Anti B-Cell Maturation Antigen CAR T-cell and Antibody Drug Conjugate Therapy for Heavily Pre-Treated Relapsed and Refractory Multiple Myeloma: Final Policy Recommendations

May 11, 2021

Policy Recommendations

Introduction

The following policy recommendations reflect the main themes and points made during the Policy Roundtable discussion at the April 16, 2021 Midwest CEPAC public meeting on the use of anti-BCMA therapies for the treatment of heavily pre-treated multiple myeloma. At the meeting, ICER presented the findings of its revised report on these treatments and the Midwest CEPAC voting council deliberated on key questions related to their comparative clinical effectiveness, potential other benefits and contextual considerations, and long-term value for money at current prices. Following the votes, ICER convened a Policy Roundtable of two patients, two clinical experts, two payers, and one representative from a pharmaceutical manufacturer to discuss how best to apply the evidence and votes to real-world practice and policy. The discussion reflected multiple perspectives and opinions, and therefore, none of the statements below should be taken as a consensus view held by all participants.

A recording of the conversation can be accessed here, and a recording of the voting portion of the meeting can be accessed here. More information on Policy Roundtable participants, including conflict of interest disclosures, can be found in the appendix of this document. ICER's report on these treatments, which includes the same policy recommendations, can be found here.

The roundtable discussion was facilitated by Dr. Steven Pearson, MD, MSc, President of ICER. The main themes and recommendations from the discussion are organized by audience and summarized below.

All Stakeholders

All stakeholders have a responsibility and an important role to play in ensuring that effective new treatment options for patients with multiple myeloma are introduced in a way that will help reduce health inequities.

African Americans are at a higher risk of developing multiple myeloma. Unfortunately, these individuals are also at a higher risk of not receiving adequate education about their condition, face a longer time between diagnosis to initiation of any therapy, are often late to receive guidance regarding new treatment options, and may have trouble accessing highly specialized therapies such as those that are the focus of this review. All stakeholders should accept and act upon their responsibility to address these disparities.

- Manufacturers should engage with a variety of people from diverse communities to help inform the design and implementation of clinical trials, ensure that patients enrolled in pivotal trials are fully representative of people of color and those from less advantaged backgrounds. Relying solely on patient organizations and representatives already engaged in ASH and ASCO meetings may provide a skewed view of the diversity of patient perspectives. Active and broad outreach should be conducted to historically underserved patient populations. In addition, manufacturers should moderate new treatment pricing. Even with insurance coverage, cost is a tremendous driver of health inequities; thus, pricing that exceeds reasonable proportions to the added clinical and contextual benefits for patients will likely exacerbate health inequities, while pricing that is viewed as responsible may provide opportunities for improved access to patients facing financial barriers to care.

- Payers should recognize that, in addition to often steep out-of-pocket costs for the treatments themselves, there are often ancillary costs which can become real barriers to care and exacerbate inequities. Specifically, these treatments may require travel to specialized centers, with the attendant travel costs and lost wages for accompanying caregivers. Payers should develop coverage that creates a broader package of benefits so that patients who face financial or logistical hurdles can have equal access to specialized care at Centers of Excellence, if desired. Another way to accomplish this goal is by expanding telemedicine coverage and creating parity (e.g., in out-of-pocket costs) between in-person and remote care, which can help patients receive care in their own communities while receiving input and second opinions from leading experts in other locations. Through one or multiple mechanisms, patients from rural and inner-city neighborhoods need broader benefit designs to give them the equal access they deserve.

- Clinicians and clinical societies should conduct (or continue to conduct) active outreach and education to underserved communities and the general oncologists and other members of the health care team serving those communities to get new, effective treatments to those patients who would benefit most. Given the difficult trade-off decisions necessary in the choices for multiple myeloma treatment, clinicians should actively engage in and encourage shared decision-making to ensure that the values of patients with diverse needs and perspectives on risks and benefits of different treatments are at the heart of all treatment decisions.

- Patient organizations for people with multiple myeloma should seek (or continue to seek) to represent diverse perspectives, requiring outreach to patients who may not be engaged by academic health systems, manufacturers, payers, policymakers, or other stakeholders. Patient groups should collaborate with organizations and people in diverse communities to build lasting relationships and trust. Patient organizations should also embrace their responsibility to address the impact of pricing of new treatment options on the ability of

patients to access care. The patient voice should always be present as society wrestles with how to find the difficult balance between incentives for innovation and affordability.

- We propose that these principles and individual considerations, explored throughout the ICER public meeting, should be the focus of a more comprehensive Multiple Myeloma Therapy Access Summit. With all stakeholders at the table, this Summit would develop these goals and specific actions further and forge them into a coordinated action plan for improvement. One element of such a plan should be transparent targets for improvement by which manufacturers, payers, clinical specialty groups, and patient advocacy groups would hold themselves and each other accountable in addressing the substantial inequities that our current health care system – and society – have allowed to persist.

Manufacturers

Manufacturers should seek to set prices that will foster affordability and good access for all patients by aligning prices with the patient-centered therapeutic value of their treatments. In the setting of these new interventions for multiple myeloma, while there is considerable hope associated with the promise of the therapies, there also remains substantial uncertainty regarding their longer-term safety and effectiveness, and the platform on which they are based has been funded in part with taxpayer money. Manufacturer pricing should also reflect these considerations in moderating launch pricing.

Drug prices that are set well beyond the cost-effective range cause not only financial toxicity for patients and families using the treatments, but also contribute to general health care cost growth that pushes families out of the insurance pool, and that causes others to ration their own care in ways that can be harmful.

Manufacturers should therefore price novel treatments in accordance with the demonstrated benefits to patients. In settings of substantial uncertainty, initial pricing should err on the side of being more affordable. This would allow more patients access, generating additional data on the real-world effectiveness of novel treatments that could be used in future assessment updates. With accumulation of evidence of substantial patient benefit, manufacturers should be allowed to increase pricing in accordance with benefit.

The initial developmental science underpinning anti-BCMA chimeric antigen receptor T-cells was conducted at the National Cancer Institute. Manufacturers should propose lower prices, particularly for public payers, in situations when a substantial part of the initial risk of drug development is borne by taxpayers.

Clinical Specialty Societies

Clinical specialty societies should advance education, policy, and practice mechanisms that facilitate awareness of treatment costs and financial burdens for patients as part of shared decision-making for individual patients.

Given the huge impact of treatment costs on both society and patients, clinicians should be aware of the costs of the treatment options they are recommending to patients and develop the tools to incorporate patients' own financial considerations into transparent shared decision-making. As a general principle, when efficacy is similar between two treatment options, and patient preferences for different side effect profiles has been fully discussed, clinicians should recommend the less expensive option.

Payers

Payers should use the FDA label as the guide to coverage policy and engage clinical experts and diverse patient representatives in considering how to address coverage issues for which there is limited or no evidence at the current time.

Given the significant uncertainty that remains about anti-BCMA therapy, it is reasonable for payers to use prior authorization as a component of coverage. Prior authorization criteria should be based on the FDA label, clinical evidence, specialty society guidelines, and input from clinical experts and patient groups. The process for authorization should be clear and efficient for providers and patients. Options for specific elements of coverage criteria within insurance coverage policy are discussed below.

Coverage Criteria: General

- Payers should offer alternatives to prior authorization protocols such as programs that give feedback on prescribing patterns to clinicians or exempt them from prior authorization requirements ("gold carding") if they demonstrate high fidelity to evidence-based prescribing. Patients should be provided information on the incentives and guidelines that clinicians consider when recommending a course of treatment.

- Payers should document at least once annually that clinical eligibility criteria are based on high quality, up-to-date evidence, with input from clinicians with experience in the same or similar clinical specialty.

- Clinical eligibility criteria should be developed with explicit mechanisms that require payer staff to document using an open and transparent process that is readily accessible to the public that they have:

    - Considered limitations of evidence due to systemic under-representation of minority populations and sought input from clinical experts on whether there are distinctive benefits and harms of treatment that may arise for biological, cultural, or social reasons across different communities;

    - Confirmed that clinical eligibility criteria have not gone beyond reasonable use of clinical trial inclusion/exclusion criteria to interpret or narrow the FDA label language in a way that disadvantages patients with underlying disabilities unrelated to the condition being treated.

Drug-Specific Considerations: belantamab

FDA Label: Adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent.

Coverage Criteria:

- **Diagnosis:** Per clinician attestation

- **Patient Eligibility Criteria:** As per the FDA label, with no need for definition of clinical terms. Key inclusion criteria in pivotal trials included ECOG status of 0-2, and ineligibility for autologous stem cell transplantation or transplantation > 100 days prior. Clinical experts did not feel these criteria were needed for inclusion in coverage language in order to prevent inappropriate use.

- **Step Therapy:** Besides the FDA label clinical requirements, there is no other treatment that could be considered a first-step treatment prior to eligibility for belantamab.

- **Exclusion Criteria:** Pivotal trials excluded patients with prior BCMA therapies or those who are on systemic high-dose corticosteroids, and those who have received allogeneic SCT. There is no evidence on the use of belantamab in patients who have had inadequate response or have recurrence following CAR-T treatment. Many payers are likely to restrict coverage pending clinical research on the risks and benefits of retreatment with anti-BCMA therapies.

- **Duration of Therapy and Renewal of Coverage:** N/A

- **Provider Criteria:** The therapy should be prescribed by an oncologist.

Drug-Specific Considerations: CAR-T (ide-cel)

FDA Label: Adult patients with relapsed or refractory multiple myeloma after 4 or more prior lines of therapy, including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent.

Coverage Criteria:

- **Diagnosis:** Per clinician attestation
- **Patient Eligibility Criteria:** As per the FDA label, with no need for definition of clinical terms. Key inclusion criteria in pivotal trials included ECOG status of 0-1. Clinical experts did not feel these criteria were needed for inclusion in coverage language in order to prevent inappropriate use.
- **Step Therapy:** Besides the FDA label clinical requirements, there is no other relevant treatment that could be considered a first-step treatment requirement prior to eligibility for CAR-T. The risks and benefits of belantamab are so different from those of CAR-T that it does not meet criteria for reasonable consideration of step therapy.
- **Exclusion Criteria:** Pivotal trials excluded patients who have received allogeneic SCT. There is no evidence on the use of CAR-T in patients who have had inadequate response or have recurrence following an anti-BCMA therapy such as belantamab. Many payers are likely to restrict coverage pending clinical research on the risks and benefits of retreatment with anti-BCMA therapies. Similarly, until further evidence is developed, payers are likely to restrict coverage to repeat CAR-T, whether a second round with the same CAR-T or a trial of a different CAR-T. Clinical experts suggested, however, that requests for consideration of repeat CAR-T are likely and will require case-by-case consideration.
- **Duration of Therapy and Renewal of Coverage:** N/A
- **Provider Criteria:** The therapy should be prescribed by an oncologist.

Medicare should consider new reimbursement strategies, including enhanced new technology add-on payments or demonstration projects that carve out pricing and payment for cell and gene therapy, to improve the chances that hospitals and clinics can provide the necessary services to deliver these novel therapies to patients safely.

The early experience with CAR-T for lymphoma demonstrated the inefficiency of the existing Medicare payment structures for novel one-time therapies with high costs. Hospitals struggled to provide CAR-T without adequate reimbursement, leading to barriers to access for many patients. Medicare should consider changes to its reimbursement system to avoid such bottlenecks in the future. Approaches that should be considered include:

a. Increasing the new technology add-on payment to 80%
b. Consider a new demonstration project where cell and gene therapies are carved out, allowing CMS to buy directly from manufacturers and negotiate a value-based payment that includes outcomes-based measures.

Clinical Research Community

The clinical research community should move rapidly to address key gaps in evidence for treatments for multiple myeloma. These gaps include whether patients can stop therapy while in response, how well the clinical trial populations reflect the target populations for treatment, data on preferences and patient-reported outcomes in historically disadvantaged populations, and the clinical characteristics of the disease and its affected populations that may be predictive of response.

Numerous important research questions remain regarding treatment options for multiple myeloma. First, nearly all studies conducted to date focus on continuing treatment until progression. Thus, it is unclear whether patients can safely stop therapy. Since therapies often expose patients to side effects and impose substantial financial costs, non-inferiority studies comparing a fixed duration of treatment to indefinite treatment until progression should be conducted. Since these studies will provide the evidence base for less drug use, manufacturers will not support these studies and public funding through entities such as the NIH will be necessary.

Second, the FDA should work with manufacturers to ensure that the studied population for any disease is representative of the population with disease. For example, the anti-BCMA studies were conducted in populations that were substantially younger and which included fewer African Americans than the US population of multiple myeloma patients, injecting additional uncertainty on whether the benefits seen in the studies will be replicated when these therapies are used in clinical practice.

Third, additional research needs to be conducted regarding patient preferences and patient-reported outcomes in African American and other historically disadvantaged populations, to better

inform accurate characterization of the impact of multiple myeloma in these groups and the potential benefits of new treatments.

Finally, additional research is needed to determine which patient characteristics predict response, so that these costly, high side effect therapies can ideally be targeted to those patients most likely to benefit.

Appendix

Appendix Tables 1 through 3 contain conflict of interest (COI) disclosures for all participants at the April 16, 2021 Public meeting of the Midwest CEPAC.

Table 1. ICER Staff and Consultants and COI Disclosures

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*No relevant conflicts of interest to disclose, defined as more than $10,000 in healthcare company stock or more than $5,000 in honoraria or consultancies during the previous year from health care manufacturers or insurers.

Table 2. Midwest CEPAC Panel Member Participants and COI Disclosures

Participating Members of Midwest CEPAC	
Alan Balch, PhD* Chief Executive Officer, Patient Advocate Foundation, National Patient Advocate Foundation	**Elbert Huang, MD, MPH, FACP*** Professor of Medicine, Director, Center for Chronic Disease Research and Policy, University of Chicago Associate Director of the Chicago Center for Diabetes Translation Research, University of Chicago
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*No relevant conflicts of interest to disclose, defined as more than $10,000 in healthcare company stock or more than $5,000 in honoraria or consultancies during the previous year from health care manufacturers or insurers.

Table 3. Policy Roundtable Participants and COI Disclosures

Policy Roundtable Member	Conflicts of Interest
Tom Bellfort, Patient Expert	No conflicts to disclose.
Harold Carter, PharmD, Vice President, Pharma Contracting, Strategy & Wholesale Markets, Express Scripts	Harold Carter is a full-time employee of Express Scripts.
Anita D'Souza, MD, MS, Associate Professor of Medicine, Medical College of Wisconsin	Anita D'Souza has received institutional research funding from Sanofi, TeneoBio, Takeda, and Caelum. D'Souza reports advisory board roles with Akcea, Imbrium Therapeutics and Pfizer and received consulting honoraria from Janssen.
Ira Gupta, MD, Vice President & Medicine Development Leader, GlaxoSmithKline R&D, Oncology	Ira Gupta is a full-time employee of GSK.
David Mitchell, Patient Expert Founder, Patients For Affordable Drugs	David Mitchell is on the Board of Directors of Friends of Cancer Research which receives grants from BMS, Bluebird Bio, and Janssen. He received honoraria from the FDA for his service on the Oncologic Drugs Advisory Committee and was part of a class action suit against Celgene to which he received a service award.
S. Vincent Rajkumar, MD, Edward W. and Betty Knight Scripps Professor of Medicine, Mayo Clinic, Rochester, MN	S. Vincent Rajkumar has held a position as a member of the Board of Directors for the International Myeloma Foundation.
Melissa Pozotrigo, PharmD, BCOP Senior Clinical Oncology Pharmacist, Oncology Analytics Inc.	Melissa Pozotrigo is a full-time employee of Oncology Analytics.