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RE: Medicare Program; Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long-Term Care Hospital Prospective Payment System and Proposed Policy Changes and Fiscal Year 2019 Rates; Proposed Quality Reporting Requirements for Specific Providers; Proposed Medicare and Medicaid Electronic Health Record (EHR) Incentive Programs (Promoting Interoperability Programs) Requirements for Eligible Hospitals, Critical Access Hospitals and Eligible Professionals; Medicare Cost Reporting Requirements; and Physician Certification and Recertification of Claims

The Alliance for Regenerative Medicine (ARM) appreciates the opportunity to comment on the Center for Medicare & Medicaid Services' (CMS) Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long Term Care Hospital Prospective Payment System and Proposed Policy Changes and Fiscal Year 2019 Rates Proposed Rule (Proposed Rule).¹ Specifically, we are writing to thank CMS for all of its proposals and thoughts related to modifying Medicare's New Technology Add-on Payment Program (NTAP). ARM appreciates that CMS has discussed a few options to improve the current NTAP and overall MS-DRG system with a focus on creating a methodology and system that balances appropriate access and cost effective care to new and innovative therapies. ARM looks forward to working with CMS to create a transparent and predictable NTAP and MS-DRG system that will continue to stimulate and reward innovation in the inpatient setting.

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.

¹ 83 Fed. Reg. 20164 (May 7, 2018).

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 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 disk 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.

What's critical about all these technologies is that many of the products are transformative – they provide a durable therapeutic benefit or even a cure with a single administration of the therapy. The potential for dramatic clinical benefit is why these innovations are changing medical care and must be considered as part of the solution and not as part of the problem of rising overall drug costs.

I. CMS Should Establish a CCR of 1.0 for CAR-T Therapies

ARM appreciates CMS' various proposals on how to appropriately reimburse providers for administering CAR-T therapies. The agency's discussions include implementing a new MS-DRG for CAR-T therapies, establishing a cost-to-charge (CCR) of 1.0, using MS-DRG 016 as a reference for the NTAP, taking into account an appropriate portion of the average sales price (ASP) for these drugs², and/or some combination of these proposals.³ In finalizing its proposal, ARM believes that CMS should establish a payment policy that complies with Congressional intent when it created the NTAP to establish an additional payment that adequately reflects the estimated average cost of such service or technology.⁴ Further, Congress instructed CMS that this additional payment might be satisfied by means of a new technology group known as an "add-on payment," that is, a payment adjustment or any other similar mechanism for increasing the amount as long as it represents the estimated average cost of such service or technology.⁵

In addition to complying with Congressional intent, ARM believes that reimbursement policies should not drive site of care. Currently, under the outpatient setting, providers are reimbursed based on the ASP methodology, which by congressional design closely mirrors actual acquisition cost.⁶ As such, the final reimbursement methodology in the inpatient setting should equally mirror hospital costs to ensure that site of care does not determine access.

CMS states that using a CCR of 1.0 for charges associated with the CAR-T therapies would help approximate hospital costs because "hospitals would be unlikely to set charges different from the costs of the CAR-T therapies."⁷ ARM agrees with this approach because it will most closely align costs of care with payment and avoid significant financial losses for hospitals. In addition, ARM believes that a CCR of 1.0 will help CMS set an appropriate coverage and payment approach for CAR-T therapies post NTAP within the overall MS-DRG system. Therefore, ARM urges CMS to finalize its payment proposal of implementing a CCR of 1.0 for the CAR-T therapies.⁸

As mentioned above, CMS also proposes to assign CAR-T cases to MS DRG 016. In the absence of a new MS-DRG, (ARM supports the establishment of a new MS-DRG, which is detailed below), CMS should finalize a CCR of 1.0 for the NTAPs assigned to this MS-DRG. ARM believes that a CCR of 1.0 will help CMS comply with congressional intent and more importantly establish a reimbursement

² ARM understands that some stakeholders may be advocating for reimbursement rate based on ASP. ARM would support that conclusion as well for the same general reasons of support of a CCR of 1.0 as a part of the final payment rate.

³ 83 Fed. Reg. 20189.

⁴ SSA §1886(d)(5)(k)(ii)(III).

⁵ SSA §1886(d)(5)(k)(v).

⁶ SSA §1847A.

⁷ 83 Fed. Reg. 20189.

⁸ ARM also urges CMS to consider applying this methodology to all current and future orphan therapies that equally represent reimbursement and access challenges to hospitals and patients respectfully in the inpatient setting.

methodology that will promote appropriate overall and site of care access by avoiding significant financial losses for hospitals.

II. CMS Should Also Establish a New MS-DRG For CAR-T Therapies

Congress also provided CMS the authority to create “a new technology group” to effectuate additional payment for new technologies eligible for a NTAP.⁹ CMS states that in considering a new MS-DRG, “it considers whether the resource consumption and clinical characteristics of the patients with a given set of conditions are significantly different that the remaining patients in the MS-DRG.”¹⁰ CMS further adds that “in evaluating resources costs, we consider both the absolute and percentage differences in average costs between the cases we select and review the remainder of cases in the MS-DRG.”¹¹ ARM believes that given the resources used for MS-DRG 016 and the clinical characteristics of the patients assigned to MS-DRG 016 as compared to CAR-T therapies that CMS must establish a new MS-DRG for these patients. The clinical characteristics, treatment process, side effects and resource utilization for patients with diffuse large B-cell lymphoma (DLBCL) who receive CAR-T differs significantly from those patients receiving a bone marrow transplant as characterized by MS-DRG 016. Specifically, patients receiving CAR-T cells may have worse comorbidities and also have less treatment options for their disease than patients receiving autologous stem cell transplants (ASCT). For example, high-dose chemotherapy with ASCT is used as second-line treatment for patients who have responded to first-line therapy and then have experienced a relapse. Patients eligible for ASCT have chemosensitive disease and are generally younger and have fewer comorbidities than patients who are not eligible for ASCT. By contrast, patients who are approved to receive YESCARTA™ have disease that is refractory or relapsed to two or more lines of therapy and are deemed chemo-insensitive; they may have already undergone a prior ASCT or may not be a candidate for ASCT due to their comorbidities. As a result of these clinical differences there is a significantly greater resource utilization for CAR-T cases relative to other cases in MS-DRG 016. Therefore, ARM urges CMS to focus on creating a new MS-DRG for CAR-T cases with a CCR of 1.0.

In addition, the creation of a new MS-DRG would establish a transparent and predictable reimbursement infrastructure for providers that would mitigate or avoid significant financial losses. The new MS-DRG would be a stable approach towards reimbursing new CAR-T therapies that will help promote access to these therapies in the inpatient setting. ARM, however, urges CMS to include both the therapy costs and all of the associated care services for the delivery of the CAR-T within this new MS-DRG. Without these important and associated costs, the new MS-DRG would not achieve its intended purpose of providing appropriate reimbursement and subsequent patient access to these novel treatments. Finally, ARM notes that many Medicaid programs rely on CMS’ policies to establish reimbursement rates for Medicaid patients such that a new MS-DRG would also have a positive impact on

⁹ SSA §1886(d)(5)(k)(v).

¹⁰ 83 Fed. Reg. 20189.

¹¹ 83 Fed. Reg. 20189.

Medicaid programs. In conclusion, ARM urges CMS to establish a CCR of 1.0 and a new MS-DRG for CAR-T therapies. The combination of these two policies will help ensure appropriate access in the inpatient setting both in the near term and the long term for both Medicare and Medicaid programs.

III. Proposed Add-On Payments for New Services and Technologies for FY 2019

Congress required that the new technology represent an advance in medical technology that substantially improves the diagnosis or treatment of individuals.¹² As stated above, regenerative medicine and advanced therapies on the market and in the pipeline epitomize Congress' statement on new technologies. Regenerative therapies, such as CAR-T have already and will continue to demonstrate substantial clinical improvement by improving health outcomes and hold the promise of reducing overall health care costs. Hundreds of regenerative medicine products in clinical trials hold similar promise to treat unmet medical needs, improve patient care, and bend the health care cost curve in ways that current forms of clinical care have not been able to achieve. Many of the diseases targeted by regenerative medicine researchers and product developers, such as heart disease, diabetes and musculoskeletal conditions, are chronic conditions that affect millions of American families and are major cost drivers for Medicare.

Congress, however, did not require the new medical technology to be a novel mechanism of action, to treat a different patient population, or have a certain clinical trial size. These criteria were developed by CMS, and ARM believes that CMS should update and/or eliminate many of these criteria as they represent a significant barrier to access to new therapies for Medicare beneficiaries in the inpatient setting.

A. CMS Should Recognize Certain FDA Approval Designations As Dispositive for Newness and Substantial Clinical Improvement NTAP Criteria

CMS' regulations implementing the NTAP provisions specify three criteria for a medical service or technology to receive the additional payment: (1) the medical service or technology must be new; (2) the service or technology must demonstrate a substantial clinical improvement over existing services or technologies; and, (3) the medical service or technology must be costly such that the DRG rate otherwise applicable to discharges involving the medical service or technology is determined to be inadequate. ARM believes that CMS' application of the first two criteria, created as part of the eligibility process, is being inappropriately applied to cell and gene therapies and therefore should be modified.

1. Substantial Clinical Improvement:

¹² 83 Fed. Reg. 20279.

Regarding substantial clinical improvement, CMS notes that the agency “evaluates whether the use of the device, drug, service or technology significantly improves clinical outcomes for a patient population as compared to currently available treatments”¹³ as a determining factor of substantial clinical improvement. ARM previously stated and continues to believe that this standard was created by Congress and CMS for medical devices as that was the prevailing new technology of the time. This standard, however, should not be applied to regenerative medicine therapies because these criteria are likely outside Congressional intent because it is inconsistent with some of the congressionally created FDA approval rules related to expedited approval programs. Specifically, the FDA defines the congressionally created “breakthrough therapy” and designates a therapy as such if it “may demonstrate substantial improvement over existing therapies.” In addition, the Regenerative Medicine Advanced Therapy (RMAT) designation is granted to products that are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and if clinical evidence shows that it has the potential to meet an unmet medical need. ARM therefore believes that CMS’ substantial clinical improvement criteria should not apply to any therapy that has a Breakthrough or RMAT designation from the FDA.

In response, CMS states that “if the technology has a status designated by the FDA that is similar to the standards and conditions required to demonstrate substantial clinical improvement under the new technology add-on payment criterion, or is designated as a breakthrough therapy, the technology should be able to demonstrate with evidence that it meets the new technology add-on payment substantial clinical improvement criterion.”¹⁴ ARM appreciates CMS’ stated connection between the FDA designation and its belief that the technology “should be able to demonstrate substantial clinical improvement criterion.” ARM, however, questions why CMS continues to raise concerns regarding the substantial clinical improvement criterion for each application that has a Breakthrough or RMAT designation from the FDA.

In raising concerns with each NTAP application that has one of the aforementioned FDA designations, it seems to ARM that CMS questions the validity of the FDA designation and the ability of the technology to meet the substantial clinical improvement criterion, which was just satisfied via FDA designation. For example, CMS continues to raise patient mortality data and few published results showing survival benefit as concerns for satisfying substantial clinical improvement. Yet, the FDA designated the therapy as RMAT or Breakthrough because it demonstrated substantial clinical improvement based on these same characteristics and then approved it based on the same criteria. The FDA has the authority to revoke the designation should the agency believe that the therapy no longer meets this criteria such that if the NTAP applicant was approved with a FDA Breakthrough or RMAT designation it should be definition satisfy the substantial clinical improvement criterion.

¹³ 83 Fed. Reg. 20279.

¹⁴ 83 Fed. Reg. 20279.

ARM believes that by continuously raising patient mortality data and few published results showing survival benefit as concerns for the NTAP, CMS seems to be contradicting itself. First, the agency states that the same data that FDA relied upon for Breakthrough or RMAT designation and subsequent FDA approval should suffice for the NTAP. Yet, the agency then questions patient mortality data and few published results showing survival benefit as concerns related to eligibility for the NTAP. ARM believes that CMS cannot state that the technology should have no problem meeting substantial clinical improvement standard for NTAP approval while simultaneously questioning the same data used to demonstrate FDA designation and approval. To reconcile this contradiction, ARM believes that if the FDA approved a therapy with a Breakthrough or RMAT designation and has not revoked the designation, the substantial clinical improvement criterion should automatically be satisfied.

i. Clinical Trial Size on a FDA Approved Therapy Should Never Disqualify a NTAP Application

In addition, in recent NTAP applications, CMS has questioned how clinical improvement can be measured and achieved via the small clinical trials that generated FDA approval. ARM is concerned that this view sets a dangerous precedent by significantly undervaluing new transformative therapies. Cell and gene therapies often target small patient populations as developers are attempting to cure rare diseases or previously untreatable subsets of patients. Therefore, by necessity, the sizes of clinical trials for these products will be small and frequently can include surrogate measures of efficacy, with long-term post-approval patient follow-up expected. The FDA recognizes this and often only requires single-arm trials with small numbers of patients for these products. It is often not feasible for product developers to provide data on a large number of patients, especially those working in rare diseases, as many regenerative and advanced therapeutic developers are.

In response, CMS states that “it accepts different types of data (for example, peer-reviewed articles, study results, or letters from major associations, among others) that demonstrate and support the substantial clinical improvement associated with the new medical service or technology’s use. In addition to clinical data, we will consider any evidence that would support the conclusion of a substantial clinical improvement associated with a new medical service or technology.”¹⁵ ARM appreciates that the agency considers a wide range of data to support substantial clinical improvement but given the FDA approval process and the nature of clinical trial design for this class of transformative products, small clinical trial size should never be a reason for CMS to deny an NTAP.

In addition, for those therapies without such designations, ARM believes that the substantial clinical improvement standard is an inappropriate clinical standard for the family of regenerative therapies as it creates a threshold that is too high and unrealistic. Requiring a vague standard such as “substantial clinical improvement”

¹⁵ *Id.*

ignores ARM's belief that innovation should be patient focused. By only qualifying new technologies that can achieve such a vague standard, CMS' policy is at cross-purposes with promoting innovation because many worthy technologies would not be approved by CMS.

2. Newness:

Similar to the substantial clinical improvement requirement, ARM believes that the current newness criteria are inappropriate for regenerative and advanced therapies. Specifically, CMS established the additional criteria requiring an applicant to show its technology is not "substantially similar" to existing technologies and does not treat the same or similar disease. As noted earlier, products that receive Breakthrough or RMAT designations are by definition determined by the FDA to be an improvement over existing therapies or treat unmet medical needs. If FDA makes this determination, it would be inconsistent for CMS to make a clinical determination that such a product is "substantially similar" to an existing product and therefore does not satisfy the newness criterion. Moreover, given the incremental nature of technological advancement, the ability of CMS to determine when a product meets a "newness" standard is not clear. For these reasons, ARM believes that products that receive a Breakthrough or RMAT designation from the FDA should automatically meet the newness criterion.

B. CMS' Application of NTAP Criteria to Current Applications

CMS provides a detailed review of the NTAP applications for Kymriah and Yescarta, which are CD-19-directed T-cell immunotherapies used to treat certain patients with aggressive variations of non-Hodgkin lymphoma (NHL). For purposes of satisfying the newness criterion, the agency concludes that the two technologies are substantially similar to each other because CMS "believes that these technologies are intended to treat the same or similar disease in the same or similar patient population, and are purposed to achieve the same therapeutic outcome using the same or similar mechanism of action."¹⁶ ARM appreciates CMS' consideration of the two NTAP applications and supports granting NTAP status to the two CAR-T therapies.

From a technology point of view, ARM has serious concerns with CMS' conclusion that the two CAR-T therapies are substantially similar to each other. As mentioned above, each therapy has separate FDA Breakthrough designations, are approved via separate Biological License Applications and will likely treat different patient populations in different sites of care (verify—not each site will administer each therapy). As such, ARM believes that for purposes of meeting the newness criterion, each NTAP application must be treated as unique. The ARM does however recognize that should the agency create a new MS-DRG for CAR-T therapies each of the CAR-T therapies will be assigned to the same MS-DRG, which ARM supports.

¹⁶ 83 Fed. Reg. 20286.

IV. CMS Should Establish a More Frequent NTAP Process

The current process provides for NTAPs to hospitals to occur only at the beginning of the fiscal year. ARM believes that this requirement unnecessarily delays access to innovative and often lifesaving therapies for Medicare beneficiaries. This delay could mean the difference between life and death. As such, ARM urges CMS to implement a quarterly NTAP approval process similar to the current outpatient pass through process.

V. Conclusion

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. Specifically, by reducing hospital care, the need for physician, clinical and professional services, nursing and home healthcare, we could substantially reduce overall healthcare expenses. The 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.

ARM supports the goals of NTAP. It is critical for CMS to develop and implement policies and programs that support use of new technologies such as a CCR of 1.0 and a new MS-DRG. This is particularly true for regenerative medicine and other advanced therapies that hold the promise of durably treating and potentially even curing disease. We thank the agency for its many proposals in the Proposed Rule and look forward to working with CMS to establish policies that promote appropriate access to regenerative medicine therapies in both the near term and long.

Sincerely,



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Alliance for Regenerative Medicine