ASTCT
American Society for
Transplantation and Cellular Therapy

March 15, 2019

Tamara Syrek Jensen, JD
Director, Coverage and Analysis Group
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

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

Dear Ms. Syrek-Jensen:

The American Society for Transplantation and Cellular Therapy (ASTCT), formerly the American Society for Blood and Marrow Transplantation (ASBMT), appreciates the opportunity to provide comments on the Centers for Medicare and Medicaid Services' (CMS) Proposed Decision Memo for Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers (CAG-00451N). ASTCT is a professional membership association of more than 2,200 physicians, scientists and other health care professionals promoting blood and marrow transplantation and cellular therapy through research, education, scholarly publication and clinical standards. The clinical teams in our society have been instrumental in developing and implementing clinical care standards and advancing cellular therapy science, including participating in trials that led to current FDA approvals for CAR-T cell therapy.

In comments submitted in June 2018 on CMS' decision to examine coverage for CAR-T therapies, ASTCT opposed the establishment of a National Coverage Determination (NCD) due to concerns that it would cause significant and ongoing barriers to providing current and future CAR-T therapies to beneficiaries in need of these breakthrough treatments. Patients who receive CAR-T have typically exhausted all other available therapies. **The Society still believes that it is premature to implement a NCD because this is a rapidly evolving area of medicine.** Several CAR-T products are under investigation, including products with better safety profile and for indications other than the ones currently approved by the FDA (lymphoma and acute lymphoblastic leukemia). **We recommend that development of a coverage policy be delayed until the field matures.** We recognize that the unprecedented costs of these innovative therapies does necessitate evaluation of alternative coverage mechanisms. However, mechanisms other than a NCD need to be considered, and the ASTCT will continue to work with CMS as they explore the same.

**If CMS proceeds despite these concerns, ASTCT recommends that the agency eliminate the CED requirement and instead implement an NCD with a data collection requirement that leverages the registry reporting currently in progress.** We believe that the CED requirement will create another barrier to patient access. The insufficient Medicare inpatient reimbursement is already creating challenges for the centers where our members practice as they determine whether they can withstand the significant financial losses associated with delivering CAR-T therapy to Medicare patients. As drafted, this coverage policy may further limit access and ultimately stifle innovation because of the associated burden on centers. ASTCT has been working with CMS to address these reimbursement challenges and is hopeful that the FY 2020 Inpatient Prospective Payment System proposed rule will include policies to improve



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CAR-T reimbursement. We welcome the opportunity to work with the Coverage and Analysis Group to ensure that a final policy meets the needs of CMS, providers, and most importantly, patients.

Please consider the following comments that outline our suggestions on how to improve this proposed decision memo to limit any negative impacts on patient access and innovation should CMS decide to proceed. There are also many aspects of this policy that require further clarification that must be provided before this policy is finalized in order to minimize any disruptions to patient care.

Patient Condition Requirements

As drafted, coverage would be limited to require that patients have relapsed or refractory cancer. **ASTCT urges CMS to expand this requirement to indications covered on the FDA approved label.** Expanding the covered indications in this manner will not only cover life-saving treatment but also help promote innovation. We are concerned that based on CARs currently undergoing clinical trials, it may be necessary for CMS to reopen the NCD within the next five years in order to provide coverage for CAR-T therapies that are likely to be approved in that timeframe, or label expansions for the current products. One example of a CAR in the pipeline that would not be covered by the relapsed/refractory requirement is the ongoing study of CAR-T in high-risk multiple myeloma.[1] Another example is for lymphoma, where the current FDA approved indication is failure of two lines of therapy. The ongoing ZUMA7 trial is studying CAR-T after failure of first line of therapy.[2] Other therapies that are pending include CD19-specific CAR-T therapy[3] and B cell maturation antigen CAR-T therapy for myeloma.[4] These examples demonstrate the innovative therapies that can save lives but will be difficult, if not impossible for patients to receive with the proposed coverage decision.

ASTCT also disagrees with the requirement that the therapy can only be provided to a patient that is not currently experiencing any comorbidity that would otherwise preclude patient benefit. It is unclear from the proposal how CMS plans to define this, or monitor for it in its claims processing system. Patients presently receiving these therapies have advanced malignancies that frequently requires ongoing therapy prior to treatment with CAR-T. We recommend that the determination whether a patient can benefit from the therapy despite having certain comorbidities be deferred to their treating clinicians, as this very sick patient population is likely to have one or more comorbidities.

We also request that CMS provide more guidance around what it means by a "new primary cancer diagnosis" and "the use of more than one therapeutic dose of a specific CAR T-cell product" for repeat treatment. The possibility exists that a patient could be diagnosed with a separate malignancy or new diagnosis of a previously treated cancer and could benefit from receiving the same CAR-T product. Moreover, if the patient relapses at some point in the future, after receiving CAR-T therapy, our clinicians

[1] https://clinicaltrials.gov/ct2/show/NCT03549442
[2] https://clinicaltrials.gov/ct2/show/NCT03549442
[3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5410390/
[4] https://ash.confex.com/ash/2018/webprogram/Paper116898.html



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should be the ones assessing whether the patient would benefit from receiving the same or different CAR-T treatment. The field of cell therapy is rapidly evolving and therefore CMS' final NCD should promote access rather than create barriers for new and innovative therapies.

CED Requirement

ASTCT understands that CMS included the CED requirement in order to gather additional data on the effectiveness of CARs in the Medicare population. However, if the agency chooses to finalize an NCD, the same objective can be accomplished with a registry reporting requirement rather than CED. We recognize and appreciate that the proposed CED requirement is less restrictive than others that CMS has implemented. However, we remain concerned that by virtue of this being a CED with additional patient reported outcomes (PRO) requirements in the outpatient setting, some centers will "opt-out", further restricting access since the agency's conditions of provider enrollment do not require participation in CED.[5] The Society requests that CMS' legal counsel confirm our analysis of the provider enrollment requirements and whether the anti-discrimination provisions in the conditions of participation require hospitals to furnish covered therapy (i.e., NCD covered therapies) to all patients in writing to avoid any confusion amongst centers. This analysis also should address whether or not patients are required to sign a notice of non-coverage (i.e, either an Advanced Beneficiary Notice (ABN) or a Hospital Issued Notice of Noncoverage (HINN)) acknowledging they have been advised that Medicare may not cover and pay for CAR-T therapy should a patient receive care at a hospital that chooses not to participate in data collection for the CED.

**The Society strongly recommends that CMS eliminate the CED requirement and instead finalize a NCD with data collection that is tied to existing registry reporting, as this will help avoid the access problems that may result from centers being able to opt-out of the CED requirement.** ASTCT strongly opposes the implementation of a coverage policy that allows centers to opt-out of participation if they perceive participation in the CED as imposing a significant burden in addition to the financial burden they already face. Again, we believe a NCD with data collection mechanism will provide CMS the opportunity to obtain data it needs to determine coverage policy for CAR-T therapy (see Registry Requirement below).

ASTCT asks for explicit clarification on the data collection and analysis requirements for the CED in order to ensure this requirement does not further limit patient access. In (3)(a)(iii), the policy states:

> *"The furnishing hospital shall address the CED requirements on all registry patients by tracking the following clinical data elements at baseline, at treatment, and at follow-up 3 months, 6 months, 12 months, and 24 months after the treatment is administered."*

It is not clear whether this language would require the furnishing hospital to analyze the data. If CMS intends for the approved registry to do this analysis, we request that this section be redrafted to state more

[5] 42 CFR 424



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precisely that the registry is required to conduct the analysis. As written, there may be confusion that the furnishing hospitals will be required to conduct their own analysis on all registry patients (i.e. their own and other hospital registry patients), and that would represent an undue burden on hospitals and present yet another reason for centers to opt-out of participation.

ASTCT also requests clarification from CMS on the patient consent requirements applicable to this coverage policy both as it applies to the registry reporting and PRO requirements. The Society believes that there would be no coverage or a coverage denial if a patient does not explicitly consent to have their data reported to the registry and requests that CMS clarify what would happen if patients do not consent. Specifically, ASTCT requests clarification on whether hospitals will be required to provide patients with a notice of non-coverage (i.e., an ABN or HINN) if the patient does not consent to their data being submitted to the registry or to having their PROs submitted if the therapy is delivered on an outpatient basis. The Society does not support coverage being contingent upon a patient's explicit consent to having their identifiable data submitted.

While it has been our general experience that most patients provide consent and are interested in having their data submitted to a registry to be a part of future scientific learning to benefit other cancer patients, CMS must recognize that there may be patients who do not want to participate, and that they have the right to refuse without penalty. As our Society members have been at the forefront of both clinical trials that led to the current product approvals, and in the first approved centers for commercial delivery of CAR-T therapy, we know that these patients have few realistic treatment alternatives, and certainly none that would potentially be curative. Knowing the poor outcomes for this disease population, and the risks of foregoing this treatment option, we are concerned how patients will perceive providers requesting patient consent regarding identifiable information in order for the patient's treatment to be covered. Instead of potentially placing patients in this position, we recommend that CMS recognize a hospitals' participation in a registry as sufficient to meeting the registry reporting requirements.

<u>Registry Requirement</u>

As proposed, the registry requirement requires furnishing hospitals to participate in "a prospective, national, audited registry that consecutively enrolls patients, accepts all manufactured products, and follows the patients for at least two years…" It also requires CMS to review and approve all registries. ASTCT believes the Center for International Blood & Marrow Transplant Research (CIBMTR) will meet the requirements to become an approved registry based on our review of the requirements and conversations with CIBMTR. **Therefore, we recommend that CIBMTR be listed as an approved registry in the final NCD, assuming they receive their approval prior to the May 17 implementation date. We also recommend that the agency accept hospital participation with the registry without requiring any other enrollment with CMS.**

CIBMTR is already collecting data for several CMS CED studies for myelodysplastic syndrome, myelofibrosis, sickle cell disease, and myeloma with great success. Our members are already familiar



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with CIBMTR through their work with patients with these conditions. Furthermore, CAR-Ts are already being provided by Foundation for the Accreditation of Cellular Therapy (FACT)-approved bone marrow transplant (BMT) programs, which are required by law to report data on allogeneic BMT to CIBMTR. The two manufacturers with approved products, Novartis and Kite/Gilead, are also using CIBMTR as the registry to meet their FDA post-approval study requirement. ASTCT believes this provides additional support for our request to have CIBMTR listed as an approved registry, which would reduce the burden to providers and institutions. ASTCT is pleased that our members are already familiar with a registry that will most likely be approved. Utilization of a registry other than the CIBMTR will increase reporting burden at centers that are providing CAR-T therapy, and will impact access as some centers may decide not to take on the additional resources and personnel required to report to another registry.

ASTCT believes it is critical that a registry be approved at the time this policy is finalized and implemented to avoid any coverage gaps. Furthermore, it is vital that the policy clarify that coverage is based on cell collection occurring on or after the effective date since there will be patients in the midst of their CAR-T episode of treatment when the policy is finalized. We do not support an effective date that would be based on cell administration that could potentially disrupt coverage of an episode of CAR-T therapy already in progress.

Patient-Reported Outcomes Requirement

In the proposed decision memo, CMS included a PRO requirement for the outpatient setting. ASTCT has several concerns and questions related to this requirement. **As we stated in our July 2018 comments regarding MEDCAC's discussion on PROs, the Society strongly objects to any mechanism that would tie patient access or provider reimbursement to the reporting of PROs, especially in the case of CAR-T therapy**.[6] The Society believes that a PRO requirement would add an additional unreimbursed, administrative burden to the patients being treated with CAR-T therapy. In particular, we believe it is premature to require PRO data for this population and are also concerned that the two PRO tools listed in the policy are not directly applicable to this patient population. Moreover, at the August 2018 MedCAC meeting, we shared that there is insufficient evidence to support the use of these tools for CAR-T patients and believe that this is still the case. The Society is also concerned that the PRO requirement turns a registry-reporting requirement into a study, which will further exacerbate the financial burden on centers. At this time, the appropriate PRO instruments, their characteristics, timing of administration and feasibility of data collection in patients receiving CAR-T therapy is not well described.

If this requirement is retained in the final policy, we request that it continue to be applied only to outpatients and the agency define "outpatient" as used in the proposed decision memo. It is unclear if the setting is based on the physician order when the cells are administered or on how the account is billed.

[6] ASBMT Comments to CMS on MEDCAC meeting held on August 22, 2018. Link to comments here: https://higherlogicdownload.s3.amazonaws.com/ASBMT/43a1f41f-55cb-4c97-9e78-c03e867db505/UploadedImages/ASBMT_CMS_Comment_MEDCAC_CAR_T_PROs_7_16_2018.pdf



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Since some patients may be administered the cells as outpatients, but billed as inpatients, it is important that CMS provide clear guidance on this issue. We also recommend that participation in the PRO component of CED studies be voluntary for patients. In addition, so that access to CAR-T therapy is not compromised, we recommend that CMS allow additional time for development of PRO data collection protocols, IRB approvals, and implementation of appropriate PRO data collection mechanisms while allowing patients to enroll on CED studies that evaluate standard clinical outcomes (other than PROs). Finally, if PROs are included, we strongly recommend that CIBMTR, as our recommended registry of record for this purpose, be the organization that develops and implements the PRO aspect of the CED protocol.

Accreditation Requirements

In the proposed decision memo, CMS included the following requirement for CED:

> *"The hospital has: a Cellular Therapy Program consisting of an integrated medical team that includes a Clinical Program Director, a Quality Manager, and at least one physician experienced in cellular therapy, and demonstrates that protocols, procedures, quality management, and clinical outcomes are consistent from regular interaction among all team members; a designated care area that protects the patient from transmission of infectious agents and allows for appropriate patient isolation as necessary for evaluation and treatment; and written guidelines when administering CAR T-cell therapy for patient communication, monitoring, and transfer to an intensive care unit."*

If CMS retains this requirement in the final NCD, ASTCT urges CMS to define a uniform mechanism for accreditation that conforms to CMS standards in order to ensure that these cells are administered within a cell therapy program as defined. We were pleased that CMS listed Foundation for the Accreditation of Cellular Therapy (FACT) in the proposed decision memo as a mechanism to accredit centers providing CAR-T therapy under the CED. **ASTCT urges CMS to require use of FACT or another broadly accepted accreditation program rather than creating a duplicative set of requirements to which centers must comply.**

The Society expects that the hospital will not be required to attest to CMS its program meets the outlined accreditation standards. We do not support a requirement that would require a hospital to actively enroll with CMS as a requirement of coverage.

Off-Label Coverage Requirements

In the proposed decision memo, CMS outlines off-label coverage requirements. ASTCT requests that CMS provide clarification on whether this triggers study participation or if the registry reporting requirement would apply. Currently, CMS recognizes off-label use of anti-cancer drugs and biologicals when they are referenced in compendia listed in the Chapter 15, Section 50.4.5 of the Medicare Benefits Policy Manual.



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**The Society urges CMS not to implement a coverage policy that restricts off-label coverage for CAR-T different from that allowed for Medicare beneficiaries receiving any other anti-cancer drugs and biologicals.** As we have repeatedly emphasized, this therapy is currently a therapy of last resort and saves patients' lives. Appropriate off-label use should not come with additional requirements beyond data collection. The Society requests that CMS clarify if the intent is for a study similar to a full clinical trial be required for off-label use, or if the requirement is similar to the registry reporting requirement already in place.

The Society also seeks clarification on why NCCN was listed as the sole applicable compendium in the proposed decision memo when CMS recognizes others in the above referenced Medicare Benefits Policy Manual.[7] ASTCT recommends that CMS cover off-label use of CAR-Ts consistent with other anti-cancer drugs and biologicals and clarify that data collection via the registry is also required.

Conclusion

ASTCT appreciates the opportunity to comment on the proposed decision memo and to provide our perspective on the best way to ensure access to medically accepted CAR-T therapies for Medicare beneficiaries. We have included a list of questions in Appendix I, which require clarification before the implementation of the policy. The Society looks forward to working with you to improve this policy to ensure that appropriate patients have access to this lifesaving therapy. If you have any questions regarding the above comments, or if we can provide any additional information, please contact Alycia Maloney, ASTCT's Director of Government Relations at amaloney@asbmt.org.

Sincerely,

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[7] 42 CFR 424



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