



September 24, 2018

Seema Verma
Administrator
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
Hubert H. Humphrey Building
200 Independence Ave, SW
Washington, DC 20201

RE: Medicare Program: Proposed Changes to Hospital Outpatient Prospective Payment and Ambulatory Surgical Center Payment Systems and Quality Reporting Programs; Requests for Information on Promoting Interoperability and Electronic Health Care Information, Price Transparency, and Leveraging Authority for the Competitive Acquisition Program for Part B Drugs and Biologicals for a Potential CMS Innovation Center Model [CMS-1695-P]

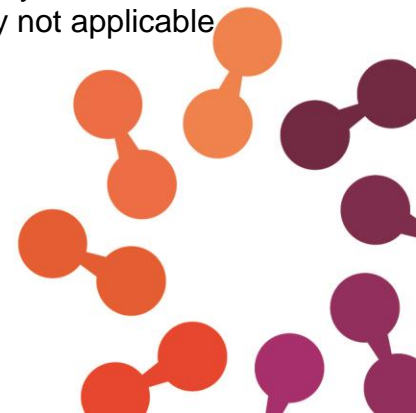
The Alliance for Regenerative Medicine (ARM) appreciates the opportunity to comment on the Center for Medicare & Medicaid Services' (CMS) recently published proposed rule entitled, "Proposed Changes to Hospital Outpatient Prospective Payment and Ambulatory Surgical Center Payment Systems and Quality Reporting Programs; Requests for Information on Promoting Interoperability and Electronic Health Care Information, Price Transparency, and Leveraging Authority for the Competitive Acquisition Program for Part B Drugs and Biologicals for a Potential CMS Innovation Center Model (Proposed Rule).¹ Specifically, ARM's comments focus on CMS' Request for Information (RFI) related to the Competitive Acquisition Program (CAP) and on a specific recommendation made by the Advisory Panel on Hospital Outpatient Payment (HOP) on August 20, 2018.²

Regarding the CAP, ARM appreciates and looks forward to working with CMS to potentially implement a new and improved CAP that would "introduce competition to improve quality of care for beneficiaries while reducing both Medicare expenditures and beneficiary's out of pocket spending."³ These principles lay at the foundation of the clinical development of ARM's member companies who are developing new and innovative therapies that treat a wide range of diseases and patient populations. ARM, however, urges the Agency to prioritize maintaining appropriate beneficiary access to therapy over cost reduction such that ARM believes that the CAP is likely not applicable

¹ 83 Fed. Reg. 37046 (July 31, 2018).

² <https://www.cms.gov/Regulations-and-Guidance/Guidance/FACA/AdvisoryPanelonAmbulatoryPaymentClassificationGroups.html>

³ 83 Fed. Reg. 37212.



to all drugs and biologicals covered and reimbursed by Medicare Part B. This priority was shared by Congress in the CAP's authorizing statute that explicitly gave the Secretary the authority to exclude therapies from the CAP that are "likely to have an adverse impact on access"⁴ to such therapy. Congress continued to recognize the importance of maintaining patient access and quality of care when it created the Center for Medicare and Medicaid Innovation (CMMI)⁵ and under which the Secretary will be designing the "new CAP." Specifically, Congress stated that "[t]he Secretary shall focus on models expected to reduce program costs under the applicable title while preserving or enhancing the quality of care received by individuals receiving benefits under such title."⁶ As such, and as detailed below, ARM urges CMS to again exclude those therapies that present potential access issues, and/or require specialized distribution models, and/or administration protocols, clarify how quality of care will be preserved within each class of drug chosen for the CAP, and delay implementing the CAP for the remaining therapies until the proposed changes to physician reimbursement are fully implemented.

Last month, the HOP panel recommended that CMS separately pay for certain newly available Category 3 codes related to CAR-T therapies. ARM agrees that providing a CAR-T therapy requires special handling and processes by physicians and institutions and supports reimbursement for work performed. However, as stated in greater detail below, ARM raises some questions and issues that it hopes the agency will clarify before finalizing the HOP panel's recommendation to separately reimburse for each of the Category 3 codes related to CAR-T therapies.

I. Regenerative Therapies Are Often Specialized to Small Patient Populations and/or Areas of Substantial Unmet Medical Need That Are Likely Not Conducive to a One-Size Fits All CAP

ARM is an international multi-stakeholder advocacy organization that promotes legislative, regulatory, and reimbursement initiatives necessary to facilitate access to life-giving advances in regenerative medicine worldwide. ARM comprises more than 275 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

⁴ Social Security Act (SSA) §1847B(a)(1)(D).

⁵ SSA §1115A

⁶ SSA §1115A(b)(2).

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 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, 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 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.

ARM appreciates that CMS specifically asks for comments on the applicability of the CAP to the "new high cost therapies"⁷ and seeks comments on how a CAP can introduce competition and strengthen negotiation to lower overall costs. ARM reminds CMS that many of the "new high cost therapies" resulting from the new technologies detailed above can represent a substantial benefit over existing standard of care by employing the most advanced science to treat or even cure disease. In particular, therapies that are intended to treat serious or life threatening conditions that are also recognized as areas of significant unmet medical need, by definition reflect indications where standard of care is inherently limited, ineffective, or unavailable for many or most patients. Many of these indications have a substantial impact on patients in terms of clinical outcomes, quality of life, and in economic terms (e.g. cost of both clinical and non-clinical care, quality of life for the patient and family members that may need to

⁷ 83 Fed. Reg. 37213.

provide home care, and overall cost burden). Innovative therapies that are targeted at such areas are, and should remain, a priority, and broadly reflect the focus of many regenerative medicine and advanced therapies.

Highly innovative regenerative medicine and advanced therapies typically require specialized manufacturing, time sensitive administration protocols, and complicated handling and/or storage criteria. In order for these types of regenerative medicine and advanced therapies to achieve their maximum clinical result each of the components mentioned above must be optimized to the therapy and the patient. Because of these factors, companies focused on the development and delivery of these medicines carefully choose distribution partners often creating a limited distribution network of specialized distributors with the necessary skill to timely deliver and care for the therapy. Therefore, ARM encourages CMS to carefully consider the impact that a CAP vendor that does not have the capability to service these types of therapies could have on all of key aspects of timely and appropriate access to the therapy before including any class of therapies in the CAP.

The potential for dramatic clinical benefit and the potential ensuing direct and indirect cost offsets---is why these innovations are changing medical care. CMS should encourage the development and commercialization of these types of therapies rather than establish policies that inject payment uncertainties or threaten continued investment incentives.

A. Due To Conflict Of Interest, the Model Vendors Should Not Also Administer Value-Based Contracts

ARM is concerned that CMS is considering “allowing private sector model vendors to enter into and administer value-based arrangements with manufacturers of separately payable Medicare Part B drugs and biologicals” because of the conflict of interest this could present. ARM is concerned that by requiring a vendor that has a financial interest in both the distribution of the therapy and the therapy’s outcome, the vendor may be more inclined to dedicate more resources behind the therapy for which it has a greater financial interest in its distribution terms. Specifically, if a vendor distributes two therapies that are at the center of a value-based contract that compares the outcomes of the competing therapies and has more favorable financial terms for one of the therapies, it could dedicate more resources to supporting the patients on that therapy in order to improve the outcomes of the patient and therefore its finances.

Further, not all vendors are equipped to implement value-based contracts. To appropriately administer these types of contracts the vendor would need access to many different types of data that it does not regularly have such as medical, pharmacy and patient outcome data. In addition to the time and expense of acquiring the data, the vendor would need specialized infrastructure and staff to appropriately negotiate and administer a value-based contract to monitor, analyze and interpret the data on some level. By requiring these functions of the CAP vendor the Agency will be limiting the number of potential vendors eligible to participate in the CAP. This seems contrary to

the spirit of the potential new CAP, which is to foster competition among potential vendors. Therefore, considering the conflict of interest and limiting factor that administering a value-based contract presents, ARM urges CMS to separate the two functions of distribution and administering a value-based contract. The CAP should singularly focus on new distribution models as this will likely be the expertise of the broadest number of vendors.

B. ARM Urges CMS to Consider the Impact of the Proposed E&M Code Changes on Physicians Before Implementing the CAP

Effective 2019, CMS is proposing to create a single payment rate for E&M visit complexity levels 2-5 for both new and established patients.⁸ These proposed changes will have varying impact on physicians depending on the acuity level of the physician's beneficiary population. Specifically, if these proposed changes are finalized, physicians who treat more complex beneficiaries will be disproportionately and negatively impacted in comparison to those who treat beneficiaries with less complex medical needs. Typically, the physicians with the higher acuity beneficiary population also prescribe and administer drugs and biologicals incident to the office visit. ARM is concerned that if CMS should implement both the CAP and the proposed changes to E&M codes at the same time, in addition to the continued changes to the MIPS program, physicians may be disincentivized to enroll in the CAP instead choosing to focus on the changes to the economics of their practice's CPT codes while not introducing changes to their buy and bill economics.

CMS states that the original "CAP also was hindered by low physician enrollment"⁹ and ARM is concerned that the same market dynamic would occur if the Agency mandates or offers so many changes to Medicare practice economics. Therefore, ARM urges CMS to delay any implementation of the CAP until the Agency has a better understanding of the impact that the E&M code changes will have on the physician's desire to participate in the CAP.

C. ARM Encourages CMS to Exempt the Same Classes of Therapies That Were Exempted from the Initial CAP For the Same Reason Which is to Protect Access

As mentioned above, ARM believes that if structured correctly and introduced at the appropriate time, the CAP can achieve the Administration's goals of reducing list prices, improving outcomes, and reducing beneficiary's out of pocket costs by introducing competition into the market. ARM, however, believes that these principles should not compromise the beneficiary's access to the most appropriate clinical therapy. Many times the most appropriate therapy has no competition, which is typically the case for patients' suffering from an orphan disease.

⁸ 83 Fed. Reg. 35704, 35839 (July 27, 2018)

⁹ 83 Fed. Reg. 37214.

CMS excluded from the initial CAP single indication orphan drugs stating “that access problems provide a sound reason for not including some orphan drugs (single indication) from the CAP.”¹⁰ The Agency further stated that this “group of orphan drugs poses much more severe access issues than other orphan drugs precisely because their use is generally limited to relatively rare orphan indications.”¹¹ CMS’ rationale for determining that, for certain orphan drugs, the potential access issues justify exclusion from CAP was well-reasoned when promulgated and may be even more compelling in the wake of the initial CAP’s failure. ARM urges CMS to apply the CAP exemption to orphan drugs that are administered to treat a rare disease, including those with more than one orphan indication or potential use.

Many if not all regenerative medicines treat small orphan patient populations and present the same potential access issues as they did thirteen years ago when CMS exempted this class of therapies from the CAP. ARM expects that given the unmet medical needs these products address, any savings opportunity in incentivizing clinicians to choose lower-cost products, or delay use of an orphan product, would frustrate, rather than further, CMMI’s statutorily defined mission¹² to improve outcomes and reduce costs. Therefore, ARM urges CMS to again exempt this class of drugs.

D. Similar to an Orphan Indication, ARM Believes That CMS Should Exempt Therapies That Focus on Serious or Life Threatening Conditions Such as Those Receiving a RMAT Designation Or Require Specialized Distribution Services and/or Beneficiary Administration Protocols

ARM believes that there are other FDA designations, like orphan designation, that reflect a specific focus on serious or life threatening conditions where there is a recognized unmet medical need that should also be exempted as a class. A class of drugs should be exempted where current medical care is ineffective or unavailable to many or most patients, because conventional treatment approaches are inherently limited or simply do not work or are unavailable for most patients, and innovative approaches and therapies are desperately needed. For example, regenerative medicine or advanced therapies that have received a Regenerative Medicine Advanced Therapy Designation (RMAT), are specifically targeted at these types of situations, and by definition, represent a fundamental advance in medical care. In order to receive this designation, the drug must be a cell therapy, therapeutic tissue engineered product, human cell and tissue product, or any combination using such therapies or products.¹³ Further, the law requires that the drug must be intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition.¹⁴ The nature of the therapies that received a RMAT designation often require a specialized distribution model and/or specified and unique patient administration protocols. Similar to orphan therapies, ARM is concerned that including therapies that have an RMAT designation in the new CAP

¹⁰ 70 Fed. Reg. 39022, 39028 (July 6, 2005).

¹¹ *Id.*

¹² SSA §1115A(b)(2).

¹³ See Section 3033 of the 21st Century Cures Act.

¹⁴ *Id.*

could present access issues and compromise quality of care by introducing a potentially inexperienced vendor that is not qualified to distribute this unique class of therapies. ARM is concerned that the integrity of the therapy could be compromised under a CAP model. CMS exempted certain classes of drugs from the initial CAP due to concerns of access and channel integrity. ARM believes that the same should hold true for the class of therapies that receive a RMAT designation.

E. Therapeutic Innovations Emerging Since CMS Implemented the Initial CAP Present Access and Logistic Issues that Warrant CAP Exclusion

In its initial CAP implementation rule, CMS acknowledged the rapidly-changing landscape for contrast agents and ultimately determined to exclude these products from its CAP implementation. CMS noted that “[w]e agree with the commenters that the rapid pace of change in this field, in conjunction with major changes in coding and payment in recent years, may pose special possibilities for confusion during the initial stage of the CAP. We, therefore, are not including contrast agents under the CAP during this initial stage of implementing the program.”¹⁵

Similar considerations certainly apply to the regenerative medicine sector, and this potential for confusion is compounded because these highly innovative regenerative medicine and advanced therapies typically require specialized manufacturing, time sensitive administration protocols, and complicated handling and/or storage criteria. For example, many regenerative medicine and advanced therapies require specialized cryogenic storage conditions to maintain product stability and integrity (i.e. at temperatures of $\leq -130^{\circ}\text{C}$ or lower), that intermediate distributors would have no relevant experience in, knowledge of, infrastructure or capacity to manage. In addition, such therapies may require time sensitive preparation protocols and processes that must be completed within a defined time frame to preserve the integrity of the product, as well as highly specialized infrastructure for product preparation (e.g. controlled rate thawing and/or final preparation in a specialized part of the hospital such as a cell processing lab) and subsequent administration (e.g. a requirement for administration of the product to the patient in a catheter lab environment). Many regenerative medicine and gene therapy products are manufactured through an individualized approach, using autologous cells and/or tissue to engineer a patient-specific therapy.

Perhaps more importantly, however, is the fact that many of these emerging therapies have a specific focus on serious or life threatening conditions where there is a recognized unmet medical need – a significant gap in clinical care. For patients requiring these products, currently available alternatives are ineffective, and innovative approaches and therapies are desperately needed. The stakes, from a patient perspective, of delayed or impeded access can be catastrophic. ARM, therefore, urges CMS to apply the well-reasoned approach adopted in devising exclusions to the initial CAP, to the evolving technologic landscape we face today. We believe that significant savings are unlikely, and access issues are likely to predominate for therapies that:

¹⁵ 70 Fed. Reg. 39028.

- Are manufactured on a patient-specific basis;
- Have specialized handling and delivery requirements; or
- Address an unmet need in treating a serious or life-threatening condition.

ARM believes these products present the same, if not more compelling, potential access issues as the products CMS exempted from the CAP thirteen years ago.

II. ARM Urges CMS To Clarify The Payment Status of The CAR-T Category 3 Codes

On August 20, 2018 the HOP panel recommended that CMS reassign the status indicators for the following Category 3 CPT codes from B¹⁶ to S¹⁷:

- CPT code 05X1T, *Chimeric antigen receptor T-cell (CAR-T) therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells, per day*
- CPT code 05X2T, *Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived lymphocytes for transportation (e.g., cryopreservation, storage)*
- CPT code 05X3T, *Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration*
- CPT code 05X4T, *Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous*

The Panel further recommended that CMS assign CPT code 05X1T and CPT code 05X4T to APC 5242, *Level 2 Blood Product Exchange and Related Services*, and CPT code 05X2T and CPT code 05X3T to APC 5241, *Level 1 Blood Product Exchange and Related Services*.¹⁸

ARM agrees that some of these services are crucial towards a successful clinical outcome for the beneficiary and must be valued. For example, ARM agrees that CMS should cover and separately pay for the leukapheresis because it requires specialized skills and is different from each of the other aspects of the CAR-T cell therapy because it is the only function that can be performed at a different facility than where the CAR-T therapy is ultimately administered. In separately paying for the leukapheresis, CMS also should clarify that the National Coverage Determination (NCD) for Apheresis

¹⁶ Status indicator B means that the corresponding CPT code is not recognized by OPPS when submitted on an outpatient hospital bill and not paid under OPPS.

¹⁷ Status Indicator S means the procedure or service is separately paid under OPPS.

¹⁸ <https://www.cms.gov/Regulations-and-Guidance/Guidance/FACA/AdvisoryPanelonAmbulatoryPaymentClassificationGroups.html>

(Therapeutic Pheresis)¹⁹ does not apply to harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells.

ARM also asks CMS to clarify the following operational issues related to the HOP panel's recommendations. Specifically, the established HCPCS Q codes for the marketed CAR-T therapies includes the dose preparation services such that it seems that CMS' reimbursement policies may be paying twice for the same service. Therefore, ARM urges CMS to reconcile the payment for the services included in the HCPCS with those that are now being recommended to be paid for separately with the new codes and provide some clarity on how this will be handled in the future.

Second, ARM is concerned that CPT code 05X4T duplicates current infusion codes that already reimburse for the administration of CAR-T therapies and asks CMS to clarify why both codes are necessary. ARM asks CMS to provide guidance in the final rule indicating that providers should use existing, separately reimbursable codes for the administration of CAR T cell therapy, consistent with CMS's approach for other drugs and biologicals.

Finally, ARM asks CMS to clarify the benefit category for each of these services. ARM appreciates that these new codes mirror those that are used for a bone marrow transplant, but those codes are part of a larger service being provided to a Medicare beneficiary. A CAR-T therapy is a biological that is separately paid for in the outpatient setting and not part of a larger service. As such, ARM asks the Agency to clarify the benefit category for each of the separately payable service.

ARM appreciates the efforts to account for all the work and services being provided in connection to the CAR-T therapy for Medicare beneficiaries but also wants to reduce confusion and eliminate unnecessary and duplicative payments in the outpatient setting.

III. 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. Our members are already developing innovative distribution models in the private sector by contracting directly with payers demonstrating our commitment to looking for alternative models that lower costs while maintaining appropriate access.

¹⁹ <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCAId=256&NcaName=Transcutaneous+Electrical+Nerve+Stimulation+for+Chronic+Low+Back+Pain&ExpandComments=y&CommentPeriod=0&ver=14&NCDId=82&ncdver=1&bc=AgBAAAAAIEAAAA%3D%3D&>

ARM asks CMS to work broadly with stakeholders in the regenerative medicine community to identify improvements to the Medicare program that will allow it to take into account the value of these new therapies more accurately in the future.

Thank you for your consideration. Please contact me at rfalb@alliancerm.org with questions.

Sincerely,

A handwritten signature in black ink that reads "Robert J. Falb". The signature is written in a cursive style with a large, sweeping initial "R".

Robert J. Falb
Director, U.S. Advocacy and Policy