal and state legislation.\textsuperscript{13} However, applying this threshold only to pharmaceutical spending assumes that the relative value of pharmaceuticals compared to the rest of the healthcare industry is constant over time. In practice, when new pharmaceuticals provide significant value to patients above the status quo, spending on pharmaceuticals treatments should increase relative to other type of health care goods and services; in periods of low or modest innovation, the share of the economy dedicated to drug spending should fall.

*Increase transparency of methodology and process*

ICER should increase the transparency of its reviews through three primary avenues: (i) refining topic selection and timing, (ii) provision of additional methodological detail, and (iii) inclusion of approaches for validation. The goal of a cost-effectiveness analysis is to identify high value treatment for a specific patient population.

1. **Topic selection and timing.** Although ICER has recently better outlined how its topics are chosen, the topic selection criteria are largely driven by the approval of new, high-cost treatments, rather than the goal of answering clinical questions for patients.\textsuperscript{14} A new cost-effectiveness analysis is of most interest in a rapidly evolving treatment landscape, but topics should be based on clinical questions of interest rather than drug cost. BMS recommends greater alignment with clinical societies on relevant questions for research. Further, it would be beneficial to all stakeholders if they were made more aware of when ICER plans to evaluate its topics. Ideally, a schedule of topics would be released well in advance of the development of any draft scoping document, rather than allowing only a few weeks for preparation as part of the open comment period.

2. **Transparency of methodological detail.** In addition, ICER should make full details of its models publicly available for replication purposes. Cost-effectiveness modelling best practices indicate that models should be both transparent and valid to help researchers understand the results and have confidence in them.\textsuperscript{15} This transparency includes the ability for other decision-makers to replicate a model and produce similar results. While ICER currently provides an overview of its methods online and has begun providing inputs and assumptions documents, these documents are not sufficiently detailed to allow for replication by interested stakeholders. For instance, in the ICER PCSK9 report, details were omitted with respect to the estimation of cardiovascular disease risk in the
secondary prevention population. ICER also should provide methodological details when it shares its preliminary analysis results with manufacturers.

3. **Peer reviewed methodology.** Peer-review of the model before it is finalized and applied in a review is recommended. Although ICER has submitted components of its reviews to peer-reviewed journals—such as publications on the treatment for familial hypercholesterolemia and the hepatitis C virus—it has not published the complete evidence-based reviews of its topics. Publication of all reviewed topics should be common practice, and ICER’s draft and final reports should reflect the rigor of the published manuscripts. Further, although ICER has begun to publish its protocol online, it should ensure that the details included allow for a full replication of the analysis.

**Improve care value methodology**

ICER could better incorporate all components of value, including those from patient and societal perspectives. Focusing primarily on medicines fails to take advantage of a much greater opportunity to evaluate value in the US healthcare system where a large majority of health spending remains unexamined.

1. **Incorporate patient priorities.** While ICER has begun to try to integrate patient and societal perspectives in the clinical-effectiveness phase of its evaluation, these perspectives generally are not included in ICER’s care value modeling, even in more recent reviews such as those in the multiple sclerosis or rheumatoid arthritis. To address this shortcoming, ICER should consider adding other components of value to patients such as worker productivity and the value of durable survival gains. Treatments that improve patient or caregiver work productivity (i.e. through reduced absenteeism or presenteeism) should also be reflected in the value calculation, as health-related lost productivity is estimated to cost over $260 billion to employers annually in the United States. For example, a recent Cancer Support Community survey found quality of life and length of life were important factors when making a treatment decision.

However, the patient’s perspective on survival gains is not adequately accounted for in the ICER framework. As a study published in Health Affairs indicates patients place significant value in survival improvements in the tail of the distribution above and beyond treatments that improve median survival. Patients surveyed were asked to compare two treatment regimens for melanoma that, statistically speaking, yielded equivalent survival gains. A large majority of cancer patients chose the regimen that offered a 50% chance of twice the survival gain over a regimen that provided assurances of a shorter survival gain. Although the “sure bet” regimen provides assurance of a shorter survival gain, and “hopeful gamble” offers a 50% chance of twice the survival gain, a large majority of cancer patients chose the latter. This value of hope cannot be ignored. In recognition of the importance of long term survival, the America Society of Clinical Oncology (ASCO) explicitly incorporates survival improvements in its revised value framework through tail of the survival curve bonus points.

Finally, ICER should rely on a patient-centric approach for valuing treatments. For example, while the clinical efficacy of a psoriasis treatment could be similar across most patients, the value of an effective treatment to a given patient may depend on the location on the body where psoriasis manifests itself. For instance, patients who experience the disease on highly visible regions of their body are likely to place a significantly higher value on treatment than other psoriasis patients where the disease manifests itself more discretely. Using a single QALY measure obscures these patient specific preferences.
2. **Incorporate patient heterogeneity into methodology.** Further, ICER should better incorporate patient heterogeneity in its methodology. Although ICER does on occasion model certain subpopulations (e.g., line of therapy for non-small cell lung cancer [NSCLC]), in other cases it will not (e.g., separating patients with squamous and non-squamous NSCLC histologies). ICER's definition of a relevant patient population is broad and ignores significant patient heterogeneity resulting from different natural history and biology (NSCLC review). NCCN guidelines state "The generic term 'non-small cell lung cancer (NSCLC)' should be avoided as a single diagnostic term". NCCN specifically separates out treatment by histology type which is due to clinical trial findings that different treatments have different risk/benefit profiles based upon histology. Further, the FDA has recognized these differences during reviews and approvals of NSCLC therapeutics.

As another example, ICER's hepatitis C virus (HCV) model did not examine how treatment effects vary based on patient comorbidities such as HIV co-infection, diabetes, renal disease, and congestive heart failure. All of these comorbidities are known to impact and be impacted by co-infection with HCV, resulting in, for example, an increase in the rate of disease progression, complications, and mortality. More generally, when evaluating a therapy or disease area, ICER should strive to identify the highest value treatment for a given patient, rather than identifying the highest value treatment for only the average patient.

3. **Incorporate caregiver perspective.** Benefits to non-patients are also not adequately incorporated into ICER's baseline cost effectiveness models. Currently 3 in 10 American households provide unpaid caregiving to a family member. Unpaid caregiving imposes a significant health and financial burden, and treatments that can reduce this burden should be valued to reflect this. Further, non-patients also value new treatments due to their "insurance" value. Non-patients that do not suffer from the disease under consideration still value the availability of treatment advances, as these innovations act as a sort of "insurance policy" in the event these individuals contract the disease of interest in the future. The value of innovative treatments to non-patients can be quite large.

4. **Prevent bias against interventions when data is not yet available.** Further, ICER's current approach is inherently biased towards finding that health care interventions are not cost-effective. ICER's general approach has been to assume that a treatment's benefits are valued at $0 if there is no evidence available at the time of the review. This type of approach, however, is problematic as it systematically underestimates the value of a treatment at drug launch, as much of the information on potential treatment benefits (e.g., change in caregiver burden) has not yet been collected. ICER should consider incorporating plausible assumptions from other treatments or other diseases related to treatment costs and benefits when no data is available.

5. **QALY thresholds inappropriate for US healthcare system.** Further, ICERS use of a QALY threshold is premature given the lack of debate in the U.S. on society's willingness to pay for new treatment innovations. Whereas ICER uses a $50,000-$150,000 value of a QALY, a number of economic analyses find that the value of an additional QALY for cancer patients is closer to $150,000-$300,000. Other research has demonstrated that patients near the end of their life have a higher willingness to pay for survival extensions compared to the average patient. Arbitrary QALY valuations can alternatively make drugs seem either cost-effective or highly non-cost effective
depending on these parameter assumptions. A broader discussion with stakeholders, including patients and other experts is needed before drugs are arbitrarily categorized as being cost-effective or not. In addition, understanding the total cost of care inclusive of therapeutic interventions and other healthcare spend (resulting in cost savings and medical cost offsets) is important to factor in.

6. **Significant uncertainty makes benchmark pricing unworkable.** Additionally, ICER should eliminate recommendations on treatment price when there is significant uncertainty in the treatment's value. In the multiple myeloma review, the differences between the low and high ends of the credible incremental cost effectiveness ratio ranges were greater than $200,000 for some treatments. Further, changes to some basic assumptions changed the incremental cost effectiveness ratios for elotuzumab by more than $200,000 between the draft and final reports. If one were to calculate prices based on the credible cost-effectiveness ranges presented, the resulting discounts would encompass such a large range that they would be—in many cases—practically meaningless.

Also, ICER’s current approach inappropriately assumes that drug prices are static. Drugs that are viewed as “expensive” today inevitably decline in price, either after competing drugs enter the market or the loss of a drug's patent exclusivity. For instance, therapeutic competition from biosimilar drugs is estimated to lower biologic drug prices by as much as a third.31 Failing to account for the likely price profile throughout the drugs lifecycle will underestimate the value to society. Finally, the “list price” that ICER assessments currently utilize does not represent the actual discounted price that is relevant to, and often negotiated, by payers.

**Incorporate stakeholder critiques into methodology and process**

ICER should also better integrate stakeholder comments into its methodology and processes. From BMS’ experience conducting research, extensive consultation with patients, caregivers, and providers helps manufacturers and other stakeholders determine what treatments are needed and what outcomes should be prioritized. For example, BMS’ research process and post-market evidence generation efforts are aimed at improving survival, quality of life, and other areas of care that patients, caregivers, and providers have deemed valuable. In addition, BMS discusses value with payers every day and we lead active dialogue with payers on all aspects of value through submissions of extensive, high quality, and transparent clinical and economic research.

In order to allow for more meaningful input, ICER should dually lengthen its public comment periods and allow for more time to incorporate these comments into their models. To date, most of the revisions ICER has made in response to stakeholder comments have been minor fixes. Given the project timelines, there generally is insufficient time for ICER researchers to fundamentally revise its methodology or approach in response to valid comments; this constraint can be problematic when comments advise changes or clarifications to the evaluation’s more time-consuming components, such as the network meta-analysis. As part of the comment process, ICER should also respond to stakeholders’ comments directly as to why or why they were not implemented in ICER’s approach in order to increase the transparency of ICER’s methodology.
BMS supports a more comprehensive and current approach to value assessment

BMS believes in, and works to promote, a comprehensive and current approach to value that incorporates key elements: patient priorities, real-world evidence, total health system value over a multi-year timeline, multi-stakeholder input, and the most up-to-date clinical science. The value of medicines evolves over time with new understanding of benefits compared to risks and changes in the evidence base, such as long-term data that becomes available only after a medication’s launch.

1. **BMS supports defining value from the patient perspective considering patient preferences, goals, and experiences.** BMS is taking action to ensure the growth of value frameworks that consider patients’ desires, goals, and experiences. We support the rubric developed by the National Health Council (NHC), which aims to assess value frameworks by considering their degree of patient partnership, engagement, transparency, inclusiveness, and diversity. The rubric also supports the use of patient-centered data sources and patient-reported outcomes in line with BMS’ push to use more real-world evidence in determining the value of rheumatoid arthritis and cancer therapeutics. In developing the rubric, NHC notes that “it is not apparent that individual patients or patient organizations were engaged throughout the creation” of new value frameworks like that of ICER.

2. **BMS is committed to generating greater evidence to improve health care decision-making and the ultimate value of care provided to patients.** BMS believes value frameworks should take into account real-world evidence as it can better reflect a therapy’s impact in the actual clinical setting. Overall, BMS participates in numerous pharmacoeconomic conversations and produces globally over 200 publications per year. For example, to better treat patients with rheumatoid arthritis (RA), BMS has published studies using real-world data from the Corrona, LLC RA registry to identify patient response to ORENCIA® based on key biomarkers. Additionally, BMS has launched the ACROPOLIS (Apixaban ExperienCe Through Real-World Population Studies) program designed to generate evidence from clinical practice settings to help improve healthcare decisions in the prevention of stroke and embolism.

3. **BMS supports a comprehensive assessment of value that looks at the full range of the patient’s healthcare experience.** BMS supports value assessments that broadly incorporate the patient’s care journey, including examining healthcare delivery and reassessing the standard of care to ensure that treatment is up-to-date and reflects the most appropriate therapies available. Value assessment should consider the impact of making progress against costly conditions. As new medicines hold the promise to reduce costly healthcare utilization for non-drug services, other contextual factors such as innovation should be considered to improve value in the long-run. In fact, many ex-U.S. health technology assessment bodies do consider innovation, extent to which a therapy addresses unmet medical need, societal preferences, and other relevant factors in their decision-making. Lastly, pharmaceutical costs are only a modest share of overall health spending. In 2014, retail and non-retail pharmaceuticals accounted for 13.8 percent of national health expenditures while hospital care, physician services, health insurance, and nursing care facilities accounted for 70 percent. In 2010, labor costs accounted for 56% of total healthcare spending in the United States. The entire care continuum cannot be overlooked when researching the value of one component in the healthcare system.
Conclusions

BMS appreciates the opportunity to comment and suggest improvements to ICER’s value framework. BMS has outlined a number of areas in ICER’s framework that, if improved, could strengthen ICER’s methodology and approach. We hope that ICER incorporates these recommendations into their modelling and processes.

Sincerely,

_______________________    _____________________
Mitch K. Higashi, PhD     Wayne M. Sichel, JD
Head of US Medical Health Economics and Outcomes Research    Head of U.S. Federal Policy
References


27 Braithwaite, R.S., et al., What does the value of modern medicine say about the $50,000 per quality-adjusted life-year decision rule? Medical Care, 2008. 46(4): p. 349-356.


