PIPC Partnership to Improve Patient Care

January 22, 2024

Honorable Bill Cassidy
Ranking Member
Senate Committee on Health, Education, Labor and Pensions
428 Senate Dirksen Office Building
Washington, DC, 20510
GeneTherapyCoverage@help.senate.gov

Dear Ranking Member Cassidy:

Thank you for the opportunity to comment in response to a Request for Information related to access to cell and gene therapies. Since its founding, the Partnership to Improve Patient Care (PIPC) has been at the forefront of applying principles of patient-centeredness to the nation's health care system – from the generation of comparative clinical effectiveness research at the Patient-Centered Outcomes Research Institute (PCORI), to the translation of evidence into patient care in a manner that achieves value to the patient. Having driven the concepts of patient-centeredness and patient engagement in the conduct of research, PIPC looks forward to bringing the voices of patients and people with disabilities to the discussion of how to advance patient-centered principles throughout an evolving health care system.

We recognize that access to cell and gene therapies is too often restricted based on a model of coverage that relies heavily on biased measures of clinical and cost effectiveness, leading to denials or onerous cost sharing that may be prohibitive for many patients. This has very real consequences for patients in the form of restricted and delayed access to novel therapies. For patients waiting for a cell and gene therapy, timely access to a treatment consistent with the FDA-approved indication is essential and delays will pose a significant long-term health risk.

Therefore, PIPC recommends the following:

- Considerations related to the value and effectiveness of cell and gene therapies should incorporate patient perspectives, avoid discriminatory and biased measures and health utilities.
- Congress should ban use of QALYs and similar measures consistently across federal programs.
- Congress should not adopt foreign government policies related to reimbursement and coverage of cell and gene therapies.
- Shared decision-making and criteria for patient-centeredness should be central tenets of policies related to how patients access cell and gene therapies.

- P&T Committees should be informed by patients with lived experience and their providers.
- Coverage and utilization management policies should not be selectively based on a person's level of disability or biased perceptions of quality-of-life, leading to discriminatory judgments about a person's worthiness of treatment.
- Exclusion from clinical trials is not a nondiscriminatory reason for coverage and utilization management decisions that deny or restrict access to care.

Considerations related to the value and effectiveness of cell and gene therapies should incorporate patient perspectives, avoid discriminatory and biased measures and health utilities.

It is a priority for PIPC to ensure that patient experiences and preferences are incorporated into analyses related to a treatment's value, both in terms of clinical and cost effectiveness. The movement to incorporate this information in the Food and Drug Administration's (FDA) Patient-Focused Drug Development (PFDD) program has already gained traction in the context of the approval pathway for new drugs. Consistently, PIPC also urges policies that engage people with lived experience in decisions that affect payer-level decisions impacting access to such FDA-approved treatments.

We are very concerned that payer-level decision-making related to coverage is increasingly informed by value assessment frameworks that take a one-size-fits-all view of treatment value, ignoring that patients may value treatments differently, consistent with known tenets of personalized medicine. Despite being banned for use in Medicare, the most frequently used type of value assessment is cost-effectiveness analysis using the Quality-Adjusted Life Year (QALY) as a generic measure of disease burden. Internationally, QALYs and similar measures are used widely by health technology assessment (HTA) bodies to determine which treatments should be financed by national health systems. In the United States, the Institute for Clinical and Economic Review (ICER) has raised millions in funds from Arnold Ventures (formerly known as the Arnold Foundation) and others to conduct value assessments for use by payers whose engagement drives ICER's value assessment agenda. By contrast, ICER's QALY-based value framework is largely criticized by patients and people with disabilities due to concerns about devaluing the lives of people with disabilities, chronic conditions and older adults, as well as their failure to measure quality of life and improvement in a manner that captures the value of treatments for people living with a disease or condition. Studies have demonstrated that ICER's methods fail to account for patient-centered outcomes in the assessment of cost effectiveness.[1]

[1] https://www.pipcpatients.org/resources/white-paper-the-use-of-patient-centered-outcomes-in-icer-assessments

PIPC and Everylife Foundation for Rare Diseases partnered in drafting a report about the need to incorporate patient perspectives in value assessment of novel cell and gene therapies.[2] While most concerns regarding traditional value assessment are applicable to a broad range of therapies, they are especially amplified for cell and gene therapies that inherently involve uncertainties, particularly for treatments addressing rare diseases with limited clinical data and significant patient heterogeneity. It is also important to consider the societal elements of value, most salient for potential cures that last a patient's lifetime and which may not be quantitively assessed in a value assessment and thereby devalues these treatments.

The methods for value assessment and HTA have been historically tailored for use by payers, focusing almost exclusively on whether the additional benefits of a given new therapy, relative to some standard of care or comparator, are justified by its costs. Payers then use these evaluations to help determine funding, coverage, and access policies for therapies. Unfortunately, this approach to value assessment has historically not captured other clinical and non-clinical aspects of value that matter to patients and caregivers, i.e. their burdens and economic outcomes. Translating this type of value assessment into a payer-level decision has the predictable outcome of justifying restrictive coverage policies.

Therefore, the inclusion of patient experience data and patient preferences must be more central to the process of determining the effectiveness and value of cell and gene therapies and decisions related to patient access to them. Cell and gene therapies tend to utilize single or short-term administration, with durable quality of life benefits potentially extending over the lifetime. Payers require information to inform short-term coverage determinations, yet patients make decisions based on longer-term considerations, such as long-term benefits weighed against short-term costs. Long-term data on clinical benefit for cell and gene therapies are usually infeasible to collect in a short-term clinical trial, and patient views and tolerance of this uncertainty are not usually a consideration in payer determinations related to coverage. These therapies are frequently indicated for rare or severe diseases, where the utility scores of various health states should be derived from extensive patient input – yet they are not.

The failure of existing measures of effectiveness lies not only in their discriminatory implications related to devaluing life extension of people with disabilities and chronic conditions, but also the utility weights that measure quality of life and improvement. The most commonly used utility weight is the EuroQoL instrument (EQ-5D). It is built on ableist, discriminatory inputs, failing to account for the full nuance in patient conditions when translating condition-specific measures into utility weights. Oftentimes, dimensions of data are lost when translating condition specific patient-reported outcome measures (PROs) into utility weights, and more frequently, entities conducting value assessment will rely on generic PROs, like the EQ-5D. It is important to consider that continued use of the EQ-5D is wholly inconsistent with NIH efforts to

[2] https://www.pipcpatients.org/resources/white-paper-value-for-whom-incorporating-patient-perspectives-into-value-assessment-for-novel-cell-and-gene-therapies

dismantle ableism in research. As an example, the EQ-5D questionnaire asks patients whether they have problems in "walking about."[3] A negative answer will thereby lower the health-related quality of life score, as inability to "walk about" is seen as equivalent to a low quality of life using the ableist standard that walking is needed for a high quality of life.

It Is important that the dimensions used by instruments such as the EQ-5D bear some relationship to the QOL of patients, as emphasized by the FDA in their guidance to industry on the use of the patient reported outcome (PRO).[4] As such, the FDA notes that "PRO instrument item generation is incomplete without a range of patients with the condition of interest to represent appropriate variations in severity and in population characteristics such as age or sex." The EQ-5D, translated into QALY utility weights, does not meet this standard as it relies upon weightings constructed by populations unfamiliar with the conditions being evaluated and therefore does not have the legitimacy obtained by consulting with patients. Criticism of this disconnect is widespread and growing.[5],[6] The EQ-5D often underestimates both the baseline burden of these diseases in patient populations, as well as the impact of treatments, compared to the more accurate disease-specific measures that were developed with those diseases in mind.[7] Studies have shown that the content of the EQ-5D is often poorly aligned with patient perceptions in diseases such as asthma[8], mental health[9] and cancer,[10] and whole population groups such as older adults.[11] Without a nuanced, patient-driven lens, a generic scale like EQ-5D will fail to account for health-related quality of life impacts outside the dimensions that are included in the scale.[12] The NCD report published in 2019 also expressed these concerns.

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[3] EuroQol Research Foundation, "EQ-5D-5L About," https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/

[4] US Food and Drug Administration Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. 2009. [2020-07-15].

[5] Cubi-Molla P, Shah K, Burström K. Experience-Based Values: A Framework for Classifying Different Types of Experience in Health Valuation Research. Patient. 2018 Jun;11(3):253–270.

[6] Helgesson G, Ernstsson O, Åström M, Burström K. Whom should we ask? A systematic literature review of the arguments regarding the most accurate source of information for valuation of health states. Qual Life Res. 2020 Jul;29(6):1465–1482

[7] Payakachat N, Ali MM, Tilford JM. Can the EQ-5D detect meaningful change? A systematic review. Pharmacoeconomics;2015;33:1137–1154.

[8] Whalley D, Globe G, Crawford R. et al. Is the EQ-5D fit for purpose in asthma? Acceptability and content validity from the patient perspective. Health Qual Life Outcomes;2018;16:160.

[9] Keetharuth AD, Rowen D, Bjorner JB, Brazier J. Estimating a preference-based index for mental health from the Recovering Quality of Life Measure: valuation of Recovering Quality of Life Utility Index. Value Health. 2021;24(2):281-290.

[10] Garau M, Shah K, Towse A, Wang Q, Drummond M, Mason A. Assessment and appraisal of oncology medicines: does NICE's approach include all relevant elements? What can be learnt from international HTA experiences? Report for the Pharmaceutical Oncology Initiative (POI) February 2009.

[11] van Leeuwen KM, Jansen APD, Muntinga ME, Bosmans JE, Westerman MJ, van Tulder MW, et al. Exploration of the content validity and feasibility of the EQ-5D-3L, ICECAP-O and ASCOT in older adults. BMC Health Serv Res. 2015;15:1–10.

[12] Avalere and The Partnership to Improve Patient Care, Use of Patient-Centered Outcomes in ICER Assessments, July, 25, 2023, http://www.pipcpatients.org/uploads/1/2/9/0/12902828/avalerepipc_icer-use-of-pcos-whitepaper.pdf.

Therefore, any new payment models intended to improve access to high quality care for patients must reflect their perspectives, requiring a process for patient engagement and data collection on outcomes that matter to them, as well as consideration of the long-term benefits for society. A traditional value assessment will not provide this information.

Congress should ban use of QALYs and similar measures consistently across federal programs.

Cell and gene therapies treat diseases and conditions that are often disabling for people that live with them. It is widely acknowledged that the discriminatory nature of the QALY and similar measures such as the equal value of life year gained (evLYG) can drive discriminatory payer policies related to coverage. While Congress barred the use of such measures in Medicare decisions, there is not a consistent federal policy across federal programs, a challenge recognized by the National Council on Disability (NCD), an independent agency advising Congress and the administration on disability policy. NCD determined that the QALY and similar measures are inconsistent with disability rights laws and recommends against their use in federal health programs.[13]

Therefore, PIPC strongly supports H.R. 485, the Protecting Health Care for All Patients Act, legislation introduced in the House of Representatives and marked up by the House Energy and Commerce Committee in 2023 that would extend the existing Medicare ban on use of QALYs and similar measures to other federal programs such as Medicaid.[14] Any policy advancing new payment models for cell and gene therapies (or any treatment or service) should clearly and consistently ban the use of QALYs and similar measures if it is to truly protect patients and people with disabilities from their use to discriminate. Such as policy would:

- Be consistent with current developments and laws and discourage confusion.
- Allow for consideration of how value assessments may discriminate by classifying people with disabilities as inferior whether in measures of life extension or in quality-of-life improvement.
- Be consistent with NIH efforts to address ableist assumptions about quality of life that may also drive value assessments.
- Spur meaningful innovation in the development and use of measures of quality of life and improvement that do not discriminate based on the assumed "worth" of patients with disabilities to treat.[15]

[13] https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf
[14] Bill as marked up by committee: https://docs.house.gov/meetings/IF/IF00/20230323/115556/BILLS-118-HR485-M001159-Amdt-8.pdf
[15] https://www.pipcpatients.org/uploads/1/2/9/0/12902828/pipc_504_comment_final.pdf

Congress should not adopt foreign government policies related to reimbursement and coverage of cell and gene therapies.

Internationally, restricted access to cell and gene therapies are the consequence of relying on biased and discriminatory measures of clinical and cost effectiveness. The NCD sent a letter to Congress in 2021 stating, "The history of restricted access occurring in countries utilizing QALY-based cost effectiveness research raised concerns that its use in the U.S. would result in rationing care to seniors and people with disabilities, leading Congress in 2009 to prohibit its use under the Affordable Care Act of 2010 (ACA)."[16] The NCD also stated, "Drug prices need to be lowered. They should not be permitted to be lowered based on the use of a pricing methodology that has unarguably been proven to be discriminatory in its use against persons with disabilities. Acceptance of foreign drug prices set in reliance on the QALY method effectively endorses the use of this discriminatory pricing methodology."[17] The Consortium of Constituents with Disabilities (CCD) also expressed concerns about reference to international prices in a letter to Congress in 2019, stating, "HR 3 relies on international prices to set an upper limit in negotiations. Many of the nations used to create the average international market price rely on QALYs to determine their coverage and prices. CCD is very concerned that these provisions effectively import a QALY-based and discriminatory system from abroad. These systems are discriminatory against people with disabilities and do not have a place in the United States health care system."[18]

In response to references to the German health system by policymakers, PIPC studied and developed a white paper related to its process for assessing the effectiveness of prescription drugs and reimbursing for their use. PIPC found that 60% of new medicines receive negative assessments in Germany. This outcome is the direct result of its biased process for assessing the effectiveness of new treatments. Germany severely limits the types of evidence that can be considered in assessments and typically uses an inappropriate comparator, selected based on cost rather than clinical similarity. Germany also restricts the types of endpoints that are acceptable to show the value of treatment, often excluding health outcomes that are important to patients and failing to capture heterogeneity of patient populations. Similar to the ICER process, patient input does not meaningfully impact the final recommendation related to effectiveness, impacting reimbursement and patient access.[19]

Foreign government structures for coverage and reimbursement of cell and gene therapies would be inconsistent with U.S. laws protecting people with disabilities against discrimination. Stories of delayed access to care are common abroad as many countries see people with

[16] https://www.ncd.gov/publications/2021/ncd-letter-qaly-ban
[17] https://www.ncd.gov/publications/2021/ncd-letter-house-committees-concerns-regarding-hr-3
[18] https://c-c-d.org/fichiers/CCD-Letter-HR-3-Final-9.24.19.pdf
[19] https://www.pipcpatients.org/resources/the-german-health-care-system-and-its-impact-on-patient-access-lessons-for-the-us

disabilities and older adults as less worthy of health care spending.[20] Therefore, PIPC agrees with the NCD assertion, "There has been increasing interest by the Federal Government in reducing the cost of health care by modeling parts of its national health insurance programs after the healthcare systems of other countries, such as the United Kingdom. Several of these countries utilize QALYs to make benefits and coverage decisions. The coverage denials and loss of access to care faced by people with disabilities in these countries illustrate what might happen if the United States made a similar choice."[21]

Shared decision-making and criteria for patient-centeredness should be central tenets of policies related to how patients access cell and gene therapies.

As part of the ACA, Congress enacted provisions of law calling for a shared decision-making program that advanced preference sensitive medicine and patient-centeredness criteria as the evaluation measure of success for alternative payment models. Patients and people with disabilities envisioned development of new resources to aid in patient-provider healthcare decision making centered on their needs and goals. These legal provisions were intended to advance the delivery of health care that achieved outcomes meaningful to patients, people with disabilities and their caregivers. Yet, the shared decision-making program has not been advanced despite the development of a Playbook on Shared Decision-Making developed in collaboration with the National Quality Forum and health care stakeholders.[22] Nor have patient-centeredness criteria been developed by CMMI on which to benchmark the success of alternative payment models. Therefore, PIPC has consistently urged CMS to focus on advancing a shared decision-making program consistent with the recommendations of the Playbook[23] and to engage patients and people with disabilities in the development of patient-centeredness criteria for alternative payment models.[24] We are still waiting.

P&T Committees should be informed by patients with lived experience and their providers.

Insurers' Pharmacy & Therapeutics (P&T) committees make decisions about coverage and utilization management typically include physicians, other prescribers, pharmacists, nurses, administrators, quality-improvement managers, and other health care professionals and staff who participate in the medication-use process.[25] Their biased perceptions related to the quality

[20] https://www.pipcpatients.org/international.html
[21] https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf
[22] https://www.qualityforum.org/National_Quality_Partners_Shared_Decision_Making_Action_Team_.aspx
[23] http://www.pipcpatients.org/uploads/1/2/9/0/12902828/sdm_comment_on_interoperabiity_final.pdf
[24] http://www.pipcpatients.org/uploads/1/2/9/0/12902828/pipc_et_al_cmmi_letter.pdf
[25] ASHP, "ASHP Statement on the Pharmacy and Therapeutics Committee and the Formulary System," https://www.ashp.org/-/media/assets/policy-guidelines/docs/statements/pharmacy-and-therapeutics-committee-and-formulary-system.ashx#:~:text=The%20P%26T%20committee%20is%20composed,in%20the%20medication%2Duse%20process.

of life of people with disabilities can result in decisions about coverage that link underlying disabilities to restricted access to care through coverage and utilization management policies. P&T committee decisions are not necessarily informed by people with lived experience or specialists in the disease or condition that would have knowledge of the clinical appropriateness of treatment for subgroups of patients that have disabilities. It is even less likely that a member of a P&T committee would be deeply familiar with the experiences of patients who are candidates for a cell and gene therapy, as they often treat rare diseases.

Therefore, PIPC strongly supports including the patient perspective on P&T Committees. A patient perspective should be required to bring a focus on the patient experience of care to the P&T committee, providing additional insight into the practical use of therapies and effect on quality-of-life outcomes. Additionally, the P&T committee process should be required to engage patients and people with disabilities and the organizations representing them as advisors that have experience with the disease or condition to ensure that outcomes that matter to patients are key considerations in payer decisions. Engaged patients and people with disabilities should have an opportunity to comment on the evidence that is being reviewed by a P&T committee, including the evidence relied upon by third party contractors that provide recommendations for formularies. Too often, third party contractors make recommendations to P&T committees based on value assessments and other studies that fail to capture outcomes that matter to patients and people with disabilities.

Coverage and utilization management policies should not be selectively based on a person's level of disability or biased perceptions of quality-of-life, leading to discriminatory judgments about a person's worthiness of treatment.

Access to novel therapies is too often restricted based on a person's disability, a practice that PIPC has raised with the HHS Office for Civil Rights as contrary to Section 504 of the Rehabilitation Act's provisions against disability discrimination. [26] Reduced access to medical treatment leading to health disparities and poor health outcomes is too often associated with coverage and utilization management policies that are barriers to medical treatment for people with disabilities. Unmet health care needs contribute to various indicators of health inequity experienced by people with disabilities and payer policies contribute to that inequity.

Policies impacting access to care must protect against biased perceptions of a person's quality of life as the basis for decisions not to treat people with disabilities or to treat them differently than others. Discrimination happens when care decisions are motivated by inappropriate consideration of cost or value judgments regarding the quality of life of individuals with disabilities. Too often, payer policy may selectively restrict coverage based on an underlying

[26] https://www.pipcpatients.org/uploads/1/2/9/0/12902828/pipc_504_comment_final.pdf

disability such as one's need for mechanical ventilation or a mobility impairment, motivated by cost or value judgements related to the quality of life of individuals with disabilities rather than clinical appropriateness. For example, a person with Duchenne Muscular Dystrophy who is considered ambulatory may be approved for a gene therapy while the same insurer restricts access to someone who is non-ambulatory. Selectively denying or restricting access to care for non-ambulatory patients that are included in the FDA-approved label indication is discrimination. The underlying disability, being non-ambulatory, does not translate into the treatment not being clinically appropriate simply because the person who is non-ambulatory may continue to need accommodations and supports and may not achieve being ambulatory in the future with treatment.[27,28,29,30] Similarly, a person with spinal muscular atrophy who is dependent on a BiPAP should not be selectively denied care when dependence on a BiPAP is not called out as disqualifying under the FDA-approved label indications. The underlying disability, being dependent on a BiPAP, does not translate into the treatment not being clinically appropriate simply because the person dependent on a BiPAP may continue to need it in the future. Yet, payers have used BiPAP dependence as an excuse to deny or restrict coverage.[31]

Any policy advanced to ensure appropriate access to cell and gene therapies must clarify that access to clinically appropriate treatment should not be denied or limited based on an underlying disability. It is contrary to U.S. nondiscrimination laws to deny care to a person with a disability based on the determination the person's quality of life is not worth the cost of treatment.

Exclusion from clinical trials is not a nondiscriminatory reason for coverage and utilization management decisions that deny or restrict access to care.

People with disabilities are too often excluded from clinical trials. Therefore, to use such exclusion as a reason to deny a patient with a disability access to a treatment or service only serves to amplify health equity concerns for people with disabilities that already experience

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27 Mass.gov, "Table 76: Neuromuscular Agents-Duchenne Muscular Dystrophy and Spinal Muscular Atrophy," https://mhdl.pharmacy.services.conduent.com/MHDL/pubtheradetail.do?id=373.

28 State of Iowa Department of Health and Human Services, "Amondys 45," https://hhs.iowa.gov/sites/default/files/Amondys%2045%20%28casimersen%29%20-%20PAM-044%20%28v.2%29.pdf.

29 Maryland Department of Health, "Exondys 51," https://health.maryland.gov/mmcp/Documents/Exondys%2051%20Clinical%20Criteria.pdf#search=exondys.

30 United Healthcare Community Plan, "Exondys 51," https://www.uhcprovider.com/content/dam/provider/docs/public/policies/medicaid-comm-plan/exondys-51-eteplirsen-cs.pdf.

31 Khrystal Davis, "Testimony," May, 4, 2021, https://docs.house.gov/meetings/IF/IF14/20210504/112551/HHRG-117-IF14-Wstate-DavisK-20210504.pdf.

tremendous health disparities. When a coverage policy differentiates those eligible for treatment based on disability simply because of a lack of evidence from a clinical trial directly related to the clinical effectiveness for the population of people with disabilities – as opposed to evidence of ineffectiveness, danger or potential harm – there is no legitimate nondiscriminatory reason to deny coverage or impose utilization management barriers that those included do not face. People with disabilities are often excluded from trials because the accommodations to include them (i.e. making forms accessible, having ASL interpreters, having accessible clinic sites) is a barrier. Researchers often view accommodations as too expensive, or do not understand what is needed to include people with disabilities in trials.[32] Therefore, new payment models for cell and gene therapies should clearly protect populations excluded from clinical trials that are otherwise included by the FDA label and for whom evidence does not indicate ineffectiveness, danger or potential harm. The ongoing exclusion of people with disabilities from clinical trials only makes it more important to gather real world evidence that will allow for improved decisions related to clinical appropriateness.

Conclusion

We appreciate the opportunity to share with you our views and concerns related to access to cell and gene therapies. We share your concerns about the need to improve and protect access to these novel treatments and look forward to continuing to engage with you.

Sincerely,

Tony Coelho
Chairman
Partnership to Improve Patient Care

[32] Bonnielin Swenor and Jennifer Deal, "Disability Inclusion as a Key Component of Research Study Diversity," https://doi.org/10.1056/NEJMp2115475.