



June 15, 2018

Katherine B. Szarama, PhD
Lead Analyst
Coverage and Analysis Group
Centers for Medicare & Medicaid Services
Department of Health and Human Services
7500 Security Blvd.
Baltimore, MD 21244

Re: National Coverage Analysis (NCA) [Tracking Sheet](#) for Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers (CAG-00451N)

Dear Dr. Szarama:

The Alliance for Regenerative Medicine (ARM) appreciates the opportunity to comment on the recently issued National Coverage Analysis Tracking Sheet for Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers.¹

ARM writes to express concern about CMS' direction and approach towards new and innovative technologies. ARM believes that the agency's National Coverage Analysis (NCA) may have a significantly chilling effect on access to the approved therapies and curtail clinical and financial investment in these technologies given the uncertainty that a NCA presents. Additionally, ARM questions the use of CMS' resources and is equally concerned that by performing this analysis, the agency is inappropriately setting the precedent that it will inappropriately conduct an NCA for every new cellular and gene technology approved by the FDA.

ARM questions the agency's decision to focus its resources on a technology that impacts so few, yet very ill Medicare beneficiaries as compared to focusing on other Medicare items and services that affect millions of Medicare beneficiaries and represents a much larger overall expense to the Medicare program. An extremely small patient population is being treated with the two CAR-T cell therapies currently on market, they have only months to live, they have exhausted all other treatment options. As such, ARM suggests that CMS rescind this NCA.

¹ <https://www.cms.gov/medicare-coverage-database/details/nca-details.aspx?NCAId=291&bc=ACAAAAAAAAAA&>

If, however, CMS continues with the NCA, ARM urges CMS to immediately clarify and remind its Medicare Administrative Contractors (MACs) that the CAR-T cell therapies that are subject to this NCA remain covered according to their respective FDA labels² and for any indication published in a CMS recognized compendia that meets CMS' evidentiary standards.³ ARM believes that this type of communication will ensure continued access to these lifesaving therapies during the NCA process by removing any uncertainty regarding coverage in the provider community.

I. Regenerative Therapies Represent the Future of Health Care

ARM is comprised of more than 290 leading life sciences companies, research institutions, investors, and patient groups that represent the regenerative medicine and advanced therapies community. ARM takes the lead on the sector's most pressing and significant issues, fostering research, development, investment, and commercialization of transformational treatments and cures for patients worldwide

The regenerative medicine and advanced therapies sector is the next frontier in the fight against some of humankind's most devastating diseases and disorders. As of year-end 2017, ARM estimates there are 850+ regenerative medicine and advanced therapies developers worldwide sponsoring 946 clinical trials across dozens of indications, including oncology, cardiovascular, central nervous system, musculoskeletal, metabolic disorders, ophthalmological disorders, and more.

First, a quick primer on the various technologies that comprise this sector.

- Cell therapy is the administration of viable, non-genetically modified cells into a patient's body to grow, replace or repair damaged tissue for the treatment of a disease. Cells can be administered allogeneically, in which the patient receives cells processed from a donor, or autologously, in which the patient receives cells from his or her own body. ARM members are currently developing cell therapy approaches to treat diseases and disorders that include chronic heart failure, Crohn's disease, ALS, ischemic stroke, diabetes, Parkinson's disease, degenerative disc disease, and more.
- Tissue engineering combines scaffolds, cells and biologically active molecules into functional tissues to restore, maintain or improve damaged tissues. Biomaterials are medical devices designed to interact with living systems, providing physical structures and support for

² Social Security Act (SSA) § 1861(t)(2)(A).

³ Medicare Benefit Policy Manual, ch. 15, § 50.4.5.

engineered tissues. ARM members are currently developing tissue-engineered products and biomaterials to treat cartilage damage and degeneration, wound repair, spinal cord injury, hernia repair, and more.

- Gene therapy seeks to modify, replace, inactivate or introduce genes into a patient's body with the goal of durably treating, preventing or even curing disease. Gene therapy techniques include genetically modifying a patient's cells outside of their body, which are then re-introduced to deliver a therapeutic effect, an approach known as gene-modified cell therapy. ARM members are currently developing gene therapy and genome editing approaches to treat inherited blood disorders beta-thalassemia and sickle cell diseases, blood cancers leukemia and lymphoma, inherited retinal disease, Huntington's disease, and more.

What is critical about all these technologies is that many of the therapies are transformative – they provide a durable therapeutic benefit or even a cure with a single administration of therapy. ARM is concerned that a NCA targeting CAR-T cell therapies in the early stages of their use is a poor use of federal resources, sets a horrible precedent and may slow adoption denying access to Medicare beneficiaries, who have no other recourse, to this life saving technology. Consequently, ARM urges CMS to rescind the NCA or, should the process continue, clearly state that these therapies are covered during the process.

II. The Law Provides for Coverage of the CAR-T Therapies

In 2017, The Food and Drug Administration (FDA) approved tisagenlecleucel (Kymriah®) and axicabtagene cileucel (Yescarta®) CAR-T-cell therapies for the treatment of certain relapsed or refractory leukemias and lymphomas.⁴ Each of these therapies was approved under a biologics license application (BLA). The Social Security Act (SSA) states that the term biologicals includes only such biologicals as are included or approved for inclusion in certain publications; or, as are approved by the pharmacy and drug therapeutics committee (or equivalent committee) of the medical staff of the hospital furnishing such drugs and biologicals for use in such hospital.⁵ Both Yescarta and Kymriah are currently administered at various hospitals across the country. ARM therefore believes that each of the CAR-T cell therapies satisfies the statutory definition of biological and must be covered consistent with the statute, which includes both the inpatient and outpatient settings as detailed below.

⁴See Tracking Sheet at: <https://www.cms.gov/medicare-coverage-database/details/nca-details.aspx?NCAId=291&bc=ACAAAAAAAAAAAA&>

⁵ SSA §1861(t)(1).

CMS notes in the NCA that each CAR-T cell therapy includes a safety monitoring program through an FDA Risk Evaluation and Mitigation Strategy (REMS) and that “the majority of patients who received CAR T-cell therapy also experienced adverse events including cytokine release syndrome and neurological effects.”⁶ ARM has two major concerns with CMS using the safety issue as support for the NCA so close to FDA approval. First, monitoring the safety and adverse event profile of any given therapy is clearly within the jurisdiction of the FDA, especially where a REMS is required. If CMS has specific concerns that certain safety issues were not reviewed by the FDA during the regulatory review process and/or are not included in the REMS, the ARM urges CMS to identify those concerns; however, the ARM does not believe this to be the case. Thus, it would not be prudent to move forward with a NCA on the grounds of safety considerations.⁷

Second, and more specifically, ARM urges CMS to clarify what safety concerns it has for Medicare beneficiaries and what data suggest that such considerations are specific to this population. These therapies have been deemed safe and effective for appropriate patients and received FDA approval. Additionally, studies show that patients 65 and older have a similar clinical and safety profile to patients under 65. CMS states in the Tracking Sheet that few Medicare patients have received either CAR-T-cell therapy. Therefore, ARM additionally asks CMS to clarify what safety issues specifically exist for Medicare beneficiaries at this juncture and why the agency’s concerns should replace the regulatory judgement of the FDA and the clinical judgement of physicians who prescribe a CAR-T cell therapy for Medicare patients, consistent with a medically accepted indication.

III. Various Types of Compendia Publication Provide Coverage

The Social Security Act (SSA) states that the term drug includes drugs or biologicals used in an anticancer chemotherapeutic regimen for a medically accepted indication, which is further defined as any use which has been approved by the FDA for the drug and such use is supported by one or more citations which are included in one or more of a CMS approved compendia with certain levels and types of evidence.⁸ ARM is concerned, based on UnitedHealthcare’s Request Letter that the agency is considering narrowing coverage to only those stated in FDA label thereby ignoring the statute and

⁶ See Tracking Sheet at: <https://www.cms.gov/medicare-coverage-database/details/nca-details.aspx?NCAId=291&bc=ACAAAAAAAAAA&>

⁷ In addition to the REMS, manufacturers also certify each site to ensure that the site can safely administer the therapy and care for the patient. This provides yet another layer of safety concern further mitigating this issue as a reason for the NCA.

⁸ SSA §§1861(t)(2)(A) & (B).

IV. Site of Care Should be Determined by FDA Label, Treating Physician and Institution

Similarly, the FDA labeling for Yescarta is agnostic as to site of care; rather, deferring to physicians to determine appropriate site of care. In light of these data from both CAR-T cell therapies, ARM urges CMS to allow physicians to continue to determine the most appropriate site of care based on the clinical needs of the individual beneficiary and not a NCA.

¹¹ <https://www.novartis.com/news/media-releases/primary-analysis-results-from-novartis-pivotal-juliet-trial-show-kymriah-tm-tisagenlecleucel-sustained-complete-responses-six-months-adults-r-r-dlbc-difficult>

In conclusion, ARM believes that the field of regenerative medicine has the potential to heal people and bend the health cost curve toward lower long-term costs and higher quality outcomes. This trend is already evidenced by several approved and marketed first-generation regenerative medicine products that are demonstrating both clinical and cost reduction value in relation to current “standards of care”. Specifically, by reducing hospital care, the need for physician, clinical and professional services, nursing and home healthcare, we could substantially reduce overall healthcare expenses. ARM is confident that meaningful improvements in clinical outcomes and cost reduction can be accomplished through regenerative medicine technologies.

Much of the dialogue around healthcare in recent years has focused on the issues of broadening access (through insurance reforms) and controlling costs through Medicare and Medicaid reimbursement reforms such as payment cuts to health providers. Clearly, reducing expenditures alone will not enable us to improve clinical outcomes and achieve enhanced patient quality of life if it hampers innovation.

It is critical for CMS to develop and implement policies and programs that support beneficiary access to new technologies when they are deemed most clinically appropriate and stimulate their continued development. This is particularly true for regenerative medicine and other advanced therapies that hold the promise of durably treating and potentially even curing chronic or life-threatening diseases.

ARM asks CMS to rescind the NCA on the basis that it was prematurely undertaken. If the Agency moves forward despite this strong recommendation, we urge CMS to address the issues identified throughout this letter in a timely fashion while maintaining beneficiary access as a priority. Regardless, ARM believes that CMS must immediately clarify to the healthcare community that the CAR-T therapies are covered and will remain so until this process is over.

Sincerely,

A handwritten signature in cursive script that reads "Robert J. Falb".

Robert J. Falb
Director, U.S. Policy & Advocacy
Alliance for Regenerative Medicine