Little Hercules Foundation

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Submitted by email to: osupharm.di@oregonstate.edu

August 25, 2026

RE: Public Comment — Duchenne Muscular Dystrophy Drug Class Update (October 1, 2026 meeting): proposed prohibition on targeted therapies following gene therapy, and on combination targeted therapy

Dear Members of the Pharmacy & Therapeutics Committee:

The Little Hercules Foundation is a nonprofit organization that helps families of children with Duchenne muscular dystrophy (DMD) access FDA-approved therapies. We write regarding two specific recommendations in the proposed October 2026 DMD class update: first, the proposal to deny coverage of targeted DMD therapies — both exon-skipping therapies and givinostat — following administration of gene therapy (delandistrogene moxeparvovec, or Elevidys); and second, the proposal to deny coverage of any combination of two or more targeted therapies. We respectfully urge the Committee not to adopt these categorical prohibitions, and instead to address these clinical situations through individualized, case-by-case prior authorization based on medical necessity.

We do not contest the updated safety criteria for Elevidys, which appropriately track the FDA's November 2025 labeling. Our concern is is that a blanket, categorical denial is an inappropriate regulatory instrument for clinical decision-making.

1. A categorical prohibition built on "absence of data" is not evidence-based.

The stated basis for both prohibitions is that there is no published data on the efficacy or safety of targeted therapy after gene therapy, and no literature evaluating combination treatment. Absence of evidence is not evidence of absence, and it is not a scientific basis for a statewide denial. When the literature does not yet address a specific clinical scenario, the appropriate response is individualized clinical judgment applied case by case — not a rule prohibiting the therapy for every patient in Oregon. Moreover, the lack of explicit combination trials is not a standard applied to combination therapies for more common, chronic disorders (e.g. heart disease, asthma, diabetes), in which such combinations are routinely prescribed based on complementary mechanism of action, without clinical trials designed to study specifically how those drugs work together.

2. The efficacy debate does not justify this prohibition.

We recognize that the Committee's review is skeptical that these therapies improve motor function on randomized endpoints, and while we disagree, we do not ask the Committee to resolve that debate in this proceeding. However, the proposed prohibition does not follow from this conclusion.

These are FDA-approved therapies. Elevidys carries traditional FDA approval for ambulatory patients, and the exon-skipping therapies and givinostat are FDA-approved for their respective indications. The FDA, reviewing this same body of evidence, determined that each met its standard

for approval. The Medicaid Drug Rebate Program directs states to cover FDA-approved drugs for their medically accepted indications; a categorical denial of such a therapy to a defined subgroup of patients is not an ordinary utilization-management tool, but a refusal to cover a medically accepted indication.

3. The prohibition overrides the treating specialist's judgment for every patient.

Each of these therapies is FDA-approved, and each request would come from a neuromuscular specialist who has determined, for an individual patient, that the therapy is medically necessary. The proposed criteria would override that determination categorically — regardless of the patient's mutation, disease course, response to prior treatment, or the specialist's clinical rationale. Oregon's existing criteria already route high-cost therapies through secondary DMAP review, which is exactly the mechanism suited to evaluating novel or uncertain requests one patient at a time. There is no need to replace that individualized review with a blanket bar.

4. The stated scientific rationale does not withstand scrutiny — for either the exon-skipping therapies or givinostat.

The proposed criteria rest on a scientific premise that "exon-skipping therapies affect mRNA splicing and their impact on transcription of the delivered micro-dystrophin gene is unknown." That premise does not support the prohibition of either class of drug.

Exon-skipping therapies are antisense oligonucleotides that act on the splicing of the patient's own dystrophin pre-mRNA — they bind specific splice sequences in the native gene to skip a targeted exon and restore the reading frame. The gene therapy does not deliver that native gene. It delivers an engineered micro-dystrophin — a compact, complementary-DNA construct built, as the Committee's own review explains, precisely because the full gene "is too large to be delivered in a viral capsid." That construct contains none of the native splice junctions that oligonucleotides are designed to target; there is no pre-mRNA splicing of the transgene for an exon-skipping drug to alter. The stated concern therefore conflates transcription with splicing and, more fundamentally, assumes an interaction between two therapies that operate on entirely different molecular elements — the patient's endogenous pre-mRNA on one hand, and a transgene on the other. Such an interaction is not supported by biology nor the chemistry of these drugs.

In the context of givinostat, the rationale does not apply at all. Givinostat is a histone deacetylase (HDAC) inhibitor. It does not act on dystrophin, on mRNA splicing, or on the micro-dystrophin transgene in any respect. As the Committee's own review states, the mechanism of givinostat is to increase muscle regeneration and reduce the replacement of healthy muscle with fat and fibrosis — pathological processes that continue in DMD even when partial dystrophin is present, including the shortened micro-dystrophin delivered by gene therapy. Combining an agent that targets inflammation and fibrosis with one that partially restores dystrophin is biologically rational, not contraindicated.

In short, the one mechanistic concern the Committee offers is unfounded as to the exon-skipping therapies and simply inapplicable to givinostat. To the extent any genuine uncertainty about

sequencing or combination remains, the answer is individualized assessment of the specific patient — not a categorical prohibition resting on a mechanism the science does not support.

5. Gene therapy is a one-time, non-curative treatment; permanently foreclosing all other options is arbitrary.

As the Committee's review acknowledges, the goal of Elevidys is to reduce symptom severity, not to cure the disease, and it is given as a single lifetime dose. A child who receives gene therapy still has Duchenne muscular dystrophy, will continue to progress, and over time will have sound clinical reasons to receive other targeted therapies. The proposed policy would permanently lock every such child out of every targeted therapy except corticosteroids, on the basis of one past treatment. For a progressive, fatal disease, a permanent categorical foreclosure of current or future FDA-approved options, disconnected from any individual patient's circumstances, is arbitrary and harmful.

6. The prohibition is in tension with EPSDT and adds a limit the FDA labels do not contain.

Under the federal Early and Periodic Screening, Diagnostic, and Treatment (EPSDT) requirement, Oregon must cover treatment that is medically necessary to correct or ameliorate a condition in a member under 21 — determined individually — regardless of limitations that would otherwise apply under the state plan. A categorical rule that denies a medically necessary, FDA-approved therapy to a child solely because of a prior gene therapy, with no individualized medical-necessity determination, cannot be reconciled with that obligation. Separately, none of the FDA-approved labels for the exon-skipping therapies or for givinostat contains any contraindication or limitation based on prior gene therapy or on concurrent use of another targeted agent. The proposed restriction is one the Committee would be adding beyond the medically accepted indications that the Medicaid Drug Rebate Program directs states to cover.

A better path: individualized review, not a categorical denial.

We respectfully ask the Committee to remove the categorical denials — the criterion denying targeted therapy after gene therapy, and the criterion denying combinations of two or more targeted therapies — and instead to evaluate these requests through the individualized, specialist-supported secondary-review process Oregon already uses, approving where the treating neuromuscular specialist documents medical necessity for the individual patient. This preserves the Committee's legitimate stewardship of high-cost therapies while ensuring that no child is categorically denied a medically necessary, FDA-approved treatment based on a rule that the evidence does not support.

We appreciate the rigor of the Committee's review and its commitment to Oregon's members. We would welcome the opportunity to provide additional clinical input, including from neuromuscular specialists who treat these patients.

Respectfully,

Kelly Maynard, President
Little Hercules Foundation

August 27, 2026

Oregon Health Authority
P&T Committee

RE: Duchenne Muscular Dystrophy Drug Class Update (October 1, 2026 meeting)

To Whom It May Concern:

I am writing to provide feedback on the proposed updated OHA criteria for Duchenne muscular dystrophy (DMD) to be reviewed in the October 1, 2026 Pharmacy and Therapeutics meeting. I am a board certified pediatric neuromuscular specialist at Oregon Health & Science University (OHSU) and director of the Ramberg Ford Center for Pediatric Neuromuscular Disorders at Doernbecher Children's Hospital. I have more than 15 years experience in caring for individuals with DMD.

I am writing as a treating physician to ask the Committee not to adopt two categorical restrictions in the proposed DMD class update: the denial of targeted therapies — both exon-skipping therapies and givinostat — after gene therapy, and the denial of any combination of two or more targeted therapies. I share the Committee's commitment to rigorous, evidence-based stewardship. My concern is that these two provisions would remove medically necessary decisions from the treating specialist and categorically deny them for every patient, including those for whom they are clinically appropriate.

Duchenne is not treated with one drug at one moment. It is managed over a lifetime with a layered, evolving regimen. A corticosteroid has historically served as the backbone; with the approval of additional therapies in recent years, we are now fortunate to have several tools in our armamentarium to offer patients in order to slow disease progression. Depending on a child's mutation, age, function, and disease course, we may add mechanism-specific therapies, together with cardiac and pulmonary care. As the disease progresses and as the evidence evolves, that regimen changes. Sound DMD care depends on the ability to individualize treatment and adjust it over time.

Gene therapy with delandistrogene moxeparvovec (Elevidys) is a single, one-time intervention offered at one point in the context of a disease that progresses over decades. It is not a cure; it partially restores a shortened form of dystrophin and slows progression. After a child receives it, he still has Duchenne muscular dystrophy, he continues to lose muscle, and he remains my patient. A rule that says a child who has received gene therapy may never again receive any targeted therapy other than a steroid — no matter how his

disease behaves over the next ten or twenty years — removes tools I may genuinely need to provide the best care for him.

I want to address the specific scientific basis offered for the prohibition, because it does not hold for either class of drug. First, exon-skipping therapies are antisense oligonucleotides that act on the splicing of a patient's own native dystrophin pre-mRNA — they bind specific sequences in the native gene to skip a targeted exon and restore the reading frame. Gene therapy, on the other hand, does not deliver that native gene. It delivers an engineered micro-dystrophin as a compact complementary-DNA construct. That construct contains none of the native splice junctions these oligonucleotides are built to target; there is simply no pre-mRNA splicing of the transgene for an exon-skipping drug to alter. The two therapies act on entirely different molecular substrates — the patient's endogenous pre-mRNA on one hand, and an intronless transgene on the other. As a clinician who uses these medications, I do not see a mechanistic basis for the concern that an exon-skipping therapy would interfere with the delivered micro-dystrophin gene.

Secondly, givinostat is further still from the stated concern, because it has nothing to do with dystrophin at all. It is a histone deacetylase (HDAC) inhibitor; it does not act on dystrophin, on mRNA splicing, or on the gene-therapy transgene. It addresses a different problem entirely — the chronic inflammation and the replacement of muscle with fat and fibrosis that continue in DMD even when some dystrophin is present. The micro-dystrophin produced by gene therapy is a shortened protein that lacks functional domains of normal dystrophin, so those downstream processes do not stop after treatment. Pairing an anti-inflammatory, anti-fibrotic agent with a therapy that partially restores dystrophin is mechanistically coherent, not contraindicated. Excluding givinostat on the basis of a dystrophin-interaction concern that does not even apply to it is not sound.

Multimodal therapy combining agents with distinct mechanisms of action is a well-established clinical practice supported by pathophysiologic rationale and society guidelines, even where head-to-head randomized trials of the specific combination are absent — a recognized and unavoidable gap because the number of possible regimens vastly exceeds what can ever be tested in dedicated trials. [1-2] Saver and Kalafut formally demonstrated the "theoretical limits of evidence-based medicine" for combination regimens: because possible combinations grow exponentially (e.g., 128 regimens from 7 agent classes in Alzheimer disease, 32 from 5 classes in ischemic stroke), exhaustively testing them would require hundreds of trials, hundreds of thousands of patients, and well over a century of enrollment. [1] They conclude that clinicians must rationally extrapolate from monotherapy efficacy and mechanistic complementarity, because dedicated combination trials for most regimens will never exist. [1] This is the central rebuttal to a denial premised solely on "no trials of the combination" — and it applies with particular force in a rare disease like DMD, where trial-eligible patient numbers are the rate-limiting resource. [3-4]

The use of two medications with similar or overlapping mechanisms of action is an established practice in other disease states, particularly when monotherapy does not achieve optimal disease control. For example, in epilepsy, patients with refractory seizures are often treated with multiple antiepileptic drugs that act on similar neuronal pathways to maximize seizure reduction. In oncology, combination chemotherapy regimens frequently include agents

targeting the same cellular processes to enhance efficacy and overcome resistance. Similarly, in rheumatology, patients with severe autoimmune disease may receive dual biologic therapies that modulate the same immune pathways when single-agent therapy is inadequate.

Finally, I would like to address a lack of similar limitations for complimentary therapy in other OHA drug class policies as prepared by OHSU Drug Information consult team.

Hematology

Sickle cell disease

OHA criteria limit exagamglogene autotemcel (Casgevy) and lovotibeglogene autotemcel (Lyfgenia) to once-in-a-lifetime treatment and disallow gene therapy after prior gene therapy or hematopoietic stem cell transplantation, but they do not categorically prohibit subsequent conventional disease-modifying treatment for sickle cell disease (SCD).[5] Under the Oregon Medicaid Preferred Drug List, hydroxyurea capsules are preferred and do not have a drug-specific prior authorization requirement, whereas crizanlizumab is nonpreferred and subject to pharmacy prior authorization.[6] Crizanlizumab's criteria require an FDA-approved indication, a 3-month trial of hydroxyurea at stable doses or a contraindication to hydroxyurea, age of at least 16 years, and at least 2 pain crises within the previous 12 months; renewal requires improvement in pain symptoms from baseline.[7] The criteria do not exclude patients based on prior SCD gene therapy or require evidence specifically supporting crizanlizumab after gene therapy. Direct evidence supporting either medication after SCD gene therapy is limited because the pivotal trials were designed to evaluate gene therapy as a stand-alone intervention. The Casgevy prescribing information requires hydroxyurea and crizanlizumab to be discontinued at least 8 weeks before mobilization and conditioning and states that there is no experience with hydroxyurea after Casgevy infusion, but it does not identify post-infusion hydroxyurea or crizanlizumab as contraindicated.[8] Notably, the original Version 1.0 CLIMB SCD-121 protocol, rather than the final Version 6.11 protocol, permitted hydroxyurea to be restarted after engraftment when a participant experienced vaso-occlusive crises or other SCD-related complications warranting reinitiation.[9] The published analysis did not report whether any participant actually restarted hydroxyurea.[10] The pivotal HGB-206 trial protocol for Lyfgenia similarly allowed hydroxyurea, crizanlizumab, and other SCD-directed therapy after transplantation only after discussion with and approval from the sponsor's medical monitor, a protocol control that limited evaluation of these therapies but did not establish that their post-gene-therapy use was unsafe or ineffective.[11-13] Thus, SCD may provide an OHA policy example in which conventional disease-modifying therapies remain potentially coverable despite limited evidence specifically evaluating their safety or efficacy after gene therapy.

Transfusion-dependent beta-thalassemia

OHA criteria similarly classify Casgevy and betibeglogene autotemcel (Zynteglo) as once-in-a-lifetime therapies and disallow gene therapy after prior gene therapy or hematopoietic stem cell transplantation, but they do not categorically prohibit subsequent conventional treatment for persistent transfusion dependence or anemia. [14] The pivotal Casgevy trial evaluated gene therapy as a stand-alone intervention and managed patients who did not achieve transfusion independence primarily through continued red blood cell transfusions and iron-removal therapy; luspatercept or another targeted erythroid therapy was not systematically evaluated after gene therapy in this study.[15] Luspatercept remains included in OHA's orphan-drug policy for its FDA-approved beta-thalassemia indication, and the general criteria support labeled use without expressly excluding patients who previously received gene therapy.[16] Therefore, this may provide an example in which OHA expressly prohibits repeat gene or stem-cell therapy but does not extend that prohibition to every subsequent disease-directed medication solely because post-gene-therapy sequencing studies are lacking.

Hemophilia B

OHA y prior authorization criteria limit etranacogene dezaparvovec (Hemgenix) to a once-in-a-lifetime dose and disallow treatment after prior gene therapy, but they do not categorically prohibit subsequent factor IX replacement therapy. [17] OHA currently classifies factor products within the Antihemophilia Factors class; however, the products listed in this class have a blank or null Preferred Drug List status, indicating that they have not been reviewed for preferred or nonpreferred placement, rather than that they are excluded from coverage.[18] The Hemgenix prescribing information does not establish the safety or efficacy of restarting long-term factor IX prophylaxis after an initial gene-therapy response diminishes, nor does it specify criteria for resuming chronic prophylaxis. The pivotal phase 3 HOPE-B trial was designed to evaluate Hemgenix against patients' prior factor IX prophylaxis, not to determine the comparative safety or efficacy of Hemgenix followed by resumed prophylaxis.[19] The HOPE-B protocol allowed or required factor IX prophylaxis after gene therapy based on endogenous factor IX activity, investigator judgment, patient preference, and clinical need.[21] In the final 5-year analysis, two participants without an adequate gene-therapy response continued prophylaxis, and one initial responder resumed continuous factor IX prophylaxis 29 months after gene therapy when factor IX activity declined to 3.6 IU/dL with concurrent bleeding. [20] The study documents this individual experience but does not establish the safety or efficacy of resumed prophylaxis through a controlled comparison or an adequately powered post-gene-therapy cohort.[21] Thus, hemophilia B may provide an example in which OHA does not impose an absolute prohibition on subsequent disease-directed treatment merely because robust evidence for the specific post-gene-therapy sequence is lacking.[22] The comparison to DMD is not exact because factor IX is replacement therapy rather than a mutation-targeted therapy. However, it demonstrates that OHA has addressed an evidence gap in another rare genetic disease through individualized clinical decision-making rather than interpreting the absence of sequencing trials as sufficient evidence that subsequent therapy must be denied.

Summary

Where explicit evidence of drugs' complementary effects is not available, the answer is individualized review— a specialist evaluating a specific patient and documenting medical necessity — not a statewide rule that denies the therapy to everyone. A categorical prohibition replaces clinical judgment with a blanket "no," and it will deny appropriate care to children in Oregon.

I respectfully ask the Committee to remove the categorical denials — targeted therapy after gene therapy, and combinations of two or more targeted therapies — and to rely instead on the individualized, specialist-supported review Oregon already uses, approving where the treating physician documents medical necessity for the individual patient. I would be glad to serve as a clinical resource to the Committee on these questions, and I thank you for your careful work on behalf of Oregon's patients.

Respectfully,

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Clinical Summary:

Secuado (asenapine) Transdermal system 3.8 mg/24 hours, 5.7 mg/24 hours, 7.6 mg/24 hours

Background

- Schizophrenia is a severe, chronic psychiatric disorder that affects more than 21 million people worldwide. It has been estimated that 1.5% to 3.0% of total U.S. national healthcare expenditures are directed towards this patient population.
- Schizophrenia has a profound impact on affected individuals, their families, and society. Patients experience multiple limitations to independent living, healthy social relationships, and successful employment, and most require caregiver support.
- Many patients with schizophrenia also suffer from other comorbid psychiatric conditions, such as major depression, drug and alcohol abuse or dependency, and anxiety disorder.
- Adult patients with schizophrenia also have a dramatically increased risk of premature mortality, commonly caused by cardiovascular disease, cancer, and accidents.
- Patients with schizophrenia are also at an increased risk of suicide.
- Adherence to antipsychotic medication use is consistently low in patients with schizophrenia.
- Pivotal drivers of patient non-adherence are the side effects and clinical limitations of existing drugs.
- Based on the limitations of existing treatments, and the high cost burden of schizophrenia, a recent critical appraisal concluded that different modes of antipsychotic medication administration are needed.
- The development of a transdermal antipsychotic option helps to address the need for different modes of administration and offers schizophrenia patients a route of administration that may contribute to improved adherence.

Secuado Safety and Efficacy

- Secuado® (asenapine) transdermal (patch) system (HP-3070) is a U.S. Food and Drug Administration (FDA)-approved atypical antipsychotic that differs from the originally approved formulation of asenapine (sublingual [SL] asenapine; Saphris®) in dosage form and approved indications. Secuado is indicated for the treatment of adults with schizophrenia.
- Available Secuado dosage strengths are: 3.8 mg/24 hours (9.0 mg asenapine Maleate per patch), 5.7 mg/24 hours (13.5 mg asenapine Maleate per patch) and 7.6 mg/24 hours (18.0 mg asenapiine Maleate per patch).
- The primary evidence supporting the efficacy of Secuado for the treatment of adults with schizophrenia was obtained from three Phase 1 trials and one Phase 3 clinical trial
- Patients treated with Secuado 9.0 mg or 18.0 mg transdermal patches for 6 weeks demonstrated significant improvements in the Positive and Negative Syndrome Scale (PANSS) and the Clinical Global Impression – Severity (CGI-S) scale compared to patients treated with placebo.
- With repeat application of the Secuado patch containing 4.5, 9.0, 13.5, and 18.0 mg asenapine maleate in patients with schizophrenia, plasma concentrations of asenapine reached steady-state in 48 to 72 hours, with minimal peak-trough concentration fluctuations.
- In the Phase 3 clinical trial, Secuado was well-tolerated; adverse events were generally mild to moderate in severity.
- The most common adverse reactions were extrapyramidal disorder, application site reaction, and weight gain.
- Observed skin irritations such as erythema, pruritus, papules, discomfort, pain edema or irritation were reported. Discontinuations due to application site reactions were infrequent (≤0.5% per treatment group).
- The comparative effectiveness of Secuado relative to other antipsychotic drugs has not been studied.

Conclusion

- Secuado (asenapine) transdermal patch is a new SGA approved by the U.S. FDA for the treatment of adult patients with schizophrenia. Secuado has a demonstrated safety, efficacy, and tolerability profile that is supported by evidence from Phase 1 and Phase 3 clinical trials, and it is the first antipsychotic therapy available as an alternative formulation in the U.S.
- Medication non-adherence poses an undue societal and economic burden for this patient population.
- Secuado represents a treatment option to address an unmet need for a more reliable mode of antipsychotic medication administration.
- Secuado transdermal asenapine provides a valuable addition to currently available atypical antipsychotic treatment options, and exhibits the potential to improve clinical, economic, and societal outcomes.