March 15, 2019

Submitted electronically to: http://www.cms.gov/

The Honorable Seema Verma, Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CAG-00451N
P.O. Box 8013
Baltimore, MD 21244-8013

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

Dear Administrator Verma:

On behalf of the Board of Directors of the Community Oncology Alliance (COA), we are submitting this comment letter regarding the Proposed Decision Memo for Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers (CAG-00451N) (the “Coverage Determination”).

As you know, COA is an organization that is dedicated to advocating for the complex care and access needs of patients with cancer and the community oncology practices that serve them. COA is the only non-profit organization in the United States dedicated solely to independent community oncology practices, which serve the majority of Americans receiving treatment for cancer. COA’s mission is to ensure that patients with cancer receive quality, affordable, and accessible cancer care in their own communities where they live and work. For more than 16 years, COA has built a national grassroots network of community oncology practices to advocate for public policies to support patients with cancer.

We appreciate the decision of the Centers for Medicare & Medicaid Services (“CMS”) to issue a proposed National Coverage Determination (“NCD”) for CAR T-cell therapy (“CAR-T”), a highly innovative and promising treatment option for patients with cancer. Providing coverage is an important step to ensuring Medicare patients have access to this treatment when recommended by their oncologist. The proposed coverage with evidence development (“CED”) will help ensure the collection of important evidence that will be crucial in determining the effectiveness and full potential of various CAR-T treatments. This will be especially important when determining future coverage and reimbursement as this emerging technology continues to evolve.

However, while we are pleased that CMS is moving in the direction of covering CAR-T therapies, we have significant concerns regarding the specific language in the proposed decision memo (“PDM”). We are concerned that the agency’s draft coverage determination is not flexible enough to accommodate advances in this rapidly developing field, recognize the progress made towards decreasing toxicity, account for ongoing research on new indications and earlier lines, and adapt existing frameworks to deliver the promise of innovation to patients in the most robust way. Our concerns are summarized as follows:
• CMS should not limit CAR-T site of care appropriateness strictly to hospitals
• Limiting patient eligibility to patients with relapsed or refractory cancer may preclude future CAR-T therapies with different indications from coverage
• CAR-T treatment is just emerging, and the NCD should not prevent CMS’ flexibility regarding future CAR-T therapies
• The draft language on off-label coverage sets a negative precedent for oncology
• While data collection around CAR-T treatment is vital, the evidence development requirements detailed in the NCD are overly onerous

Our detailed comments on the NCD follow. COA requests the opportunity to meet with the appropriate CMS staff to discuss our comments in detail and to educate staff on the complex cancer care provided by community oncology practices, especially those utilizing CAR-T therapy and/or currently participating in CAR-T clinical trials.

Detailed Comments on the NCD

CMS Should Not Limit CAR-T Site of Care Appropriateness Strictly to Hospitals

We are very alarmed by the proposal reiterated throughout the NCD to limit CAR-T therapy coverage to the hospital setting, or more specifically to a subset of hospitals electing to participate in the CED study mechanism. Limiting coverage to the hospital setting will exclude other viable settings of care and limit patients’ options when trying to locate a provider. We urge CMS to revise the language in the PDM to allow for any well-staffed and experienced sites that are able to meet the quality, safety, and operational prerequisites for delivery of CAR-T treatment to be able to participate. CAR-T should be covered in any setting equipped with important core capabilities as appropriate to the patient characteristics and the product utilized.

While Initially Focused Exclusively on Inpatient Care, CAR-T Treatment Has Been Slowly Moving to the Outpatient Setting

In the draft NCD, CMS appears focused on the fact that initial clinical studies were limited to inpatient hospital sites, but in the case of Kymriah approximately 26% of adult patients in trials were infused in the outpatient setting. In addition, one study from Juno Therapeutics showed decreased resource utilization for patients receiving CAR-T infusion in the outpatient setting, including a 40% decrease in their number of hospital days.

A major focus of ongoing research is on improving the safety of cellular therapies and reducing toxicities, so CAR-T treatment is carefully and slowly transitioning to the outpatient setting. Some CAR-T preparations have been reported with little or no cytokine release syndrome or neurotoxicity, including for cases of glioblastoma and pancreatic cancer. There are many non-hospital specialized cancer centers with the qualifications and experience to administer CAR-T treatment, and these settings of care must be included in the NCD.

Many Community Oncology Practices Have the Experience and Capabilities to Administer CAR-T

COA and our members share in CMS’ goal to ensure patient safety and we understand and agree that safety is of paramount importance when making decisions around site-of-care eligibility. We note that similar concerns and guardrails have been previously debated with other complex treatments and high-risk procedures.

That said, it is important to understand that there are state-of-the-art community oncology practices that have significant experience and capabilities in administering highly complex treatments. For example, stem cell transplants, which are similar in complexity to CAR-T therapy, are performed successfully in the community oncology practice setting. Such procedures often require the same infrastructure that CAR-T requires, with a designated care area that protects patients from transmission of infectious agents and allows for appropriate evaluation and treatment. In cases, community oncology practices conduct these complex procedures on their own. In other cases, they do so in partnership with hospitals. For those practices that would need to partner with hospitals to administer CAR-T therapy, those relationships and capabilities are already in place.

Another example of community oncology practices’ experience with treatments similar in complexity to CAR-T is bispecific antibodies (“BITEs”), which have similar potential toxicity profiles as CAR-T. BITEs are typically administered in the outpatient setting and are already being administered in community, nonacademic settings of care in both hematologic malignancies and solid tumors. There are at least four studies in hematologic malignancies and five in solid tumors.

With this reality, the Cell Therapy Program requirements detailed in the NCD are well within the scope and experience of many community oncology practices. Basic requirements to administer CAR-T therapy, including apheresis, cell processing and infusion, and lymphodepleting chemotherapy, as well as toxicity management, are activities frequently performed in the outpatient setting. As for organizational capabilities to run such a program, community oncology practices have experience with requirements such as REMS programs, distance policies, CAR-T specific nursing support and patient education, registry reporting, and more.

It is extremely important to understand that some community oncology practices already have or are currently participating in studies on CAR-T, as well as T-cell receptor and antibody-coupled T-cell receptor, which are different technologies than CAR-T but that are also considered immune effector cell therapies. As an example, one of our member practices has already participated or is currently participating in 15 such trials for hematologic malignancies and eight for solid tumors. Practices’ direct experience conducting scientific research in CAR-T and related treatment areas demonstrates their ability, in many cases, to meet and exceed the research and evidence generation requirements outlined in the proposed NCD.

We certainly acknowledge that CAR-T administration requires a high level of expertise and infrastructure that not all settings of care possess. However, hospitals are not the only settings of care that meet the necessary qualifications, and CAR-T coverage must encompass those qualified non-hospital settings. We can assure you that community oncologists certainly will take the proper precautions needed to administer CAR-T therapy and will only provide this care after having put in place the appropriate safeguards and requirements. We welcome the opportunity to help CMS develop the appropriate criteria that ensure safety and efficacy while also expanding access to CAR-T therapy. Based on our practices’ collective expertise and experience, we are confident we can offer valuable insights.
Covering CAR-T Therapy in Community Clinic Settings Would Benefit Patients and Medicare

As numerous studies have already confirmed, community oncology practices are also less expensive settings of care for both Medicare and beneficiaries. Studies on cancer treatment show that the cost of care and the rate of emergency department utilization are lower for patients in the community setting than those in hospital outpatient departments. Providing coverage in appropriate non-hospital settings will save patients with cancer and Medicare money.

COA’s members are not only skilled at advanced research and high-quality cancer care, but they are also innovators in the area of payment and delivery reform. To that end, many community oncology practices are highly focused on value-based care, including reducing preventable hospitalizations and have a proven commitment to improving outcomes, enhancing quality, and lowering costs.

Limiting Patient Eligibility to Patients with Relapsed or Refractory Cancer May Preclude Future CAR-T Therapies with Different Indications from Coverage

We are concerned by the fact that the proposed NCD would restrict CAR-T therapy coverage to patients who have “relapsed or refractory cancer.” While this limited patient eligibility may make sense in the context of the current FDA-approved CAR-T therapies, it does not encompass the full universe of future CAR-T therapies, some of which may become indicated for patients in earlier disease stages.

In fact, there are already studies accruing in the non-refractory setting in both lymphoma and myeloma (KTE-C19-107 or Zuma-7, and BB2121-MM-003 or KarMMa-3, respectively). Furthermore, there is a study accruing using CAR-T as consolidation in front-line treatment of multiple myeloma patients at higher risk of relapse post-transplant (BB2121-MM-002 or KarMMa-2). If early signals are positive, there are plans for large randomized studies in the front-line settings as well. As it is written, the proposed NCD would not include coverage for patient populations and FDA indications for earlier stages of cancer.

We are also concerned that CMS does not define “relapse or refractory cancer” in the NCD. The absence of a definition may cause hesitancy among oncologists to prescribe CAR-T therapies out of concern that they are not sure of the requirements for a patient’s cancer to qualify as “relapse or recovery.”

To avoid the patient access issues caused by limiting coverage to patients with relapse or refractory cancer, we urge CMS to broaden the NCD to provide coverage of CAR-T therapies for approved indications in accordance with the FDA label, rather than limiting to relapsed or refractory cancer. This will create flexibility to cover future CAR-T therapies with different indications, reducing potential access barriers and provider prescribing concerns in the future.

CAR-T Treatment is Emerging, and the NCD Should Not Prevent CMS’ Flexibility Regarding Future CAR-T Therapies

While CAR-T treatment is innovative and offers significant potential for patients with cancer, it is a new, emerging technology with only two FDA-approved products to date. Future CAR-T therapies will vary from the products approved today, potentially with different indications for more types of cancer and/or patients.

Given the long timeline and significant agency resources required for a potential NCD reconsideration process, it is important that a final NCD not limit CMS’ future coverage flexibility as new CAR-T therapies are approved by the FDA. Maintaining flexibility will ensure that this NCD does not create a barrier between future products and the patients who need them.

It is also important to prevent the NCD from creating barriers for patients because they will face an NCD appeal process that is more complex than the Medicare claims appeal process. It requires that a Medicare beneficiary in need of coverage denied based on an applicable NCD directly initiate a review by filing a written complaint with the Department of Health and Human Services Appeals Board. This process will be very burdensome for sick patients with cancer seeking CAR-T treatment and should be avoided. **Ensuring flexibility in the NCD now will help prevent this situation.**

**The Draft Language on Off-Label Coverage Establishes a Negative Precedent for Cancer Treatment**

The proposed NCD states that off-label use of CAR-T treatment will only be permitted when indicated for use in the National Comprehensive Cancer Network (“NCCN”) Drugs & Biologics Compendium with a grade of 2 or 1, and that the patient must be enrolled in a CMS-approved clinical trial and followed for at least two years to access off-label uses. While we understand it is very important to ensure that there is no inappropriate off-label use of CAR-T therapy, we are very concerned that the additional requirements envisioned in the PDM would represent a departure from CMS’ prior treatment of permissible off-label use of oncology drugs.

CMS has had a long-standing policy of providing flexible coverage of anti-cancer therapies that defer to physicians with expertise in the field on the clinical appropriateness of treatment. Medicare typically covers oncology drugs for medically accepted uses per the Food & Drug Administration (“FDA”) approved label as well as compendia-supported off-label uses, but this proposal is much more restrictive. We want to ensure that off-label limitations do not depart significantly from Medicare’s overall policy on off-label coverage and are flexible enough to allow for off-label use supported by appropriate compendia.

**To this end, we encourage CMS not to adopt a standard that designates only one compendium as a source for off-label indications. Instead, the NCD should allow for coverage of off-label indications that are in accordance with guidelines from any of the five compendia deemed acceptable for decisions related to off-label uses in Medicare statute.** While we recognize that the NCCN compendium is the only current source for evidence-based clinical guidelines that address CAR-T therapy, it would be shortsighted to assume that the other four compendia will not develop guidelines for CAR-T treatment in the future. While off-label use should be carefully considered and appropriately restricted, the NCD should not preclude future evidence-based clinical guidelines produced by other compendia from coverage.

**While Data Collection Around CAR-T Treatment is Critical, the Evidence Development Requirements Detailed in the NCD are Overly Onerous**

Given the intensive and specific focus on safety by the FDA, manufacturers, and providers, the requirements in the proposed NCD for evaluating the safety of CAR-T treatments may be duplicative to existing post-marketing studies that are already required. The CED requirements would add additional administrative processes and patient consents on top of those that are required by other entities.

We are concerned that the fact that the studies outlined in the NCD would not be funded by CMS, resulting in providers assuming additional costs to administer CAR-T treatments, which may further adversely restrict
access. The strict and complex registry approval requirements that are outlined in the NCD would require additional infrastructure investments from providers. **If CMS chooses to move forward with a CED decision, COA urges the agency to utilize an observational study format that remains flexible and evolves with newly approved indications and new CAR-T products.**

We appreciate the opportunity to comment on this proposed NCD and look forward to discussing our comments and concerns further with you and your staff. We are extremely willing to work with CMS to ensure that the final NCD is appropriately flexible for patients and qualified providers, including community oncologists, and that it appropriately recognizes the full future potential of emerging CAR-T treatments.

Please do not hesitate to reach out with any questions. We repeat our request to meet with the appropriate CMS staff to discuss our comments and concerns in greater detail.

Sincerely,

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President

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Executive Director

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