

ALLIANCE_{for} *Regenerative Medicine*

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My name is Michael Werner and I am co-founder and Senior Policy Counsel for The Alliance for Regenerative Medicine (ARM). Thank you for the opportunity to make the following comments today. 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 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.

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. This potential for a dramatically greater clinical benefit is how these innovations are changing medical care.

Let me give you a few examples:

Emily Whitehead was diagnosed with an aggressive form of cancer called acute lymphoblastic leukemia (ALL) at the age of 5 in 2010. She had relapsed twice after chemotherapy and was near death when she was treated at the Children's Hospital of Philadelphia (CHOP) with an experimental chimeric antigen receptor T cell (CAR-T) gene therapy that saved her life. Her dad reports that she is now 5'6" tall and in 7th grade and she just made high honor roll on her report card last week. Subsequently published data has shown that, similar to Emily, a high percentage of patients with relapsed refractory ALL treated with the same type of CAR T-cell therapy had their disease go into complete remission.

Nicole Gularte has survived leukemia (ALL) seven times. On October 26, 2010, she began treatment at Stanford University Cancer Center. After years of various treatments that weren't effective, and being told by doctors that she only had 3-5 weeks to live, she too received a CAR T-cell therapy. On October 4, 2016, she achieved a full remission.

As reported last November, doctors in Germany used gene therapy to regrow a boy's skin, saving his life. The boy, Hassan, suffered from severe junctional epidermolysis bullosa, a genetic mutation which causes fragile, blister- and tear-prone skin, leading to infections and skin cancer, causing patients severe pain and lifetime of covering their wounds with extensive, expensive specialized bandaging. Now two years later, the boy is healthy and leads a normal life.

Although Congress could never have anticipated gene therapy in 1983, surely it did not intend the Medicare program to supplement reimbursement for new technologies used in the hospital inpatient setting (the New Technology Add-On Payment or "NTAP") to be a barrier rather than a facilitator of new therapies like these.

NTAP History:

In 1983 when Congress created the Inpatient Prospective Payment System, regenerative and advanced technologies were closer to science fiction than the clinical reality they are today. As such, Congress likely did not find the need to include a mechanism or methodology that adequately reimburses hospitals for providing these types

of new and innovative technologies. However, in efforts to recognize the value of new technologies, Congress, in 2000, required CMS to establish a mechanism to recognize the costs of new medical services and technologies in the inpatient setting for discharges beginning on or after October 1, 2001.

Specifically, Congress instructed CMS to “provide for additional payment...in an amount that adequately reflects the estimated average cost of such service or technology.” 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.

Congress also required that the new technology represent an advance in medical technology that substantially improves the diagnosis or treatment of individuals. As stated above, regenerative medicine and advanced therapies on the market and in the pipeline epitomize Congress’ payment approach for new technologies. Regenerative therapies have already demonstrated substantial clinical improvement by improving health outcomes. They also 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.

Importantly, Congress did not require the new medical technology to be a novel mechanism of action, to treat a different patient population than existing therapies, or have a certain clinical trial size. These criteria were developed by CMS, and ARM is here today to urge CMS to update and/or eliminate many of these criteria as they represent a significant barrier to access to new regenerative therapies for Medicare beneficiaries in the inpatient setting. Without updating some of the NTAP’s eligibility criteria and changing the current reimbursement rate to be more in line with congressional intent, many of the technologies described above will be out of reach for Medicare beneficiaries, or worse, never be developed due to CMS’ insufficient eligibility criteria and payment rate.

ARM therefore urges CMS to modernize the NTAP Program with a particular focus on promoting timely beneficiary access to regenerative and advanced therapies. Specifically, ARM has concerns with CMS’s payment rate, the substantial clinical improvement requirement, and the agency’s definition of newness when applied to “new technologies.”

NTAP Payments:

Regarding NTAP payments, CMS implemented the Congressional requirement of “adequately reflect[ing] the estimated average costs” by reimbursing the lesser of two amounts, 50 percent of the amount by which the total covered costs of the case exceed the

MS-DRG payment, or 50 percent of the costs of the new technology, as determined by CMS. This is meant to compensate for CMS determining that payment for the new technology or service under the existing DRG is “inadequate” ARM believes that these payment amounts are inconsistent with the language and intent of the statute and insufficient in the context of regenerative therapies.

Simply put, 50 percent of the costs or the amount over the total DRG payment is not an accurate valuation of these new technologies. Consequently, it provides a dis-incentive for these products to be used in the hospital setting. That, in turn, will limit patient access to these products in the short term and could stifle the development of similar therapies in the long term. This is inconsistent with the statutory language and Congressional intent behind NTAP.

ARM appreciates that when CMS developed the 50 percent standard, no one could have envisioned the power of new regenerative therapies. It is that unprecedented clinical benefit, however, that provides the rationale for why CMS must change its payment approach for these therapies to either increase the payment rate or create congressionally authorized new technology DRG groups that capture the entire costs of the patient’s cost of care.

NTAP Criteria:

CMS’ regulations implementing the NTAP provisions specify two additional criteria for a medical service or technology to receive the additional payment: (1) the medical service or technology must be new; and (2) the service or technology must demonstrate a substantial clinical improvement over existing services or technologies. ARM believes that CMS’ application of these criteria, created as part of the eligibility process, is inappropriate when applied to cell and gene therapies, and therefore should be modified.

Substantial Clinical Improvement:

Regarding substantial clinical improvement, CMS historically has noted that a new technology is an appropriate candidate for an additional payment “when it represents an advance that substantially improves, relative to technologies previously available, the diagnosis or treatment of Medicare beneficiaries.”

This standard was created by Congress and CMS for medical devices as that was the dominant new technology of the time. But it should not be applied to regenerative medicine therapies because it is likely outside Congressional intent as it is inconsistent with Congressionally created FDA expedited approval programs. Specifically, the FDA will designate a product as a “breakthrough therapy” if it “demonstrate[s] substantial improvement over existing therapies.” In addition, the Regenerative Medicine Advanced Therapy (RMAT) designation established by Congress in the 21st Century Cures Act 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 addition, for those regenerative therapies without such designations, ARM believes that the substantial clinical improvement standard is as it creates an unrealistic and vague threshold. It ignores ARM's experience that innovation is achieved incrementally. By only qualifying new technologies that can achieve this standard, CMS' policy is at cross-purposes with promoting innovation because many worthy technologies will not be not approved by CMS and society therefore never has the chance to learn and otherwise benefit from those technologies.

In recent NTAP applications, CMS has questioned how clinical improvement can be measured and achieved via the small clinical trials that generated FDA approval. Applying this standard of clinical improvement is inappropriate and 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. Given the transformative nature of the products, this should not be a reason for CMS to ever deny an NTAP payment.

Newness:

Similar to the substantial clinical improvement requirement, ARM believes that CMS' application of 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 to 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. In addition, simply because a new therapy treats the same disease as an existing approach, this does not mean it is not considered "new". Moreover, given the incremental nature of technological advancement, the ability of CMS to determine when a product meets a "newness" standard is not clear.

Conclusion:

In conclusion, 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, overall healthcare expenses could be substantially reduced, since together these categories comprise 62 percent of all healthcare-related expenses.

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. This is particularly true for regenerative medicine and other advanced therapies that hold the promise of durably treating and potentially even curing disease. We ask the Agency to work broadly with stakeholders in the regenerative medicine community to identify improvements to the program that will allow it to take into account the value these new therapies more accurately in the future.

Thank you.