American Society of Gene + Cell Therapy

January 22, 2024

The Honorable Bill Cassidy
United States Senate
455 Dirksen Senate Office Building
Washington, DC 20510

Dear Ranking Member Cassidy,

The American Society of Gene and Cell Therapy (ASGCT) welcomes the opportunity to respond to your request for information on improving Americans' access to gene therapies. ASGCT is a nonprofit professional membership organization comprised of more than 6,200 scientists, physicians, patient advocates, and other professionals. Our members work in a wide range of settings including universities, hospitals, government agencies, foundations, and biotechnology and pharmaceutical 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 ASGCT's mission is to advance the discovery and clinical application of genetic and cellular therapies to alleviate human disease. To that end, ASGCT supports policies that foster the adoption of, and patient access to, new therapies, which thereby encourage continued development of these innovative treatments.

If you have questions about any of the information provided below, please contact Margarita Valdez Martínez, Director of Policy and Advocacy, at mvaldez@asgct.org.

Sincerely,

David Barrett, JD
Chief Executive Officer
American Society of Gene & Cell Therapy

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American Society of Gene + Cell Therapy

Request for Information from Stakeholders on Improving Americans' Access to Gene Therapies

Which Treatments Should Be Included?

1. How should lawmakers define an "ultra-rare" disease or disorder to determine when cell or gene therapies should be eligible for inclusion in new coverage or contracting requirements for those patients with an ultra-rare disease or disorder? What definitions should lawmakers consider?

In the United States, a rare disease is statutorily defined as a condition affecting fewer than 200,000 individuals (~0.06% of the population).[1] Patient advocates, product developers, and other stakeholders may also refer to "ultra-rare" diseases. While this is not term of art or currently defined, it is generally understood to refer to exceedingly small patient populations. There is not, however, universal agreement on whether this term should be defined by federal law or what a cutoff should be. ASGCT does not have a formal position on whether it would be advantageous to create a statutory definition of "ultra-rare disease," and our leadership will continue to evaluate the question.

There are several definitions of ultra-rare disease that the Committee could consider if it were to have continued interest in this topic:

- The Ultra-rare Gene-based Therapy (URGenT) Network at the National Institute of Neurological Disorders and Stroke defines an ultra-rare disorder as one that affects fewer than 6,000 people.[2] Based on current population levels, that metric equates to approximately 0.002% of the country's population.

- Outside the US, the National Institute for Health and Care Excellence (NICE) in the UK defines an ultra-rare disorder as one that affects 1 in 50,000 people,[3] and the Scottish Medicine Consortium created an "ultra orphan medicines" pathway for diseases affecting *fewer* than 1 in 50,000 people.[4] Meanwhile, Italy's Health Technology Assessment (HTA) agency considers a disease prevalence of one per million to represent an ultra-rare disease.[5]

- There are also a subset of diseases that arise from genetic mutations that are unique to a single individual, also known as "N of 1" diseases.

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[1] Morris, J.A. et al. (2021). Next-generation strategies for gene-targeted therapies of central nervous system disorders: A workshop summary. *Molecular Therapy, 29*(12), 3332-3344. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8636163/

[2] National Institute of Neurological Disorders and Sroke. (2021). *Ninds Launches URGenT: A Network to Accerlate the Development of Treatments for Ultra-rare Neurological Diseases.* https://www.ninds.nih.gov/news-events/directors-messages/all-directors-messages/ninds-launches-urgent-network-accelerate-development-treatments-ultra-rare-neurological-diseases

[3] Morris, J.A. et al. (2021). Next-generation strategies for gene-targeted therapies of central nervous system disorders: A workshop summary. *Molecular Therapy, 29*(12), 3332-3344. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8636163/

[4] Stafinski, T. et al. (2022). HTA decisión-making for drugs for rare diseases: Comparison of processes across countries. *Orphanet Journal of Rare Diseases, 17*. https://ojrd.biomedcentral.com/articles/10.1186/s13023-022-02397-4

[5] Usher, C. et al. (2019). Analysis of Health Technology Assessments of orphan drugs in Ireland from 2012 to 2017. *Pharmacoeconomics - Open, 3*(4), 583-589. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6861405/

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In the genetic disease community, the term ultra-rare often invokes both a disease's low prevalence and limited opportunities for therapeutic development and commercialization. In 2021 ASGCT hosted a *Forum on Gene Therapy for Underserved Populations*, in which panelists addressed approaches to creating alternative sustainable business models for development. These included the Bespoke Gene Therapy Consortium (a public-private partnership) and several different non-profit biotechnology models.[6]

What is the Current Practice for Patients with Ultra-Rare Diseases or Disorders?

ASGCT is a proud partner of many patient advocate organizations in the rare disease and gene therapy spaces. We believe their voices are best placed to answer the questions in this section (#3-10).

How Do Plans and Payers Currently Manage Financial Risk?

11. What does coverage for these therapies typically look like? What does the landscape look like for coverage of these therapies?

In 2023 ASGCT undertook an assessment of Medicaid coverage practices across a sample of 16 states and 3 MCOs. Our peer-reviewed white paper[7] was conducted against the backdrop of a robust pipeline of gene therapies in development[8] for conditions that will have large Medicaid populations. The one-time nature of these therapies, which result in durable benefits by treating the underlying cause of disease, result in high upfront high costs that will be difficult for state budgets to handle despite the long-term savings. In addition to identifying Medicaid coverage policies in the selected states, we sought to quantify common barriers to coverage access from a multi-stakeholder perspective and discuss federal policy options that could improve coverage to ensure equitable patient access in the Medicaid program.

Our white paper's key takeaway is that that states are not always adhering to the requirements to provide coverage for products to their "medically accepted" indication. States are narrowing coverage to populations covered in clinical trials, despite broader labeled indications; and many states require additional information or eligibility criteria that is not indicated in the drug's label.

ASGCT has no information to share at this time on the coverage landscape for private insurers.

How Do Physicians Provide Access to These Therapies?

ASGCT has been pleased to connect HELP staff with several of our physician members to provide feedback on the questions in this section (#34-38). Should the Committee seek additional insight on clinical issues, we would be happy to arrange further conversations.

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[6] American Society of Gene & Cell Therapy. (2021). *Forum on Gene Therapy for Underserved Populations.* https://asgct.org/events/underserved-populations-forum

[7] Allen, J. et al. (2023). Medicaid coverage practices for appvoed gene and cell therapies: Existing barriers and proposed policy solutions. *Molecular Therapy: Methods & Clinical Development, 29,* 513-521. https://asgct.org/ASGCT/media/about/Medicaid-paper.pdf?ext=.pdf

[8] American Society of Gene & Cell Therapy, Citeline. (2024). *Gene, Cell, & RNA Therapy Landscape: Q4 2023 Quarterly Data Report.* https://asgct.org/publications/landscape-report

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What is the Future of Access for These Therapies?

39. What is the appropriate role of the federal government in ensuring access to these therapies in the commercial market? How can any steps taken on the federal level ensure expanded access while not hurting innovation in this area?

ASGCT does not have specific information or recommendations to share about actions the federal government might take in the commercial insurance market, as ASGCT's members are broadly not subject matter specialists in that area. However, based on our previously referenced Medicaid study,[9] we can extrapolate that there are also likely challenges in the commercial market related to coverage for gene therapy products' full labeled indications. From our paper:

> "Federal law sets overarching requirements for state Medicaid programs, which mandate coverage of certain medical benefits. However, the bulk of the operational decisions are left at the discretion of each state, including enrollment eligibility, reimbursement methodology, and service coverage. Once approved by the Centers for Medicare and Medicaid Services (CMS), state Medicaid programs may draw down federal funds based on the federal medical assistance percentage (FMAP). Under the Medicaid Drug Rebate Program (MDRP), states that include prescription drug coverage in their Medicaid programs—which all states do—must cover all drugs approved by the Federal Drug Administration (with limited statutory exceptions) according to their 'medically accepted indications,' and in return manufacturers provide rebates on their products to the states, which are then shared between the states and the federal government…
>
> Despite general coverage to the labeled indication being mandated by federal law, variations in state plans, policies, and practices have created anecdotal inconsistencies regarding how therapies are covered, which populations they cover, and how quickly coverage is approved for individual patients. This leads to patient access issues, as denials or delays in coverage lead to delays in treatment. These disparities and delays all culminate into an unsustainable public payor system that undermines Medicaid's objectives to improve the care and health of its beneficiaries."

40. Should the federal government mandate coverage of these therapies? What markets (e.g. small, large group markets) or plans should be required to cover these therapies?

As noted above, federal law already requires that state Medicaid programs provide general coverage to the labeled indication. ASGCT has no official position at this time on federal coverage mandates for private insurers.

42. How should anticipated benefits from these therapies be evaluated against the potential costs of these therapies?

Gene therapy offers new and unique approaches to treating previously intractable diseases. Rather than treating disease symptoms, gene therapy can address the root causes of the

[9] Allen, J. et al. (2023). Medicaid coverage practices for appvoed gene and cell therapies: Existing barriers and proposed policy solutions. *Molecular Therapy: Methods & Clinical Development, 29,* 513-521. https://asgct.org/ASGCT/media/about/Medicaid-paper.pdf?ext=.pdf

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disease by modifying expression of a patient's genes or by repairing or replacing abnormal genes. From a strictly medical standpoint, independent reviews of gene therapy products have shown that over the course of a patient's lifetime, gene therapies can result in savings over traditional treatment options despite high upfront costs.[10] The anticipated durability of gene therapies – from several years up to a lifetime – is atypical among current disease treatments and would confer significant value. Time is needed to confirm the total longevity of these products, but we are starting to reach major milestones in these post market assessments. For instance, the first pediatric patient treated with a CAR T-cell therapy reached the ten years post-treatment milestone in 2022.[11]

There are a number of non-medical factors that also increase gene therapies' value.[12] Patients with chronic genetic illnesses often struggle with significant interruptions of their schooling, jobs, and social lives. Alleviating their symptoms or halting progression can allow them to lead a much more normal life. ASGCT hosted two congressional briefings on sickle cell disease (SCD) in 2023, during which ASGCT members shared the toll of severe pain crises on patients.[13] One of our speakers, a patient enrolled in a clinical trial for a since-approved gene therapy, described his life before and after treatment. He shared that he was forced to drop out of college after his pain crises caused him to miss too much class time. His choice of school and degree track had already been limited by SCD, as he needed to enroll within reach of his home hospital and could only pursue degrees that would keep him behind a desk for his whole career. Since his gene therapy treatment approximately a year ago, that young man is preparing to re-enroll in college, and said he is excited to be able to explore a wider range of career paths than he previously thought open to him. Asked about the most exciting change post-treatment, he said that he was thrilled to be able to join his friends playing basketball at the gym for the first time. ASGCT would be pleased to facilitate an introduction between the Committee and this patient, plus his treating physician, to share more details about his lived experience.

Families and caregivers also experience a toll from genetic diseases, and can see personal and economic benefits after a patient's gene therapy treatment. At that same SCD briefing, the patient's mother described how she was pushed to completely change her career to give her more flexibility to care for her young son. Financial concerns, both in terms of direct expenses and opportunity costs from employment challenges, are very common for caregivers. Additionally, it is physically and emotionally taxing to provide care for family members or friends who are suffering from genetic illnesses, in some cases without being able to walk, breathe, or swallow on their own. Treatment with gene therapy may relieve many of those caregiving burdens.

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[10] Udeze, C. et al. (2022). Projected lifetime economic burden of severe sickle cell disease in the United States [Poster]. *HemaSphere, 6,* 1585-1586. https://journals.lww.com/hemasphere/Fulltext/2022/06003/P1704__PROJECTED_LIFETIME_ECONOMIC_BURDEN_OF.1585.aspx

[11] Children's Hospital of Philadephia. (2022). *Emily Whitehead, First Pediatric Patient to Receive CAR T-Cell Therapy, Celebrates Cure 10 Years Later.* https://www.chop.edu/news/emily-whitehead-first-pediatric-patient-receive-car-t-cell-therapy-celebrates-cure-10-years

[12] American Society of Gene & Cell Therapy. (2018). *Addressing the Value of Gene Therapy: Enhancing Patient Access to Transformative Treatments* [White Paper]. https://www.asgct.org/ASGCT/media/about/18GeneEdit_WP_FINAL.pdf

[13] American Society of Gene & Cell Therapy. (2023). *Sickle Cell Disease (SCD).* https://asgct.org/global/documents/advocacy/asgct-infographic-on-scd.aspx

44. How can future payment or coverage models for these therapies be designed in a way that drives down total health costs for the patient?

Current federally financed coverage and reimbursement mechanisms for new medical products are outdated in their ability to accommodate those gene and cell therapies that consist of a onetime biologic product, plus services to provide the therapy. With more than 60 durable cell and gene therapies likely to be approved in the US by 2030,[14] it is critical these mechanisms are reformed to keep pace with innovation.

To this end, the Centers for Medicare and Medicaid Services (CMS) has enacted regulations that will enable value-based, risk-sharing arrangements that tie payment to product performance. ASGCT supports this concept as such arrangements could provide cost savings to patients and payers, including state Medicaid programs. In addition, doing so redistributes some risk of uncertain outcomes from payers to manufacturers and distributes costs more equitably based on individual patient outcomes. In addition, ASGGCT supports allowing for value-based purchasing (VBP) arrangements that include a pay-over-time component. Enabling payment models that combine the two concepts would be useful by, for example, allowing payers to make installment payments upon patient attainment of benchmarks of efficacy. Doing so ties a portion of product value to durability over time.

In 2023 CMS' Center for Medicare and Medicaid Innovation (CMMI) announced three new models for development.[15] One, the Cell and Gene Therapy (CGT) Access Model, has the potential for far-reaching impact on the CGT field. If implemented properly, the CGT Access Model could help Medicaid beneficiaries gain access to potentially life-changing therapies. ASGCT is currently engaging with CMMI to share the unique nature of CGTs and the realities of many patients' experiences under the current system: that transformative potential is often hindered or blocked altogether by administrative insurance roadblocks.

CMMI also announced the Accelerating Clinical Evidence Model in mid-2023. In that proposal, CMS, in consultation with the Food and Drug Administration (FDA), is considering developing payment methods for drugs approved through accelerated approval to "encourage manufacturers to complete confirmatory trials" – suggesting differential payment rates for drugs approved through this pathway. Accelerated approval allows FDA to make treatments available earlier based on a surrogate endpoint if they address an unmet medical need for a serious condition, contingent on post-marketing trials that demonstrate the drug offers a clinical benefit and an improved patient outcome. Notably, the 2022 Omnibus included reforms to the accelerated approval pathway that requires greater reporting on post-marketing study progress as well as a refined withdrawal pathway.

ASGCT is concerned that this second model, if developed, could harm the integrity of the accelerated approval pathway and slow access to the next generation of gene and cell therapies. Many gene therapies have the potential to be approved through the accelerated pathway, as their outcomes may not be possible to assess within the duration of a traditional

[14] NEWDIGS FoCUS Project. (2020). *Updated Projection of US Durable Cell and Gene Thearpies Product-indication Approvals Based on December 2019 Development Pipeline.* https://newdigs.tuftsmedicalcenter.org/wp-content/uploads/2022/06/NEWDIGS-Research-Brief-2020F207v51-PipelineAnalysis.pdf
[15] Centers for Medicare & Mediacid Services. (2023). *Lowering Prescription Drug Costs for Americans, Response to President Biden's Executive Order.* https://www.cms.gov/priorities/innovation/data-and-reports/2023/eo-rx-drug-cost-response-report-summary

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clinical trial. ASGCT believes post-market surveillance is necessary to ensure approved products remain safe and efficacious. However, efforts to ensure confirmatory trials should not have the unintended consequence of impeding the development of new therapies and patient access. It is ASGCT's current understanding that the Accelerating Clinical Evidence Model is on hold within CMMI, but we remain concerned about the underlying philosophy that prompted the model.

47. How quickly should these covered therapies be made available to patients?

Therapies should be covered and made available to patients promptly upon FDA approval. For patients with genetic diseases, it is imperative that they receive a swift diagnosis and access treatment as soon as possible. Early diagnosis and treatment is especially important for indications where damage to organs and other body systems can accumulate over time; damage may be halted or prevented by early intervention but cannot be reversed. Both Medicaid and Medicare need to improve their practices to make this a reality for patients.

Within Medicaid, states are not always adhering to the federal requirements to provide timely coverage for these therapies to their medically accepted indications. This is especially problematic as many patients who would benefit from cell and gene therapies are Medicaid recipients. Furthermore, private insurers often follow suit for Medicaid's coverage policies. Our 2023 white paper[16] revealed multiple common barriers to access including, but not limited to:

- States are narrowing coverage to populations covered in clinical trials, despite the broader labeled indication (see question #39 for additional information on this point);
- States require additional medical information, or have or eligibility criteria that are stricter than the labeled indication;
- States have difficulty anticipating the timing of new advanced product approvals;
- Appeal processes for patients and physicians are slow and burdensome, compounding issues with delays in time to treatment.

To combat these barriers, ASGCT recommends that CMS should issue additional guidance to states reiterating the expectations of current requirements relating to coverage to label. To aid in these efforts, Congress should work with CMS to reinforce timely coverage of gene and cell therapies and limit the unnecessary, and time-consuming, demands for additional criteria to be met beyond the FDA-approved labeling. CMS should also consider reforms to prior authorization and precertification policies to minimize the burden on providers and patients and expedite decisions.

Within Medicare, recent regulatory changes that are slated to take effect this year will compound patient access challenges for cell and gene therapies. In a recently finalized rule, CMS made significant changes to the new technology add-on payment (NTAP). Specifically, CMS now requires that drugs have an FDA marketing authorization deadline of May 1, rather than July 1, to be considered for the NTAP in the upcoming year. In changing this deadline for FDA approval, CMS has placed new limitations on which products can be considered for the NTAP, which may have significant impact on the ability of Medicare beneficiaries to access new

[16] Allen, J. et al. (2023). Medicaid coverage practices for appvoed gene and cell therapies: Existing barriers and proposed policy solutions. *Molecular Therapy: Methods & Clinical Development, 29,* 513-521. https://asgct.org/ASGCT/media/about/Medicaid-paper.pdf?ext=.pdf

therapies coming to market in a timely fashion. For instance, a product approved on May 2 , 2024, would not be eligible to receive NTAP until January 1, 2026.

Following the FDA's 2017 approval of the first Chimeric Antigen Receptor (CAR) T-cell therapies, it took CMS three years, until 2020, to establish a new MS-DRG specifically for CAR T-cell therapy. Before granting a new DRG the Agency awarded the NTAP for two CAR T-cell therapy products. This decision provided a critical access bridge for these products, ensuring that providers could continue to make the products available to patients. The Society is concerned that CMS has significantly underestimated the downstream impact to beneficiary access associated with restricting the products eligible for the NTAP. The pipeline for CGTs is robust, and there are numerous therapeutic treatment options that could be adversely affected by this change.

51. Are additional regulatory requirements or flexibilities needed to promote health plan or payer coverage of these therapies?

ASGCT supports 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. While greater systemic reforms are needed, we have supported efforts to establish an automatic communication requirement between FDA and CMS for products using expedited regulatory pathways as a positive first step. We would also support discussion of ways for Congress to encourage CMS to provide a more streamlined, consistent approach to providing immediate and uninterrupted coverage for these potentially lifesaving treatments.

More granularly, ASGCT supports efforts to address barriers that impede coverage and adequate reimbursement for new therapies that receive Breakthrough Therapy designation, Fast Track designation, accelerated approval, and RMAT designation. The commencement of FDA communication with CMS upon granting 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.

There also need to be special considerations for N of 1 diseases. Developing gene therapy products for those populations is extremely complicated. FDA's attention to antisense oligonucleotides (ASOs) as a possible treatment avenue for N of 1 diseases is appreciated;[17] but more broadly, additional flexibility from FDA is needed to allow sponsors to pursue treatments for these indications as efficiently as possible while maintaining safety and efficacy. To address challenges associated with developing individualized ultra-rare products for patients, the Agency could explore alternative pathways that capture promising treatments without the need for full-scale commercialization. This approach would enable the development of treatments that may not be financially viable for traditional commercialization but still hold significant promise for the individuals who desperately need them. The goal is to create a

[17] American Soceity of Gene & Cell Therapy. (2021). *Comments for Docket No. FDA-2020-D-2199: IND Submissions for Individualize Antisense Oligonucleotide Drug Products: Administrative and Procedural Recommendations.* https://asgct.org/ASGCT/media/about/Comments-to-FDA-IND-Submissions-for-Individualized-ASO-Products-Guidance.pdf?ext=.pdf

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regulatory framework that encourages and supports the development and availability of these treatments.

53. Please provide feedback on payment and contracting options for health plans, payers, and manufacturers that would provide access to these therapies for patients. These contract options could include value-based models, warranties, annuities, shared savings models, or other risk-based contracting models. Please provide any relevant examples based on existing models.

ASGCT has previously served as a convener for conversations on this topic. At our 2019 Policy Summit we hosted a panel on *Advances in Novel Payment Solutions for Public & Private Payors.*[18] We would be pleased to make a recording of that session available to the Committee.

[18] American Society of Gene & Cell Therapy. (2019). *Policy Summi Agendat: Perspectives on Payment Policies for Gene Therapies.* https://asgct.org/advocacy/policy-summit/policy-summit-archive/2019-policy-summit/payment-policies-november-5-asgct-policy-summit

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