American Society of Gene + Cell Therapy

October 21, 2020

The Honorable Diana DeGette
2111 Rayburn House Office Building
Washington, DC 20515

The Honorable Fred Upton
2183 Rayburn House Office Building
Washington, DC 20515

Dear Congresswoman DeGette and Congressman Upton,

The American Society of Gene and Cell Therapy (ASGCT) appreciates the opportunity to provide feedback on the 21st Century Cures 2.0 concept paper. ASGCT is a nonprofit professional membership organization comprised of more than 4,400 scientists, physicians, and other professionals working in gene and cell therapy in settings such as universities, hospitals, and biotechnology companies. Many of our members have spent their careers in this field performing the underlying research that has led to today's robust pipeline of transformative therapies.

A core portion of the Society's mission is to advance the discovery and clinical application of genetic and cellular therapies to alleviate human disease. Therefore, the development and accessibility to patients of such therapies is of paramount importance to ASGCT. The Society supports robust research funding; full coverage, and sufficient reimbursement of providers, for approved therapies; and payment models that foster patient access. These positions do not imply endorsement of any individual pricing decisions.

ASGCT submitted comments to the Cures 2.0 Call to Action in December 2019. We now expand upon those comments to answer several of the questions posed in the resultant concept paper to support policy development.

General Coverage and Reimbursement Modernization and Gene and Cell Therapies

Are there current coverage and reimbursement rules for new medical products under federally-financed health programs that are outdated or in need of reform? If so, what are they?

Are the current coverage and reimbursement approaches to new medical products or other modern technologies adequate to keep up with the pace of innovation? If not, why?

Are there barriers that impede or otherwise slow coverage for new cell and gene therapy products? If so, what are they?

Are there improvements that can be made under federally-financed health programs to improve coverage and patient access of these therapies?

Current federally financed coverage and reimbursement mechanisms for new medical products are outdated in their ability to accommodate the gene and cell therapies that consist of a one-time biologic product, plus services to provide the therapy. These mechanisms create limitations to patient access, as evidenced by the low numbers of patients treated by CAR T-cell therapies, especially in the Medicare population. Only 94 Medicare beneficiaries received inpatient CAR T-cell therapy outside of clinical trials per the September 2019 update of the FY 2019 MedPAR data file that reported ICD–10–PCS procedure codes XW033C3 or XW043C3.[1] Only 24 Medicare patients received CAR T-cell therapy in 2019 on an outpatient basis.[2]

With over 60 durable cell and gene therapies likely to be approved in the US by 2030,[3] it is critical these mechanisms are reformed to keep pace with innovation. There are several components of federal coverage and reimbursement policy in need of reform in order to provide patient access and continue to incentivize the development of a robust pipeline of gene therapies that we will address in our comments: (1) Medicare inpatient payment system, (2) novel payment models, (3) coding, and (4) rapid and clear coverage determinations While we appreciate that CMS has taken steps to address some issues for particular products, the system is not sufficiently nimble to be able to incorporate multiple new therapies into the healthcare system.

Medicare Inpatient Payment System

The limitations of inpatient Medicare reimbursement rules were demonstrated with the process of reimbursement of the CAR T-cell therapies approved in 2017. First, addressing reimbursement decisions within the annual rulemaking cycle for the inpatient prospective payment system resulted in delays until FY 2019 of CAR T-cell therapy assignment to a consistent MS-DRG and approvals of new technology add-on payments (NTAPs). This situation led to highly significant gaps in reimbursement levels to providers, limiting their ability to provide them.

In addition, the partial solutions CMS enacted were specifically for CAR T-cell therapies, with uncertainty as to how the Agency will approach future gene and cell therapies. We support a more holistic approach that provides a clear sense to stakeholders—patients, providers, and

[1] Centers for Medicare & Medicaid Services (2020). FY 2021 IPPS Final Rule. Page 58452. Available at: https://www.govinfo.gov/content/pkg/FR-2020-09-18/pdf/2020-19637.pdf
[2] Centers for Medicare & Medicaid Services. (April 6, 2020). *Announcement of Calendar Year (CY) 2021 Medicare Advantage (MA) Capitation Rates and Part C and Part D Payment Policies.* Available at: https://www.cms.gov/files/document/2021-announcement.pdf
[3] MIT NEWDIGS FoCUS Project. (July 29, 2020). *Updated projection of US durable cell and gene therapies product-indication approvals based on December 2019 development pipeline.* Available at: https://newdigs.mit.edu/sites/default/files/NEWDIGS-Research-Brief-2020F207v51-PipelineAnalysis.pdf

manufacturers—regarding how Medicare will cover and reimburse for new cell and gene therapies coming to market.

The most likely solution to provide the most appropriate reimbursement level for new gene and cell therapies would be to pay the biologic acquisition cost separately as a pass-through payment in the inpatient setting, as is done in the outpatient setting. This reimbursement approach would also promote comparability between the inpatient and outpatient settings, significant in encouraging site selection based on the safety and medical needs of individual patients, without the potential for cost considerations. A similar approach is being used for gene and cell therapy reimbursement by some state Medicaid programs, such as the state of New York,[4,5,6] and has precedent in the Medicare reimbursement of hemophilia blood clotting factors. In the absence of such wholesale change, we recommend reforms of the following inpatient payment system components.

New Technology Add-On Payments (NTAPs)

The NTAP should be more immediately accessible for new technologies coming to market, including through alteration of the timing of consideration for those new products. The current system's tie to the annual rulemaking process is of particular concern. Timing for FDA approval is based upon time of application filing and not an annual cycle. The NTAP process should be reformed to match a product's marketing approval, not an annual rulemaking cycle.

ASGCT therefore recommends:

- The current NTAP process to allow for quarterly review of NTAP-qualifying products approved by the FDA, regardless of the approval pathway. The current NTAP process window (i.e., FDA approval requirement of July 1) is much too narrow, as CMS has already recognized for certain antimicrobial, antibacterial, and antifungal products.
- Manufacturers to be allowed to apply for NTAP when they have data to complete an NTAP application and "pend" those applications deemed to meet the applicable NTAP criterion until the FDA has approved the product, and manufacturers have had an opportunity to bring the products to market.
- An increase in the cap for NTAP amounts from 65 percent to 100 percent or use uniform NTAPs equal to the product acquisition cost for gene and cell therapies. The Society appreciates the recent actions of CMS to increase the NTAP cap in FY 2020

[4] New York State Department of Health. (2017). New York State Medicaid Update, Volume 33, Number 11. Available at: https://www.health.ny.gov/health_care/medicaid/program/update/2017/201711.htm #tisagenlecleucel. Accessed May 6, 2018.
[5] New York State Department of Health. (2018). New York State Medicaid Update, Volume 34, Number 1. Available at: https://www.health.ny.gov/health_care/medicaid/program/update/2018/2018-01.htm#yescarta. Accessed May 6, 2018.
[6] New York State Department of Health. (2018). New York State Medicaid Update, Volume 34 - Number 3. Available at: https://www.health.ny.gov/health_care/medicaid/program/update/2018/2018-03.htm#luxturna. Accessed May 6, 2018.

from 50 percent to 65 percent; however, even the 65 percent level does not sufficiently fill the gap in reimbursement to providers.
- Extending the length of NTAP eligibility to three full years to allow increased collection of cost data for the small populations often treated by gene and cell therapies, prior to rate-setting.

Establishment of New MS-DRGs

Because the process for establishing new MS-DRGs is dependent upon CMS having sufficient data on charges for a therapy, the creation of DRGs for gene and cell therapies for rare diseases with small populations can be delayed well past the NTAP period. If CMS intends to pay for future gene and cell therapies in a similar fashion to CAR T-cell therapy through NTAP assignment as applicable, followed by the establishment of new DRGs, CMS must continue to recognize the limited patient populations (especially for products indicated for rare diseases) when considering the number of cases, excluding clinical trials cases, sufficient to establish a new DRG. ASGCT encourages Congress to clarify that DRGs should be established prior to NTAP expiration and to identify the case parameters to utilize to prevent patient access challenges.

Charge Compression

The issue of charge compression creates an added layer of uncertainty in the gene and cell therapy markets. CMS employs cost-to-charge ratios (CCRs) to determine reimbursement under the assumption that hospitals will mark up the cost of their charges. Yet, CMS policies around price transparency push incentives in the opposite direction, leaving many hospitals with a difficult decision—to either appear to be inflating the cost of products or be exposed to the impact of a CCR.

To create a more fair and balanced system that does not have troublesome incentives for providers or negative impacts on patient access to high-cost, single-administration, transformative gene and cell therapies, Congress should charge CMS with creating a new national cost center specific to capturing charges for FDA-approved cell therapies reported using revenue code 0891. This will allow CMS to create a more robust and accurate CCR that would be used in future rate-setting to reduce revenue code 0891 billed charges to costs with significantly mitigated charge compression. This modification is especially important to setting the most accurate relative weight possible, which will be particularly important to those treatment centers in low wage-index areas, as they will not receive an upward adjustment through the application of the wage-index adjustment to help offset acquisition costs.

Novel Payment Models

Our current insurance system was not designed with the prospect of curative drugs and biological products in mind. State Medicaid programs, which need to fit into a balanced state budget each year, are even harder pressed to adapt to absorbing the cost of a one-time curative

treatment, rather than to continue to pay for chronic care. To this end, many policymakers have proposed allowing value-based, risk-sharing arrangements that would spread the payments of these therapies over a specified period, provided the product continues to demonstrate predicted outcomes. ASGCT supports this proposal, as such arrangements could provide cost savings to state Medicaid programs by tying all or a portion of cost to successful patient outcomes, thereby redistributing some risk of uncertain outcomes from payers to manufacturers, and distributing costs more equitably based on individual patient outcomes.[7]

Medicaid Best Price reporting requirements pose potential barriers to these kinds of novel payment models for gene and cell therapies for both state Medicaid programs and private payers. CMS recently issued a proposed rule to adjust these reporting requirements to delineate separate best prices for value-based purchasing arrangements and for standard payments.[8] This proposed rule does not, however, enable payment over time, which would address the intended one-time nature of gene therapies. Under such arrangements, combined with value-based payment, if a product stops providing benefit, the payer would stop making payments, thereby also tying a portion of cost to product durability.

CMS has clarified they believe that legislation is needed to establish the mechanisms to prevent partial payments made through an installment arrangement from being reported as if they are full payments, to be averaged into the average manufacturer's price (AMP) for the determination of Medicaid best price.

Legislation could also be used clarify that these novel payment methods do not violate the Anti-Kickback Statute and Stark Law. An existing safe harbor allows the provision of rebates up to 30 months after treatment; extending the safe harbor for rebates beyond this time frame would allow rebates for products to be provided if efficacy ceases after a number of years.

As payment-over-time arrangements are developed, policymakers should make sure to consider the role of providers in the purchasing scheme of gene and cell therapies. To prevent the patient access barriers due to insufficient payment for future products that were seen for CAR T-cell therapy, payments should be made either directly between payers and manufacturers, or if providers are also able to pay the manufacturer for a therapy in installment payments if reimbursement is made in installment payments.

Because the CMS proposed rule does not have a deadline for finalization, and because important aspects like the ability to pay over time may require legislative changes, the Society encourages Congress to consider a legislative means for enabling novel payment models for gene and cell therapies.

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[7] As a scientific research association, ASGCT recognizes the challenges of identifying appropriate outcome measures for use as indicators of treatment success. We offer the scientific expertise of our membership as a resource to you and to CMS in assessing the appropriateness of proposed outcomes measures within value-based purchasing arrangements.

[8] Department of Health and Human Services. (2020). *Proposed rule: Establishing Minimum Standards in Medicaid State Drug Utilization Review (DUR) and Supporting Value Based Payments (VBP) for Drugs Covered in Medicaid (CMS-2482).* Available at https://www.reginfo.gov/public/do/eAgendaViewRule?pubId=202004&RIN=0938-AT82

Coding

Under Medicare, barriers that impede or slow coverage of new cell and gene therapy products include a lack of expedient assignment of new reporting and procedure codes. Coding confusion and resulting potential errors can lead to delays in coverage that can significantly affect patient outcomes, with potentially fatal consequences. We encourage the development of a consistent, transparent, and timely approach to coding decisions for new products that minimizes uncertainty in the process.

Clear Pathway to Medicare Coverage Upon FDA Approval

Currently, Medicare coverage of gene therapies is initially determined by local Medicare Administrative Contractors (MACs). In many cases this system works well; however, the experience with coverage of CAR T-cell therapy calls into question whether there needs to be a more streamlined and coordinated coverage process for these therapies.

After FDA approval, local MACs offered coverage for on-label uses of CAR-T therapies. In parallel, CMS began a national coverage determination process which resulted in a proposal to offer coverage with evidence development (CED). While we support post-market data collection, the CED scheme as proposed could have led to providers opting out of CED participation and thereby not providing the therapy to Medicare beneficiaries. This proposal was not finalized, but it raised questions about how the Agency will address coverage decisions for future approved products.

Providing sufficient coverage requires consideration of factors such as patient eligibility requirements, treatment or site criteria, and REMS or other marketing obligations already required by FDA. We therefore recommend expediting and streamlining Medicare coverage processes for innovative products in collaboration with FDA. This type of process has been proposed by CMS for breakthrough-designated medical devices – and we believe this model could be applied to RMAT or breakthrough designated drug and biological products to allow for prompt and ongoing patient access to gene and cell therapy products.[9]

Medical Products for Small Patient Populations

What are the biggest impediments to new cures development for these important populations?

What steps can policymakers take to address these impediments, if any?

Many of the diseases for which gene therapy offers great promise are rare inherited disorders. Of the 7,000 rare diseases that exist, which collectively affect 10 percent of the US population, 95

[9] Centers for Medicare & Medicaid Services. (2020). *Proposed Medicare Coverage of Innovative Technology (CMS-3372-P).* Available at https://www.cms.gov/newsroom/fact-sheets/proposed-medicare-coverage-innovative-technology-cms-3372-p

percent have no current treatment.[10] In addition to the scientific challenges to the development of treatments for these rare diseases the small patient population also presents policy and economic impediments. We suggest specific steps to overcome these barriers below.

Continue investment in basic research to build the scientific underpinnings of gene therapy which support the development of these transformative treatments

While NIH funding increases have been generous over the past five years, the need remains to maintain global leadership in medical innovation. Continued strong funding for multiple institutes and centers of the NIH supports basic, translational, and early clinical research on these rare diseases.

Specifically, as the genetic mutations for more rare diseases are identified, there is greater need for funding to support translational research to ready potential new gene therapy approaches for further clinical research. While gene therapies have reached the market, there is still a great scientific need to investigate the preclinical application of gene therapies to treat new diseases and improve the design of vector technologies.

The 21st Century Cures Act created the Regenerative Medicine Innovation Project (RMIP) to fund this type of research. The innovation project, which provides funding solely for early translational regenerative medicine research, helps to prioritize research into potential gene therapy products for diseases with small populations. While funding for the RMIP expires on September 30, we are encouraged that the goals of the program are being considered for codification in the Public Health Service Act as part of the TRANSPLANT Act (H.R. 4764). ASGCT encourages funding this critical research at NIH at $10,000,000 per year.

Support the Accelerating Medicines Partnership in Gene Therapy Program

A major barrier to the development of gene therapies for small populations is that the current costs associated with product development preclude commercial viability of products that would be used in less than approximately 100 individuals each year, posing an enormous challenge to development of treatments for these ultra-rare diseases.[11] ASGCT supports the 2021 launch of the Accelerating Medicines Partnership in Gene Therapy Program, a public-private partnership led by the Foundation for the NIH, that will fund research on gene therapy for 5-6 ultrarare diseases over five years using a standard menu of vectors, vector manufacturing processes, delivery methods, and clinical protocols, to advance them into the clinic (with NIH as the IND holder). The development of standard protocols for the development of gene therapy for ultrarare diseases that this project will support also has the potential to streamline gene therapy

[10] Institute of Medicine (US) Committee on Accelerating Rare Diseases Research and Orphan Product Development; Field, M.J., & Boat, T.F., editors. *Rare Diseases and Orphan Products: Accelerating Research and Development.* Washington (DC): National Academies Press (US); 2010. Available from www.ncbi.nlm.nih.gov/books/NBK56189. doi: 10.17226/12953.

[11] Marks, P.M. & Witten, C. (2020). Toward a new framework for the development of individualized therapies. *Gene Therapy.* Available from https://www.nature.com/articles/s41434-020-0143-y. doi: 10.1038/s41434-020-0143-y

development in general, to benefit the development of additional applications. ASGCT recommends robust support of this program.

Consider rare disease development risk when contemplating new policies

Diseases that have small populations of 100 or more do have the potential to be commercialized, but the level of risk involved for manufacturers and investors is a potential barrier to development. The entirely of a product's lifecycle plays into the risk calculation of product development, and thus many policies impact the development of transformative therapies for rare diseases even if that is not their stated goal. As Congress weighs reforms to insurance systems, drug pricing, and FDA process, ASGCT recommends that policymakers consider the impact these policies can have on the development of potentially curative therapies for small populations and avoid de-incentivizing development in this promising area.

Breakthrough Coverage

Are there barriers that impede coverage of technologies and therapies approved through FDA's breakthrough technologies and therapies pathways?

How do we expedite coverage while at the same time ensuring that additional evidence can be collected?

The barriers that impede coverage and adequate reimbursement for new gene and cell therapies described above are the same barriers faced by many FDA breakthrough-designated technologies. While greater systemic reforms are needed, we believe that the policy proposal in the concept paper to establish an automatic communication requirement between FDA and CMS for products granted Breakthrough Therapy Designation is a positive first step. The commencement of FDA communication with CMS upon the grant of these designations could facilitate better understanding regarding expectations for both payers and product developers, and therefore more timely data collection and coverage of gene and cell therapies. We recommend expanding this requirement to therapies that receive the Regenerative Medicine Advanced Therapy (RMAT) Designation, for which preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for a serious condition.

We further recommend greater coordination between CMS and FDA regarding the confirmatory evidence needed to fulfill post-marketing obligations and demonstrate effectiveness. These measures would allow for expedited coverage with subsequent collection of evidence through mechanisms that are already in place. The Society encourages consideration of additional ways for CMS and/or Congress to provide a more streamlined, consistent approach to providing immediate and uninterrupted coverage for these potentially lifesaving treatments.

Because gene therapies demonstrate a potential for substantial improvement over available therapies, or may become the first and only available therapy, for serious or life-threatening conditions, expeditious development is imperative and often leads to limited clinical trial populations to develop the evidence needed to support labeled indications. The potential for limited clinical trial populations is warranted to make transformative treatments available to

patients quickly but can cause payer misconceptions that after approval, only patients that meet the clinical trial criteria should be covered, rather than covering to the label. Under Medicaid, known problems exist with states failing to cover therapies to FDA-labeled indications, despite a federal requirement to do so.

Medicaid coverage for gene and cell therapies varies widely state-to-state. For CAR T-cell therapy, only 24 states have publicly available coverage policies. Coverage criteria are often more restrictive than the FDA label indication statements for both tisagenlecleucel (Kymriah) and axicabtagene ciloleucel (Yescarta), another approved CAR T therapy, and nearly half of states have site-of-care coverage restrictions (some for inpatient and some for outpatient administration). Barriers to Medicaid access are especially concerning for patients with potentially fatal and/or progressive diseases, for which early administration of a therapy may prevent, but not reverse, morbidities and mortality. State program denial of coverage for therapy for non-medical reasons is not appropriate. Enforcement of the requirement for Medicaid programs to cover gene therapies to the FDA-labeled indications would be a significant step in improving coverage and access to breakthrough- and RMAT-designated therapies.

ASGCT Support for Additional Policy Proposals

The Society is appreciative of your efforts to support treatments with curative potential, such as gene and cell therapies. In addition to the proposed policy on breakthrough designation mentioned above, we strongly support the following policy proposals in the concept paper:

- The policies listed to improve diversity in clinical trials, since we are aware of disparities in participation of minorities in clinical trials, which should be remedied.
- The technical provision to extend eligibility for breakthrough and RMAT designations to sponsors without an active IND in place that have collected scientifically valid preliminary clinical evidence from clinical studies in foreign countries, due to small patient populations for rare disease.

Thank you for your consideration of these comments. Please contact Betsy Foss-Campbell, Director of Policy and Advocacy, at bfoss@asgct.org with any questions. We look forward to further engaging with you in your legislative development process.

Sincerely,

Stephen Russell, MD, PhD
President
American Society of Gene & Cell Therapy