Advancing Transfusion and Cellular Therapies Worldwide

March 15, 2019

Tamara Syrek Jensen
Director, Coverage and Analysis Group
Center for Clinical Standards and Quality
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Proposed Decision Memo for Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers (CAG-00451N)

Dear Ms. Jensen:

AABB appreciates the opportunity to submit comments in response to the Proposed Decision Memo for Chimeric Antigen Receptor (CAR) T-Cell Therapy for Cancers. AABB is an international, not-for-profit association representing individuals and institutions involved in the field of transfusion medicine and cellular therapies. The association is committed to improving health through the development and delivery of standards, accreditation and educational programs that focus on optimizing patient and donor care and safety. AABB individual membership includes physicians, nurses, scientists, researchers, administrators, medical technologists and other health care providers.

AABB values that the Food and Drug Administration (FDA) recently approved two CAR T-cell therapies and recognizes that other cellular therapies, including additional CAR T-cell products, are in development. We appreciate the clinical significance of these new therapies, as well as the challenges they present related to reimbursement. We believe it is imperative for the Centers for Medicare & Medicaid Services (CMS) to ensure that Medicare coverage and reimbursement policies do not restrict beneficiaries' access to these life-saving therapies. AABB believes that a national coverage determination (NCD) is premature and has the potential to negatively impact patients' access to important, innovative therapies. Thus, we recommend that CMS refrain from implementing an NCD for CAR T-cell therapies at this time.

If CMS decides to move forward with an NCD, we encourage the agency to: (1) adopt flexible language that can accommodate new technologies and which does not restrict patients' access to appropriate treatment options; (2) recognize and pay for all the services that must be provided throughout the CAR T-cell treatment protocol; and (3) permit standards-setting and accreditation organizations, including AABB, to continue to ensure the safety and quality of these therapies. In addition, we recommend that CMS replace the reference to the July 2016 *Circular of Information for the Use of Cellular Therapy Products* with the updated *Circular of Information for the Use of Cellular Products*, which was released in October 2018.

Finally, if CMS decides to move forward with an NCD, we encourage the Agency to specify that the Center for International Bone and Marrow Transplant Research (CIBMTR) is the registry referenced in the NCD. CIBMTR already collects outcomes and post-market surveillance data for several organizations and has a registry set up for this type of information. In addition, CIBMTR has experience with CEDs and data collection studies that it does with CMS and other agencies.

AABB urges CMS to adopt flexible language that provides Medicare beneficiaries with access to novel immune effector cell therapies and medically necessary treatments.

AABB believes that CMS' proposed decision to cover "autologous treatment with T-cells expressing at least one chimeric antigen receptor (CAR) through coverage with evidence development (CED)" when certain criteria are satisfied is far too restrictive and may unnecessarily restrict Medicare beneficiaries' access to available treatment options. For instance, AABB encourages CMS to broaden the coverage language from "autologous treatment" to "FDA approved treatments" since this is a rapidly evolving field and the broader language increases the likelihood that the NCD will apply to future products without needing to be reopened. We are concerned that the proposed decision memo will not allow for repeat CAR T-cell therapy if a patient's cancer recurs. In addition, the proposed decision memo limits coverage for CAR T-cell therapies to patients with relapsed or refractory cancer. While these eligibility criteria are aligned with the FDA-approved labels for the currently approved CAR T-cell therapies, FDA may approve CAR T-cell therapies for different indications in the future. Thus, we encourage CMS to broaden the eligibility criteria in the NCD by generally providing coverage that is consistent with the requirements in an FDA-approved label. Similarly, we believe CMS should consider using a data collection requirement that is consistent with an FDA post-approval study, rather than CED requirements. We believe that broader eligibility criteria that is consistent with FDA approval and post-approval studies will encourage innovation and expedite patients' access to novel therapies.

In addition, AABB encourages CMS to consider broadening the language in the NCD by referencing "CAR T and related immune effector cell therapies" rather than CAR T-cell therapies. This alternative language would enable the NCD to cover other novel cell-based therapies that are not derived from T-cells, such as newer products from Natural Killer (NK) Cells. We are concerned that if the narrow language in the draft proposed decision memo is finalized, CMS will need to reopen the NCD each time a new CAR T and related immune effector cell therapy becomes available.

AABB questions whether CMS' decision to cover CAR T-cell therapy through CED has the potential to limit beneficiaries' access to care. The CED process is historically slow and takes years to result in coverage or non-coverage decisions. Additionally, if Medicare covers CAR T-cell therapies through a CED with patient reported outcomes, it is possible that some providers may "opt out" of furnishing these treatments, which will restrict patients' access to care. In addition, we understand that including patient reported outcomes as part of a registry is quite burdensome. While patients must provide clinical data, patients are not required to report data and it is difficult to collect the required data after a patient leaves a provider.

AABB urges CMS to clarify that there must be appropriate coverage and reimbursement for all items and services required throughout a CAR T and related immune effector cell therapy treatment protocol.

We commend CMS for recognizing that CAR T-cell treatment protocols involve several essential steps, which the Agency summarizes as:

> (1) lymphocyte harvesting from the patient with cancer;
> (2) creation of cancer-targeting lymphocytes in vitro using various immune modulators;
> (3) selection of lymphocytes with reactivity to cancer antigens using enzyme-linked immune-assay;
> (4) depletion of the patient's remaining lymphocytes using immunosuppressive agents; and
> (5) transfusion of the cancer-targeting lymphocytes back into the patient with cancer-this transfusion represents one treatment.

Thus, CMS acknowledges that CAR T-cell therapies involve separate and distinct processes outside of the in vitro cell manipulations. Importantly, each of these five steps are labor intensive, requiring the expertise of physicians and other health care professionals, oversight and monitoring. In addition to these steps, monitoring for and treatment of therapy related complications, such as cytokine release syndrome and neurotoxicity, are important aspects of CAR T-cell therapy protocols. We urge CMS to recognize that appropriate coverage and reimbursement is necessary for all items and services furnished throughout the continuum of CAR T and related immune effector cell therapy treatments.

AABB encourages CMS to recognize AABB and other qualified standards and accreditation programs in the NCD.

The draft proposed decision memo recognizes a single accreditation program, which is overly restrictive and may provide one accreditor with a competitive advantage. AABB recommends that CMS specifically recognize in the NCD multiple qualified cellular therapy standards programs, including AABB's Standards for Cellular Therapy Services (CT Standards). The CT Standards are written in a way to allow accredited facilities to be nimble in their ability to add new products and protocols, including the manufacture and provision of CAR T and related immune effector cell therapy treatments. AABB's CT Standards include all elements of product manufacture, including collection, storage, transport, testing and processing of these products. In addition, the CT Standards contain requirements that focus on the clinical care of the recipient, including cytokine release syndrome, most commonly associated with the infusion of CAR T-cells and potentially, other immune effector cell therapies in the future. Therefore, whether a facility collects these products for further manufacture at another facility or engages in the complete manufacturing process, the CT Standards address important requirements for product quality and patient safety from donor evaluation to product manufacture, infusion and follow up.

Notably, AABB and other standards setting organizations ensure that good manufacturing practices safeguard the quality of CAR T and related immune effector cell therapies. Without a robust laboratory accreditation program, the quality of a CAR T or a related immune effector cell therapy may be compromised due to low product yields, contamination, and logistical and quality mishaps in handling and processing the cells. Not all CAR T or related immune effector cell therapies will be collected, manufactured and infused at a single facility with a Cellular Therapy Program. Rather, it is possible that the collection, manufacture and infusion of CAR T or related immune effector cell therapies will occur at up to three different facilities. In fact, the two currently approved CAR T-cell products are not manufactured in a Cellular Therapy Program. We encourage CMS to adopt a flexible policy that enables qualified facilities to be able to collect, manufacture **or** administer CAR T and related immune effector cell therapies.

CMS and the State of California have given deemed status to the AABB Accreditation Program for Cellular Therapies, which is based on the CT Standards. In addition, the Health Resources and Services Administration (HRSA) and the National Marrow Donor Program recognize the AABB Accreditation Program for Cellular Therapies as well as the Foundation for the Accreditation of Cellular Therapy (FACT) accreditation. The AABB Accreditation program is accredited by the International Society for Quality in Healthcare (ISQua). AABB is proud of its stellar record as a deemed accreditation organization. We urge CMS to ensure that any policies related to cellular therapies, including CAR T and related immune effector cell therapies, continue to support AABB's important role in ensuring product quality and patient safety throughout the treatment protocols.

* * * *

Thank you for the opportunity to provide feedback related to the proposed decision memo for CAR T-cell therapy for cancers. If you have any questions or need additional information, please contact Leah Stone, Senior Director, Public Policy and Strategic Partnerships, at lmstone@aabb.org or 301-215-6554.

Sincerely,

Debra BenAvram
Chief Executive Officer
AABB