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March 11, 2021

Steven D. Pearson, MD  
President  
Institute for Clinical and Economic Review  
Two Liberty Square, Ninth Floor  
Boston, MA 02109

Re: Institute for Clinical and Economic Review – Anti B-Cell Maturation Antigen CAR T-cell and Antibody Drug Conjugate Therapy for Heavily Pre-Treated Relapsed and Refractory Multiple Myeloma Draft Evidence Report and Voting Questions

Dear Dr. Pearson,

On behalf of the Cancer Support Community (CSC), an international nonprofit organization that provides support, education, and hope to people impacted by cancer, we appreciate the opportunity to respond to the request for comments regarding ICER's draft evidence report and voting questions regarding Anti B-Cell Maturation Antigen CAR T-cell and Antibody Drug Conjugate Therapy for Heavily Pre-Treated Relapsed and Refractory Multiple Myeloma.

I appreciated the opportunity to serve as an expert reviewer on the patient and caregiver perspectives section of the draft evidence report. Feedback included encouraging ICER to more robustly outline the process and methodology for reporting on the patient and caregiver perspectives, particularly in terms of the full breadth of qualitative findings which we believe are vital to ICER's work. We appreciate ICER's additions to this section and look forward to continuing to work with you to improve upon the process of analyzing and fully presenting patient insights.

However, as we have stated in previous letters, we believe this value assessment is premature, particularly as pricing is not yet available for the CAR T-cell therapies. We also strongly believe that ICER reports would be strengthened through additional real world data and ample patient feedback once the therapies are available outside of the clinical trial setting. Additionally, we strongly support ICER's use of real-world data and evidence in value assessments. As ICER noted in the draft 2020 framework document, "randomized controlled clinical trials have their own limitations and are often inadequate to address all questions relevant to assessments of comparative clinical effectiveness." We look forward to working with ICER as such information becomes available in order to revisit and update this report.

### ***Patient Experience***

As a leading patient advocacy organization, we are pleased to see innovative new options for patients living with multiple myeloma, particularly as the disease can cause significant quality of

life, logistical, psychosocial, and financial repercussions for many patients, survivors, and caregivers. As ICER states in this draft evidence report

the mainstays of current MM treatment include immunomodulatory agents (thalidomide, lenalidomide or pomalidomide), proteasome inhibitors (bortezomib, carfilzomib or ixazomib) and anti-CD38 monoclonal antibodies (daratumumab or isatuximab). While numerous combinations of these agents can lead to remission, most patients will relapse. These patients with relapsed or refractory multiple myeloma (RRMM) often cycle through different combinations of agents, which may increase both their clinical and economic burden. When a patient's disease is no longer responsive to agents in each of these three classes of medications, the disease is referred to as "triple-class refractory" MM (TCRMM). TCRMM patients have limited treatment options and limited survival.

We believe that in addition to limited treatment options and limited survival for TCRMM patients, it is vital that ICER take into account the full spectrum of patient experience factors with current multiple myeloma treatment options which we've outlined below.

### ***Health Equity***

As we stated in our open input letter, risk factors for multiple myeloma include being older than 65 years, being male, being of African descent, family history, radiation exposure, workplace exposure, and ancestral background (Smith, Ambs, & Landgren, 2018). Obesity also appears to be a risk factor for the disease (Marinac et al., 2020). Incidence rates of both MGUS and multiple myeloma are greater among patients of African descent, with multiple myeloma rates among patients of African descent about twice those among patients of European descent (Smith, Ambs, & Landgren, 2018). Blacks are also diagnosed at younger ages (Marinac et al., 2020). We would like to reiterate that it is critical to better understand the perspectives of Black and African American multiple myeloma patients and survivors. We support equitable access for *all* patients to the most innovative, effective therapies that can prove lifesaving and/or improve the quality of a patient's life.

### ***Symptom Burden and Side Effects***

Symptoms of multiple myeloma include frequent infections, calcium elevation, bone pain, fracture or damage, fatigue, impaired kidney function and kidney failure, low blood cell count, impaired immune function, anemia, weakness, difficult breathing, weight loss, loss of appetite, headaches, confusion, blurred vision, amyloidosis, and/or hypercalcemia (Mayo Clinic, 2019; International Myeloma Foundation, 2019; Cancer Support Community, 2019; Multiple Myeloma Research Foundation, n.d).

Side effects from current multiple myeloma treatments can include blood clots, peripheral neuropathy, gastrointestinal problems, myelosuppression, diarrhea, deep vein thrombosis, shingles, decreased blood counts, and other symptoms (International Myeloma Foundation, 2019; Multiple Myeloma Research Foundation, n.d). Additional complications include pain from bone destruction, height reduction and body shape changes (Kvam & Waage, 2015). These symptoms can lead to a substantially reduced health related quality of life (HRQoL) (Paul et al.,

2014). According to a recently released study conducted by researchers at CSC and leading expert in the disease:

Patients with MM experience substantive concerns about the physical, emotional, and practical impact of the disease. Symptom burden significantly predicted poorer QoL outcomes, including depression, anxiety, and social satisfaction. Moreover, perceived lack of control over illness was associated with greater anxiety and depression among our national sample of patients with MM. As long-term survival for patients with MM improves, the need to address symptom burden, integrate palliative care, and enhance social and emotional support becomes ever more important (Zaleta et al, 2020).

CSC's Multiple Myeloma Specialty Registry participants were asked about their experiences with the disease and subsequent treatment. We reported these findings in our open input and scoping document comments and reiterate them here:

**Physical Symptoms and Side Effects:** 25% of respondents do not report their side effects to their doctor because they do not believe that anything can be done about their side effects of symptoms, however comfort levels with speaking to their doctor about side effects and symptoms were over 99% positive. When asked how often side effects of treatment affect their decisions about treatment for multiple myeloma, 5% said always, 9% said often, and 28% said sometimes. When asked how well respondents felt that their health care team prepared them to manage side effects, 33% said very much, 26% said quite a bit, and 22% said somewhat.

**Kidney Disease:** 12% of respondents had kidney disease because of their multiple myeloma

**Peripheral Neuropathy:** 24% of respondents experienced peripheral neuropathy in the past 7 days. 13% of respondents said peripheral neuropathy interfered with their lives very much; 8% said quite a bit; and 16% said somewhat. 7% of respondents said that peripheral neuropathy interfered very much with their ability to participate in social activities; 8% said quite a bit; and 14% said somewhat.

**Pain and Bone Pain:** 48% of respondents experienced bone pain in the past 7 days. 19% of respondents experienced pain always; 15% experienced pain often; and 25% experienced it sometimes. 13% of respondents said that it interfered with their lives very much; 10% said quite a bit; and 18% said somewhat. 8% of respondents said that pain interfered very much with their ability to participate in social activities; 11% said quite a bit; and 22% said somewhat.

**Fatigue:** 70% of respondents experienced fatigue in the past 7 days; 20% of respondents experienced fatigue always; 32% experienced it often; and 29% of respondents experienced it sometimes. 16% of respondents said that fatigued interfered with their lives very much; 21% said quite a bit; and 26% said somewhat. 8% of respondents said that fatigue interfered very much with their ability to participate in social activities; 19% said quite a bit; and 25% said somewhat.

**Gastrointestinal Toxicity:** 46% of respondents experienced gastrointestinal toxicity in the past 7 days. 9% of respondents experienced gastrointestinal toxicity always; 18% said often; and 20% said sometimes. 7% of respondents said that gastrointestinal toxicity interfered with their lives very much; 9% said quite a bit, and 15% said somewhat. 2% of respondents said that gastrointestinal toxicity interfered very much with their ability to participate in social activities; 7% said quite a bit; and 12% said somewhat.

**Infection:** 12% of respondents experienced infection in the past 7 days. Since being diagnosed with multiple myeloma, 31% of respondents were diagnosed with 1-2 infections, 6% were

diagnosed with 3-4 infections, and 4% were diagnosed with more than 4 infections. When asked if they were afraid of getting an infection because of their multiple myeloma diagnosis, 10% of respondents said very much, 20% said quite a bit, and 26% said somewhat. **Sleep Disturbance:** 53% of respondents experienced sleep disturbance in the past 7 days. 10% of respondents experienced sleep disturbance always; 25% of respondents experienced it often; and 30% of respondents experienced it sometimes. 2% of respondents said that sleep disturbance interfered very much with their ability to participate in social activities; 8% said quite a bit; and 18% said somewhat. **Steroids:** 11% of respondents experienced elevated pressure in the eyes (glaucoma) as a result of steroid use. 44% of respondents experienced flue retention, causing swelling in the lower legs as a result of steroid use. 46% of respondents experienced mood swings as a result steroid use. 66% of respondents experienced sleep disturbance as a result of steroid use. 51% of respondents experienced weight gain as a result of steroid use. 14% of respondents said that steroids and their side effects always negatively affect their ability to sleep; 25% said often; and 24% said sometimes. **General Psychosocial Impacts:** When asked how often respondents felt that it would sometimes be better if they were not around, 5% said always, 11% said often, and 17% said sometimes. When asked if they were reluctant to ask for help, 43% of respondents said yes. **Mood Swings:** 31% of respondents experienced mood swings in the past 7 days. 12% of respondents experienced mood swings very much; 24% of respondents experienced it often; and 1% of respondents said sometimes. When asked how often side effects of treatment affect their decisions about treatment for multiple myeloma, and 5% said always, 9% said often, and 28% said sometimes. **Concern about Relapse:** Regarding the impact of event scale regarding intrusive thoughts about relapse of multiple myeloma, 27% of respondents had such thoughts. **Financial Concerns:** When respondents were asked if they feel upset about money and the cost of care, 19% said always, 23% said often, and 21% said sometimes. When respondents were asked if they feel overwhelmed by the demands of paying for medical care, 8% said always, 19% said often, and 29% said sometimes. When respondents were asked if they are worried that they won't be able to leave any assets to their family when they are gone, 9% said always, 13% said often, and 22% said sometimes. 63% of respondents had received financial assistance related to their multiple myeloma. 55% of respondents said that a member of their health care team talked to them about resources related to getting financial help or financial counseling. When respondents were asked how helpful financial counseling would be for someone with multiple myeloma, 52% said very much, 29% said quite a bit, and 12% said somewhat. When asked if people in the community had donated money to them, 14% of respondents said yes. **Isolation:** When respondents were asked if they feel that they are alone, 9% said always, 22% said often, and 22% said sometimes. When respondents were asked if they feel that they have brought too much hardship on their family, 14% said always, 31% said often, and 24% said sometimes. **Relationships:** When asked how supportive their family is in respect to their cancer, 60% said very much, 25% said quite a bit, and 9% said somewhat. When asked how supportive their friends are in respect to their cancer, 37% said very much, 28% said quite a bit, and 23% said somewhat. When respondents were asked if they feel that they are not being the best spouse/partner they could be, 4% said always, 19% said often, and 19% said sometimes. When respondents were asked if they feel that they are not being the best parent they could be, 8% said always, 20% said often, and 17% said sometimes. When respondents were asked if they feel that they are not being the best friend they could be, 9% said always, 23% said often, and 25% said sometimes. When respondents were asked if their friends do not understand, 10% said always, 22% said often, and 23% said sometimes. When respondents were asked if their family

do not understand, 7% said always, 22% said often, and 23% said sometimes. When respondents were asked if they are worried that they will be a burden on their family as their disease progresses, 21% said always, 30% said often, and 19% said sometimes. When respondents were asked if they have had limited contact with friends because of their multiple myeloma, 41% said yes. When respondents were asked if they have had limited contact with family members because of their multiple myeloma, 31% said yes. When asked if they feel like they don't have enough close friends or family members, 25% of respondents said yes. When asked if they have fewer people they can rely on before cancer, 27% said yes. **Work:** When respondents were asked if they were upset because they fall behind at work and others have to fill in, 4% said always, 9% said often, and 15% said sometimes. When respondents were asked if they have forgone a job opportunity or career advancement because of multiple myeloma, 40% said yes. **Treatment Decision Making:** When respondents were asked if they feel they had a choice about where to receive medical treatment for multiple myeloma, 82% said yes. When respondents were asked how much of an impact the distance from home had on deciding where to seek medical treatment, 20% said very much, 17% said quite a bit, and 16% said somewhat. When respondents were asked how much of an impact had insurance coverage or cost had on deciding where to seek medical treatment, 33% said very much, 17% said quite a bit, and 12% said somewhat. When respondents were asked how much of an impact the sense of trust or familiarity with the doctor or the practice had on deciding where to seek medical treatment, 39% said very much, 22% said quite a bit, and 12% said somewhat. When respondents were asked how much of an impact the experience of specialization of the physician had on deciding where to seek medical treatment, 55% said very much, 24% said quite a bit, and 5% said somewhat. When respondents were asked how much of an impact access to clinical trials had on deciding where to seek medical treatment, 17% said very much, 8% said quite a bit, and 16% said somewhat.

Recent research from CSC also shows that, among patients with multiple myeloma, poorer physical function and greater symptom burden are associated with worse depression, anxiety, and social satisfaction (Zaleta et al., 2020), underscoring the critical connection between patients' experience of burden and their quality of life.

We appreciate the opportunity to provide these comments and would be pleased to continue to serve as a resource to your work. I can be reached at [efranklin@cancersupportcommunity.org](mailto:efranklin@cancersupportcommunity.org).

Sincerely,



Elizabeth F. Franklin, PhD, MSW  
President  
Cancer Support Community Headquarters

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