



March 17, 2019

Tamara Syrek Jensen, J.D.
Director, Coverage & Analysis Group
Centers for Medicare & Medicaid Services
Mailstop S3-02-01
7500 Security Blvd.
Baltimore, MD 21244

Sent electronically

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

Dear Ms. Syrek Jensen:

The Personalized Medicine Coalition (PMC), a multi-stakeholder group comprising more than 230 institutions across the health care spectrum, appreciates the opportunity to submit comments regarding the Centers for Medicare & Medicaid Services (CMS)' proposed decision memo for coverage of chimeric antigen receptor (CAR) T-cell therapy for cancer with evidence development.¹ CAR T-cell therapies represent a significant advancement in cancer care, and we urge you to revise the decision memo to ensure timely beneficiary access to approved therapies, minimize provider burden and continue to foster continued innovation in this therapeutic class.

Personalized medicine is an evolving field that uses diagnostic tools to identify specific biological markers, often genetic, to help determine which medical treatments and procedures will be best for each patient. By combining this information with an individual's medical history, circumstances, and values, personalized medicine allows doctors and patients to develop targeted prevention and treatment plans.

Personalized medicine is helping to shift the patient and provider experience away from trial-and-error and toward a more streamlined process for making clinical decisions, which will lead to improved patient outcomes, a reduction in unnecessary treatment costs, and better patient and provider satisfaction. As noted above, PMC's members are leading the way in personalized medicine and recommend that patients who may benefit from this approach undergo appropriate testing and tailored treatment as soon as possible during their clinical experiences.

PMC Statement of Neutrality

Many of PMC's members will present their own responses to CMS and will actively advocate for those positions. PMC's comments are designed to provide feedback so that the general concept of personalized medicine can advance, and are not intended to

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impact adversely the ability of individual PMC members, alone or in combination, to pursue separate comments with respect to the proposed decision memo on CAR T-cell therapies for cancer.

Current Landscape and CAR T-cell Therapies

PMC recently released *Personalized Medicine at FDA: A Progress & Outlook Report*. The report documents a record number of new personalized medicine approvals by the U.S. Food and Drug Administration (FDA). This marks the fifth consecutive year that personalized medicines accounted for more than 20 percent of all new drug approvals.ⁱⁱ FDA has developed new structures for evaluating cell and gene therapies and has demonstrated remarkable speed in bringing CAR T-cell therapies to market in the last two years. The CAR T-cell therapies approved by FDA are intended to treat children and young adults with acute lymphoblastic leukemia (ALL) and adults with diffuse large B-cell lymphoma (DLBCL).

The expected survival for adults with relapsed ALL is less than six months. Among children with cancer, relapsed ALL is a leading cause of cancer-related death.ⁱⁱⁱ Treatment with CAR T-cell therapy for ALL resulted in complete remissions in up to 90 percent of adults and children with this disease. In contrast, other available treatments for relapsed ALL have a response rate of 30 percent to 43 percent, depending on the type of treatment. In some patients, remissions have lasted up to two years. Such durable remissions offered many patients the chance to undergo bone marrow transplants, a procedure that can be curative.^{iv}

DLBCL is the most common type of non-Hodgkin lymphoma. In a multicenter clinical trial of patients with DLBCL that worsened after at least two prior therapies, the cancer responded to a CAR T-cell therapy called tisagenlecleucel in 59 percent of 51 patients and the cancer went into remission in 43 percent of patients. At 6 months, 79 percent of patients had not had a recurrence of lymphoma. In a different clinical trial, patients with relapsed or refractory DLBCL, refractory primary mediastinal B-cell lymphoma, or transformed follicular lymphoma received another CAR T-cell therapy, axicabtagene ciloleucel. Among the first 92 patients who were treated, the response rate was 82 percent, with complete remissions occurring in 54 percent of patients.^v

Considerations for CMS in Revising the Proposed Decision Memo

ALL and DLBCL are cancers with a very poor prognosis, and CAR T-cell therapies have made a profound impact in extending the lives of some people with these cancers. CMS has signaled a belief that CAR T-cell therapies show promise in improving health outcomes for patients with its thorough investigation of the space since initiating a national coverage analysis. We appreciate the opportunity to provide feedback on how CMS' coverage with evidence development (CED) proposal should be modified. We respectfully ask you to revise your proposal and address the following considerations in your final National Coverage Determination (NCD).

- Final national coverage policy should not negatively impact patient access

PMC stated in its comments submitted to CMS on June 15, 2018, that patients and providers are faced with navigating daunting coverage challenges for CAR T-cell therapies. Our hope was that

the NCD process would provide coverage for CAR T-cell therapy in both the inpatient and outpatient settings without further complicating care. It is our understanding that CED requirements in the transplant space have led some facilities to opt out of participation and decline subsequent treatment of Medicare beneficiaries. We therefore believe that implementation of the CED requirement should not be overly burdensome for facilities. If this principle is not adhered to, we fear that the CED requirement may encourage facilities to opt out of Medicare coverage for CAR T-cell therapy.

We are also mindful of the lag time between the issuance of a final NCD and CMS' approval of CED registries. Because CAR T-cell treatment protocols are multi-step, we are particularly concerned about patients who have started CAR T-cell therapy but have not yet received CAR T-cell infusions at the time the coverage decision is finalized. Adding a Patient-Reported Outcome (PRO) tool to the CED requirement, as proposed by the decision memo, may further extend the time it will take registries to launch. CMS should take steps to ensure that the data collection elements of the NCD do not delay patient access to treatment, which should be the priority. We urge CMS to eliminate the PRO reporting requirement as a condition for coverage. The Center for International Blood and Marrow Transplant Research (CIBMTR) began a PRO pilot program for in the summer of 2018. CMS should consider future collaboration with the CIBMTR to address symptom function and health-related quality of life questions related to CAR T-cell treatment.

Finally, the proposed decision memo states that eligible patients for coverage will not be experiencing any of seven comorbid conditions. However, some patients with comorbidities identified on the proposed list, such as active Hepatitis B and C, are currently receiving CAR T-cell treatment. By including these patient eligibility limits, the coverage proposal may exclude some patients who could benefit from treatment. In place of the current patient eligibility requirements, PMC urges CMS to require that the patient have a cancer that is treatable with an FDA-approved therapy, according to an FDA indication.

- Final coverage should be well aligned with FDA Risk Evaluation and Mitigation Strategies (REMS) requirements

Sponsors of existing FDA-approved CAR T-cell therapies have agreed to commitments for extensive post-market surveillance to better understand the long-term benefits and toxicities of these therapies. These REMS requirements are of larger size and longer duration than studies of traditional cancer treatments. While CMS has pointed to limited data available on CAR-T therapies in the Medicare population, emerging data from the post-market studies of currently-approved CAR-T products will produce data to further demonstrate health outcomes for Medicare beneficiaries. Additional data collection requirements should align with, and not duplicate, information gathered from these post-market studies and should be limited to facilities reporting specified clinical data elements to a centralized registry operated by a professional organization.

The CIBMTR conducts post-market surveillance collection for a number of organizations and has implemented CMS CED studies. If the CED requirement moves forward, CMS should consider naming CIBMTR or a similarly qualified entity experienced with data collection studies as a centralized registry for this NCD.

- National coverage policy should mitigate the downstream impact on this new class of therapies

Current CAR T-cell therapy is most often a third-line treatment. As such, CAR T-cell treatment is addressing the individual needs of patients who are without other options. CMS has stated that the data collected through the CED for CAR T-cell therapy will inform future decisions by the agency regarding coverage of CAR T-cell treatments for cancer. This raises concern that CMS is regulating a new class of therapies based on what is known from a review of just two therapies.

Experts anticipate that advancement in CAR T-cell therapy will lead us to viable first-line therapy in areas like B-cell malignancies. Clinical trials are already underway to explore whether CAR T-cell therapy is more effective than an autologous stem cell transplant in adult diffuse large B-cell lymphoma. The hope is that CAR T-cell therapy could one day replace chemotherapy and stem cell transplants altogether. This long-term goal will be achievable through earlier detection and treatment of the right patients, a hallmark of personalized medicine. There are also ongoing research studies looking at CAR-T in myeloma, glioblastoma, prostate cancer and breast cancer. Some clinical trials are even looking at whether patients can safely and effectively receive CAR T-cell therapy in the outpatient setting, depending on individual patient characteristics.

There will continue to be specialized considerations for the delivery of each CAR T-cell therapy and for newly approved indications of existing CAR T-cell therapies. CMS' final coverage decision must ensure that findings on treatment with existing therapies are not applied in ways that have a downstream effect of hindering future innovation. The NCD must be broadened beyond relapsed and refractory cancer patients so that it does not have to be re-opened for future indications. CMS should also establish site requirements that can adapt to rapidly evolving scientific advances in CAR T cell therapy.

Conclusion

Thank you for soliciting a wide range of stakeholder views on the proposed decision memo and for considering our comments. PMC welcomes the opportunity to serve as a resource as you formulate your final decision on coverage of this important class of therapy. We hope that CMS' coverage decision on this issue can achieve the goal PMC shares with the agency of delivering appropriate, efficient, and accessible health care to every patient in need of treatment. If you have any questions about the content of this letter, please contact me at 202-589-1769 or cbens@personalizedmedicinecoalition.org.

Sincerely,



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ⁱ Centers for Medicare & Medicaid Services. *Proposed Decision Memo for Chimeric Antigen Receptor (CAR) T cell Therapy for Cancer*. February 15, 2019 <https://www.cms.gov/medicare-coverage-database/details/nca-proposed-decision-memo.aspx?NCAId=291&bc=ACAAAAAAQCAA&>

ⁱⁱ Personalized Medicine Coalition. *Personalized Medicine at FDA 2018 Progress Report*. February 12, 2019 http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_at_FDA_A_Progress_and_Outlook_Report.pdf

ⁱⁱⁱ American Society of Clinical Oncology. *At the Leading Edge of Precision Medicine: Souped-up Immune Cell*. April 5, 2017. <https://www.asco.org/about-asco/press-center/cancer-perspectives/leading-edge-precision-medicine-souped-immune-cells>

^{iv} American Society of Clinical Oncology. *At the Leading Edge of Precision Medicine: Souped-up Immune Cell*. April 5, 2017. <https://www.asco.org/about-asco/press-center/cancer-perspectives/leading-edge-precision-medicine-souped-immune-cells>

^v American Society of Clinical Oncology. *Clinical Cancer Advances of 2018*. January 30, 2018 <https://www.asco.org/sites/new-www.asco.org/files/content-files/research-and-progress/documents/CCA-2018-Report.pdf>