The Honorable Bill Cassidy, Ranking Member
Senate Committee on Health, Education, Labor, and Pensions

Dear Ranking Member Cassidy,

In service of the neuromuscular disease (NMD) community, the Muscular Dystrophy Association (MDA) thanks Senator Bill Cassidy and the Health Education Labor and Pensions Committee for the opportunity to comment on the Committee's Request for Information (RFI) regarding cell and gene therapies.

MDA is the #1 voluntary health organization in the United States for people living with muscular dystrophy, ALS, and related neuromuscular diseases. For over 70 years, MDA has led the way in accelerating research, advancing care, and advocating for the support of our community. MDA's mission is to empower the people we serve to live longer, more independent lives.

The majority of NMDs are genetic in nature and are progressive. Therefore, it is vitally important for those in the NMD community to receive access to appropriate and timely care, and cell and gene therapies are a large part of that process. Please see below for our answers to some of Ranking Member Cassidy's questions from the patient advocacy perspective.

How should lawmakers define an "ultra-rare' disease or disorder 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?

MDA does not have a specific definition to offer Ranking Member Cassidy to consider for eligibility within ultra-rare-specific coverage or contracting requirements. Without further evidence, we do not believe a specific prevalence cut-off should be chosen, and instead, if eligibility requirements must be set at all, that requirements centered on the challenges to coverage, contracting, and access should be crafted instead.

There remains disagreement within the rare disease stakeholder community on how to differentiate ultra-rare diseases from non-ultra-rare diseases, and a prevalence or incidence cutoff used in coverage and contracting may not be the place to start. Further study and discussion is needed before choosing a prevalence or incidence-based definition for ultra-rare diseases.

Are there other criteria that lawmakers should consider in determining which therapies should be included in new coverage or contracting models? Examples could include treatment characteristics (e.g. curative treatments or treatments reaching a certain cost threshold) or treatments fitting certain patient profiles (e.g. pediatric patient populations or the fatality of the disease) If so, what definitions should lawmakers consider?

There are a number of criteria that MDA would find challenging and potentially problematic if pursued for these uses. For example, "curative" is a very subjective term and potentially fraught with ethical implications of what the therapy's goal truly is. Many people with genetic diseases often see aspects of their disease experience as part of who they are, and do not wish to be "cured" of part of their identity. We would similarly caution against using other efficacy criteria as the efficacy of a gene therapy often varies within a population.
Using population-based criteria (such as pediatric versus adult) could prove problematic as such an approach would inherently disadvantage some compared to others based upon an immutable and otherwise inconsequential variable such as age.

We would again encourage the Ranking Member to consider criteria that are meaningful to the problems with covering gene therapies. These include the durability of the product stretching our year-based, non-portable coverage and contracting system. By choosing criteria directly related to the challenges at hand, any policy pursued will better solve the problems at hand.

How do patient populations currently access and pay for these therapies?

Cell and gene therapies are accessed via specialty clinics (such as those run by MDA), where in all likelihood, patients already see their multidisciplinary care team. Most patients are covered by Medicaid or commercial insurance with a few on Medicare. Cost-sharing on the high end is usually capped when it runs into Medicaid's Maximum Out-of-Pocket amount (MOOP) and is otherwise relatively low.

What, if any are the utilization management tools (e.g. step therapy, prior authorization) that patients are typically subject to when paying for and accessing these therapies? If not the patient, what individual or entity typically works through the process of obtaining approvals?

The use of step therapies is not a major issue in the NMD community with regard to cell and gene therapies due to the small number of available treatments. Prior authorization does, however, present a significant barrier to accessing cell and gene therapies. In the last year, we've seen delays in care for Elevydis, Spinraza, and Zolgenzma, among others.[1] While an approved therapy may slow or stop a patient's progression, no therapy can reverse what a patient has lost while waiting for appropriate care. Between the progressive nature of NMDs, and the small number of approved therapies, those living with a NMD are left with the choice of paying for these incredibly expensive therapies out of pocket or waiting for the approval process to resolve. Regardless, while patients wait, their condition continues to progress.

[1] See, MDA statement on insurance denials https://www.votervoice.net/MDA/BlogPosts/5325

In terms of working through the approvals for cell and gene therapies, physicians and their teams take on much of the load of working through the paperwork and communication with payers. It should also be noted that denials require a patient to divert their focus from managing their condition to accessing their therapy through an appeals process which is often difficult to navigate. Patients must understand that denials are not final and then follow their physicians through the appeals process, and organizations, such as MDA's gene team, play an important role in helping patients through the appeals process. To that end, the specialists (i.e. the physician(s) with specialized knowledge of the specific NMD treating the patient) should continue to be the experts when it comes to a determination of medical necessity rather than payers.

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

MDA has commissioned a study from Tufts University Medical Center looking at the coverage landscape for a number of therapies across multiple NMDs in both private and public markets. While that data is not yet available for widespread use and not all the therapies considered are relevant here, skewing the data for these purposes somewhat, we can share high-level impressions. Of the 1,204 plan-drug-indication combinations the vast majority had publicly available coverage policies indicated, the vast majority had publicly available coverage policies, so we can infer coverage of therapies, generally, is not an imminent issue. However, that does not mean that the coverage landscape does not pose some problems for accessing these therapies:

There were, unsurprisingly, a wide variety of initial coverage requirements across private and public plans. Most commonly these requirements pertained to respiratory function, motor function, activities of daily living (ADL), symptom duration, and scores on indication-specific clinical assessment measures. Here, it is notable that there was a high degree of variability across states and plans for how these variables were used and to what extent meeting each requirement impacted the overall coverage decision. There was also there was high variability across states and plans for requirements for continuing coverage in terms of proof of benefit.

In general, what can be gleaned from early data is that limitations to access exist across plan types, but those limits are not easily generalizable beyond the broad characterization above.

How does a physician or health system initiate the process of prescribing a patient with an ultra-rare disease or disorder one of these therapies?

It's important to note that before a physician prescribes a cell or gene therapy, one of the biggest barriers to accessing a therapy is receiving a diagnosis in the first place. According to a study commissioned by the Everylife Foundation, on average, it can take up to six years for a patient to receive a diagnosis, and medical costs and productivity loss in the pre-diagnosis years is between $86,000 and $517,000 per patient cumulatively for the years of delay.[2] During this time, patients

[2] *See generally, The Cost of Delayed Diagnosis in Rare Disease: A Health Economic Study iv-v* *https://everylifefoundation.org/wp-content/uploads/2023/09/EveryLife-Cost-of-Delayed-Diagnosis-in-Rare-Disease_Final-Full-Study-Report_0914223.pdf*

will often travel to multiple specialists (a cost not included in Everylife's study *see, footnote 2) incurring not only the high costs mentioned above, but also significant emotional strain while waiting for a diagnosis and appropriate care. To receive a diagnosis, most patients see a genetic counselor (which can be difficult in and of itself)[3] who can perform genetic and whole exome sequencing and interpret the results. Once a diagnosis is given, accessing appropriate follow-on care can also be challenging due to the often limited number of specialists in a given NMD field.

Once a patient finds aqualified specialist, the patient needs to meet various criteria to ensure the treatment can be effective, such as disease progression and ensuring they do not have certain antibodies which could result in a dangerous immune reaction. Once these requirements are met, healthcare providers or systems reach out to the manufacturer and payer to begin the process of obtaining the therapy and to move through any remaining utilization management requirements from the payer.

Do physicians or health systems bear any financial risk as part of prescribing a patient with an ultra-rare disease or disorder these therapies? If so, as part of what program or what type of contract?

One-way physicians or health systems may bear the financial risk as part of prescribing a cell or gene therapy is through buy-and-bill practices. Buy-and-bill is a reimbursement model most typically used for specialty drugs in the injectable or infused space. Typically, how the process works is that a healthcare provider or system will buy the therapy up front, administer the therapy and then seek reimbursement from the patient's insurer(s) themselves at a negotiated rate. Healthcare providers or systems incur risk in two broad areas throughout this process. Firstly, by virtue of paying for these therapies upfront, they both incur the immediate risk of paying for the therapy. And secondly, they risk potential cash flow concerns due to the investment and given the high cost of these therapies. Therefore, these financial risks could be substantial. The second area of risk is similar to risks that would otherwise be incurred (and in some senses still are) incurred by the patient. Under a buy-and-bill model, purchasing healthcare providers or systems still navigate the prior authorization process, and may encounter further insurance issues on the patient side as patients must still navigate the approvals process for appointments to specialists and patients do incur cost-sharing for any additional cost not covered by the previously mentioned negotiation. Whether the barriers to access present for the provider during prior authorization or for the patient, both add to the risk for providers under a buy-and-bill model as both may delay or prevent access to a therapy increasing cost and risk for the provider.

[3] " How Accessible Are Genetics Providers and How Can Access Be Increased? " Centers for Disease Control, https://blogs.cdc.gov/genomics/2020/10/05/how-accessible/

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?

There are a number of policy areas in which the federal government should consider further involvement to increase access in the commercial market. First, re-insurance remains one of the more promising mechanisms for protecting small commercial payers from the potential adverse selection of covering gene therapies, particularly if a disproportionate number of individuals in their covered population seek a gene therapy. The federal government could ensure re-insurance and similar risk pooling mechanisms are widely available.

The federal government can continue to reduce barriers to amortizing value-based payments, particularly across plan years and even portably across plans. All payers, regardless of whether they are public, commercial, or self-insured, are challenged by paying millions of dollars up front for a gene therapy without potential cost-recovery if the therapy is less effective than desired and/or the patient departs the plan and the future savings derived from better health are realized by a different payer altogether.

We believe commercial payers, and particularly self-insured plans, would benefit greatly from a robust approach for amortizing value-based payments across plan years and across plans, and the federal government could be instrumental in creating such an approach.

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?

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There are three coverage mandates the federal government could, and should, make to ensure appropriate access to cell and gene therapies across all markets and plans. The federal government should ban accelerated approval discrimination by insurers. As noted above, we have documented an alarming number of private insurers who have used a therapy's status as approved via the accelerated approval pathway to deem the drug "not medically necessary" or experimental. The suggestion that these determinations underscore that therapies approved under the accelerated approval pathway not only lack efficacy, but also undermine the accelerated approval process, which is vital for the development for therapies for the rare disease community.

Similarly, the federal government should mandate coverage in private and public settings to the FDA-approved label of the therapy in question. Using Elevydis as an example of how failing to mandate coverage to the label could be harmful; if the label for Elevydis is expanded from children ages four to five to a more expanded range this expansion would be transformative but could also pose problems in terms of coverage. As we have seen, payers have been reticent to supply timely coverage to these therapies. It is conceivable that payers would put in place similar barriers for a cell or gene therapy with an expanded label if not mandated otherwise by the federal government. It is important to remember that changes in a therapy's label are a normal

part of medicine and are meant to reflect evolving medical understanding and that the FDA is the authority on these determinations and not payers.

Finally, we have heard from multiple stakeholders that state Medicaid programs have been slow to add cell and gene therapies to their formularies and that there has been some delay in establishing J codes for cell and gene therapies at a national level, presumably, due to concerns about the high cost of these therapies. We would suggest working with CMS to promulgate a reasonable timeline for Medicaid programs to adjust their formularies and codes. The current paradigm of nebulous timelines leaves patients and healthcare providers unnecessarily unsure of their access to care in an environment where timing is everything.

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

Traditionally, only the cost savings through improved health are considered by payers when evaluating the cost-effectiveness of potential therapies. While some evolution has occurred with broader benefits of new therapies being considered by payers and health technology evaluators (such as the Institute for Clinical and Economic Review [ICER]), such as patient experience data provided by communities, often the scientific, population, and societal benefits that new therapies, particularly transformative gene therapies, are ignored.

Colloquially known as the "value flower", Lakdawalla et al. published on the variety of benefits new therapies bring, including advancements in science and positive impacts on family members, friends, classmates, communities, and more. There are methods developed by health economists to measure these benefits and consider them when evaluating the cost-effectiveness of gene therapies. We strongly encourage these benefits to be considered alongside the cost of these therapies.[4]

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

There are several ways coverage models for cell and gene therapies could be modified to drive down cost for patients, primarily centered on reducing administrative burden and costs. Administrative spending is estimated to account for 15 to 30 percent of healthcare spending in the US,[5] and given the often-complex nature of providing cell and gene therapies to healthcare providers and patients, it is not unreasonable that the administrative burden involved in accessing these therapies is high. A major factor in these administrative costs is prior authorization and utilization management in general. Utilization management, which creates a huge amount of

[4] https://www.valueinhealthjournal.com/article/S1098-3015(17)33892-5/fulltext

[5] "The Role Of Administrative Waste In Excess US Health Spending, " Health Affairs Research Brief, October 6, 2022. https://www.healthaffairs.org/do/10.1377/hpb20220909.830296/#:~:text=and%20administrative%20waste.-,Administrative%20Spending%20Accounts%20For%2015%E2%80%9330%20Percent%20Of%20Health%20Care,in%20cost%20reports%20or%20budgets.

medical expenditure on its own,[6] is also a huge driver of administrative costs as it requires hours of documentation to be completed and reviewed by both healthcare providers and payers.[7] Additionally, the appeals process brought on by prior authorization further adds to burden and costs. Finally, given the relatively few qualified healthcare providers and facilities to administer cell and gene therapies, travel remains a cost driver for patients as many have to travel across state lines to receive care. While we work to increase the accessibility of providers this issue could be addressed by expanding access to modalities such as telehealth where appropriate, including follow-up care.

Which entity should accept the majority of the financial risk when providing access to these therapies? Why?

As noted in previous answers, no one party is going to be able to provide or access cell and gene therapies without some level of financial risk. While it is not for MDA to dictate exactly who carries what level of risk, it certainly should not be the patient carrying the brunt of that risk as the most vulnerable population involved. Not only could a delay in access lead to continued disease progression for these patients, but also there are several other factors such as the need for other specialty care, home and community-based services, and durable medical equipment which all serve as additional costs for patients. We should not be adding to the financial burden of a rare disease by having patients accept significant financial risk for the treatment they need and deserve.

What role should utilization management tools play in providing access to these therapies?

While there are certainly many instances where utilization management should be treated with a fair degree of skepticism, there are absolutely times when utilization management tools should be utilized. When considering cell and gene therapies it is important to confirm the proper genetic mutation as well as the absence of problemmatic antibodies to the AAV for eligibility, and if or when redosing is needed there will be other similar utilization management tools that should be utilized. Other modalities such as step therapy and arbitrary approval standards such as requiring ambulation, not based in science, however, should not be implemented.[8] In short, the

[6] Quantifying The Economic Burden Of Drug Utilization Management On Payers, Manufacturers, Physicians, And Patients https://www.healthaffairs.org/doi/abs/10.1377/hlthaff.2021.00036#:~:text=Based%20on%20a%20compilation%20and,contesting%2C%20and%20navigating%20utilization%20management.

[7] *Id.*

[8] For examples, of policies with inappropriate requirements see, Premera Blue Cross Pharmacy/ Medical Policy, Pharmacologic Treatment of Duchenne Muscular Dystrophy, https://www.premera.com/medicalpolicies/5.01.570.pdf. UnitedHealthcare Commercial Medical Benefit Drug Policy for Exondys 51, https://www.uhcprovider.com/content/dam/provider/docs/public/policies/comm-medicaldrug/exondys-51-eteplirsen.pdf (last accessed Nov 20, 2022); Anthem. Clinical Criteria. Exondys 51 (eteplirsen). Publish date 09/19/2022. Available at https://www.anthem.com/ms/pharmacyinformation/Exondys.pdf. Accessed on November 26, 2022; Excellus. Pharmacy Management Drug Policy. Duchenne Muscular Dystropy (DMD). Policy Number Pharmacy -85. Available at

FDA and the treating physician with specialized knowledge of the condition in question and it is they who should be placing guardrails around when a therapy is appropriate for what patients, not payers.

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

Immediately! Again, NMDs are often progressive, irreversible diseases. Delays equate to muscle and nerve loss and/or damage in our population. Where muscle and/or nerve damage has occurred it presently cannot be reversed, and for some, delays may be as severe as the difference between life and death.

What other considerations should be made around benefit design to ensure access to these therapies (e.g. deductibles, cost-sharing)?

As mentioned previously MDA is highly supportive of considering how MOOP limits can be used in other benefit designs. We would encourage the ability to amortize costs without interest or debt accrual as is the case with MOOP. While we do not have a specific position on what a potential deductible would entail from a cost perspective, we would suggest that copay accumulators and maximizers should not be used under any circumstances. Copay accumulators and maximizers can drastically drive-up costs for patients, and considering how expensive these therapies already are, we should not add to that burden by allowing health plans to, essentially, double dip on payments.[9] Any payments (patient or otherwise) need to count toward a patient's deductible and MOOP.

What role should patient assistance programs play in providing access to these therapies?

It is incredibly likely that patient assistance programs will play an important role in ensuring access to cell and gene therapies for patients. The point of caution we would add is that these programs need to ensure that they are increasing access and defraying costs while staying within the bounds of the law. To be clear, patient assistance programs should absolutely be allowed to continue their work and in most cases, patients should be encouraged to seek them out. However, federal and state governments should make patient assistance programs' obligations under anti-kickback statutes, patient protections under the ACA and HIPAA, the False Claims Act, IRS regulations governing charitable functions, and the bevy of applicable state laws as clear and easily navigable for patients and assistance funds as possible, particularly given the complexity of the finances at play for cell and gene therapies.

https://provider.excellusbcbs.com/documents/20152/127109/Duchenne+Muscular+Dystrophy+D MD.pdf/36d6fc5f-746a-1739-e0f9-b5f378252915?t=1664373611447

[9] For a quick example of how copay accumulators and maximizers increase costs see, https://www.hemophilia.org/sites/default/files/document/files/Patient%20cost%20scenarios.pdf and see also generally, https://www.hemophilia.org/advocacy/federal-priorities/make-all-copays-count

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

One additional regulatory consideration would be implementing the framework for value-based purchasing agreements contemplated in Representative Brett Guthrie's MVP Act (HR, 2666). The MVP Act codifies the existing "multiple best price" rule that allows manufacturers to report multiple best prices for therapies that are subject to value-based purchasing arrangements when patient benchmarks are met. The MVP Act clarifies that the best price under a value-based arrangement is the maximum possible price paid, assuming all patient outcome benchmarks are satisfied. Importantly, this does not mean that Medicaid programs are prohibited from collecting rebates or other price concessions under a value-based arrangement when the treatment fails to meet its benchmarks. The bill also expands the use of value-based agreements to therapies administered in an inpatient setting. Currently these agreements only apply in outpatient settings. While there are relatively few cell and gene therapies for rare diseases at this time, as therapies continue to come through the pipeline, programs such as this one will become even more cogent, setting up the framework now will be well worth it.

How should policymakers consider other eligibility criteria for access to these therapies for populations such as individuals with long-term disabilities or complex medical needs who are eligible for Medicaid based on disability? What role should commercial insurance play in the long-term for covering these patients who may no longer have the disability that made them Medicaid eligible?

MDA is committed to access for all FDA-approved therapies. Where a therapy has been approved by the FDA, patients should have access to that therapy with as few barriers to access as possible. Where a therapy's administration is within the label, no other eligibility requirements should exist. When considering how commercial insurance interplays with Medicaid eligibility, it's important to remember that Medicaid eligibility, ***even if*** therapies could be entirely curative, is not entirely based on medical necessity. Therefore, again, where a therapy is within the label, there should be no additional eligibility requirements.

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.

As noted throughout our responses, we are supportive of value-based models, amortization schemes, shared savings models etc. One potential challenge to these models is how value is measured. We have noted concerns with how health economists value the lives of people with disabilities.[10] Should these contracting models be utilized it is imperative that the value of a therapy considered in the context of the benefit to whole patient.

[10] Quality-Adjusted Life Years and the Devaluation of Life with Disability at Letter of Transmittal, National Council on Disability (Nov. 6, 2019), https://ncd.gov/sites/default/files /NCD_Quality_Adjusted_Life_Report_508.pdf. See also, ICER. Deflazacort, Eteplirsen and Golodirsen for Duchenne Muscular Dystrophy: Effectiveness and value.

How could the federal government leverage existing alternative coverage models in order to promote commercial access to these therapies? For instance, interested parties could contemplate changes to independent, non-coordinated excepted benefits, which could allow health plans and payers to subsidize add-on benefits for these therapies.

Non-coordinated excepted benefit models have very specific uses for those that need a health plan to bridge them from one comprehensive coverage plan to another. More often than not, when excepted benefit plans are used for more than just a temporary bridge between comprehensive plans, patients end up having less robust coverage than they think they do and much more out-of-pocket than they can actually afford.[11] For these reasons, if non-coordinated plans must be used, we would suggest putting strong guardrails in place to ensure patients know what they are buying into and are protected, but in general we would suggest not using excepted benefit plans for this purpose.

How could the federal government modernize existing health insurance requirements in order to promote access to these therapies? For instance, interested parties could contemplate modifications to the portability requirements under the Health Insurance Portability and Accountability Act (HIPAA) which could allow patients to take their policy from plan to plan. In addition, interested parties could contemplate modifications to Essential Health Benefit (EHB) requirements to ensure coverage of these therapies.

We would be supportive of modifying HIPAA to allow both portability of policies and amortization of costs across plans which benefits both payers and patients. We also support modification of EHB(s) to include cell and gene therapies, as the EHBs' current construction do not contemplate specialty therapies. EHBs has been vital to ensuring that patients receive the coverage they need and deserve and adding cell and gene therapies to the list of covered medications is a big step in assuring that they can be appropriately accessed.[12]

What variables should lawmakers consider when evaluating which party should bear the greatest financial risk under different contracting or coverage models?

As above, it is not currently for MDA to say which parties should bear the greatest financial risk for cell and gene therapies under the many options for contracting and coverage. However, under no circumstances should that party be patients and their families. As noted in the introduction of this RFI, these are already our most vulnerable patients who are dealing with high stakes where a lack of access means irrevocable harm. These patients should not then also have to manage the

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2019. Available at https://icer.org/assessment/duchenne-musculardystrophy-2019/ and https://icer.org/wp-content/uploads/2020/10/Corrected_ICER_DMD-FinalReport_042222.pdf.

[11] *See generally,* Under-Covered: How Insurance Like Products are Leaving Patients Exposed, https://www.lls.org/sites/default/files/National/undercovered_report.pdf

[12] https://votervoice.s3.amazonaws.com/groups/mda/attachments/01.30.2023%20Coalition%20Comments%20to%20HHS%20on%20Essential%20Health%20Benefits.pdf

burden of unmanageably high cost for treatment in addition to the cost of receiving a diagnosis in the first place,[13] the cost of potentially necessary durable medical equipment and home modification, and more ancillary costs such as missing time from work and school to receive treatment, among many others.

We greatly appreciate the opportunity to provide feedback on the Ranking Member's consideration of access to cell and gene therapies. Should you need any further information please contact either Paul Melmeyer, Vice President of Public Policy and Advocacy at pmelmeyer@mdausa.org or Joel Cartner, Director, Access Policy at jcartner@mdausa.org.

Sincerely,

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[13] https://everylifefoundation.org/wp-content/uploads/2023/09/EveryLife-Cost-of-Delayed-Diagnosis-in-Rare-Disease_Final-Full-Study-Report_0914223.pdf