CUTANEOUS LYMPHOMA FOUNDATION

Steven D. Pearson, MD, MSc, FRCP
President
Institute for Clinical and Economic Review
One State Street, Suite 1050
Boston, MA 02109 USA

April 21, 2016

RE: ICER Review of Drug Therapies for Multiple Myeloma

Dear Dr. Pearson:

The undersigned organizations advocate on behalf of Americans with cancer and other life-threatening diseases whose life expectancy and quality of life have significantly improved due to innovative therapies. While we appreciate your efforts to engage in an expanding dialogue around value, in our opinion there is currently no mechanism to calculate the "value" to individual patients of less suffering and longer life. Suffice it to say that for the estimated 14.5 million cancer survivors today, the return on investment from more time with loved ones, a higher quality of life, increased productivity and the ability to work, travel and be active is incalculable.

Among these cancer survivors are the more than 88,000 Americans who currently have or are in remission from multiple myeloma (MM), an incurable blood cancer where the introduction of novel treatments has led to dramatic survival gains. In fact, due to innovations in MM therapies, 5-year survival rates increased from 25% in 1975 to 44.9% in 2014. Moreover, with the approval in 2015 of three drugs for relapsed or refractory MM, clinicians now have new weapons to address the ongoing challenge of treatment resistance, which remains the major obstacle to keeping myeloma in remission for longer periods of time.

However, as the tide begins to turn in combatting myeloma, we are concerned that a "one-size fits all" approach to assigning an economic value to different MM drugs will turn back the clock for patients and physicians. Further, as organizations speaking broadly for cancer patients and those with serious conditions, we are also concerned that the Institute for Clinical and Economic Review's assessment of novel myeloma treatments may be the beginning of a systematic process to restrict access to targeted therapies for many other cancers and hard-to-treat diseases. As such, we have identified specific issues with the design and ultimate impact of ICER's upcoming report on new therapies for refractory myeloma that we hope can lead to a productive dialogue between ICER and our organizations. Our specific concerns are summarized below.

1. The Beneficiaries of ICER's Value Benchmarks Will Be Payers and Not Patients

As with other healthcare stakeholders, we are concerned about the rising cost of medical care. However, efforts to limit the utilization of specific medicines based on cost have the potential to harm patients by narrowing available treatment options and impeding physicians' best clinical judgement. The consequences are especially worrisome for patients with multiple myeloma and other similar cancers, where many patients become refractory to existing drugs and continued survival requires making treatment decisions customized to the circumstances of each patient.

2. ICER's Model Does Not Reflect the Reality of Treating Refractory Multiple Myeloma
As documented in the scientific literature, multiple myeloma is a hard-to-treat blood cancer in which relapses are inevitable. Thus, even as novel therapies have extended survival significantly over the last decade, the reality is that each successive regimen results in a briefer, and less dramatic benefit, reflecting acquired drug resistance. Moreover, refractory MM patients often have comorbidities and difficulties in tolerating certain treatments, limiting the choice among therapies.

For these reasons, in October 2015 the International Myeloma Working Group (IMWG) published updated diagnostic criteria laying out certain treatment decisions based on genetic differences and validating the biological rationale for the use of more precise and accurate targeted therapies with novel mechanisms of action that can be sequenced and used in different combinations to help a majority of patients break through the ceiling and duration of response to treatment. Reflecting this new consensus, the Food and Drug Administration has approved 10 myeloma drugs so clinicians can integrate more novel therapies into the treatment armamentarium. Yet, ICER's assessment fails to take IMWG's criteria into account and instead, uses what we consider to be outdated population-wide data to develop "value-based price benchmarks" that will only make it harder for clinicians to sequence and combine regimens individualized to each patient's characteristics. In our view, this runs counter to quality cancer care and subjects patients to cost control rather than offering them the benefit of potentially more effective therapy.

3. ICER's Model Does Not Put Patients at the Center of the Value Equation
When it comes to assessing the "value" of new multiple myeloma drugs, we are concerned that the use of the cost per quality-adjusted life year (QALY) metric will lead to determinations that limit treatment choices for MM patients and their physicians. This is because the QALY is a rigid measure with many known limitations, especially the inability to assess the value of medicines for rare diseases like refractory myeloma where there are many DNA alterations in myeloma cells that frequently differ from patient to patient.

Therefore, the very nature of myeloma requires models that determine value in terms of the health outcomes achieved from a therapeutic regimen, such as increased survival, improved quality of life and fewer costly hospitalizations. When these health improvements were factored into a recent assessment of new myeloma therapies, a 2015 study published in *Health Affairs* showed that although the these agents increased treatment cost by $72,937 between 2004 and 2009, the improvements in outcomes from these drugs were valued at $140,800. Thus, the net cost of health actually decreased by $67,863.

4. Concerns About the Limitations of ICER's Methodology
In reviewing ICER's proposed scope for evaluating different therapies for relapsed and refractory myeloma, we have also identified a number of problems with the study's design that we believe should be addressed:

- ICER's assessment of new MM therapies involves comparing these drugs against one of two older treatments (lenalidomide or bortezomib in combination with dexamethasone) now widely used as first or second line therapies. Yet, the clinical trials for many of these novel agents involve patients who are refractory to both older drugs. As a consequence, ICER's

value determinations will not reflect the different subpopulations of myeloma patients and the sequencing of therapy approaches based on the configuration of the disease.

- While cost-effectiveness can inform decisions about different therapies, relying solely on this analysis to determine what myeloma treatments should be offered to patients is counter to good clinical practice. Not only does the trajectory of myeloma vary from patient to patient but there are well-known problems with cost effectiveness analysis that may led to questionable findings – from the quality of the data analyzed to difficulties in generalizing from clinical trials populations to patients in real world settings.

- ICER's methodology does not take into account individual patient characteristics that clinicians must factor into decisions about MM treatment. This includes the frailty and vulnerability of the patient, the specific adverse event profile associated with each treatment and challenges with transportation when patients are unable to drive or live in rural areas.

- We have become aware that ICER will not include several new MM therapies in its review, which suggests that the organization's simulation models to assess the lifetime cost-effectiveness of the new treatment regimens will be incomplete.

Because ICER's purpose is to influence payers decisions about which myeloma treatments should be available to patients and clinicians, we believe the impact of the upcoming report will limit patients' treatment options, make it more difficult for oncologists to practice quality cancer care and stall the progress made in extending the survival of patients with refractory disease. For these reasons, we strongly encourage ICER to confer with leaders in the myeloma and cancer communities and address existing concerns before finalizing a report and pricing recommendations that could have serious and unintended repercussions for myeloma patients.

We appreciate your consideration of the issues raised in this letter, and look forward to a continued discussion on this important matter.

Sincerely,

Alliance for the Adoption of Innovations in Medicine (Aimed Alliance)
CancerCare
CancerConnect
Community Oncology Alliance
Cutaneous Lymphoma Foundation
E-Race Cancer
MDS Foundation
Myeloma Crowd
National Patient Advocate Foundation
Patients Rising
Patient Services, Inc.