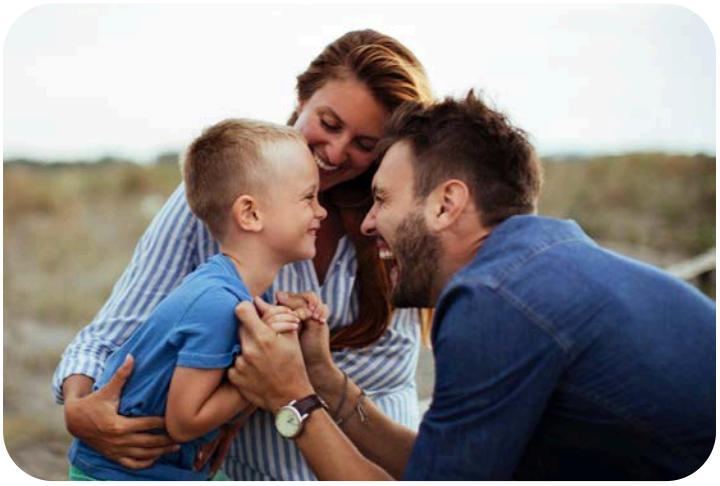
A Comprehensive Family Guide to Gene Therapy for Duchenne Muscular Dystrophy

Gene therapy is a treatment option that may help slow the progression of Duchenne muscular dystrophy (DMD). This type of therapy involves a one-time infusion designed to help muscle cells produce a shortened form of dystrophin, a protein important in muscle function. Deciding whether to consider gene therapy is a personal and medical decision that requires time, information and close partnership with a care team.

Evolving knowledge

Gene therapy for DMD and research into its efficacy (how well it works) and durability (how long it works) is very new. Factors such as disease progression, the person's age at the time of treatment, and their specific genetic variant, are just a few of the factors that may affect the level and type of benefit a person receives from the treatment. Gene therapies may also cause serious side effects, so the preparation, monitoring, and follow-up require significant amounts of time and communication between families and their care teams. Understanding safety and efficacy of gene therapy products helps all parties make informed and empowered decisions about treatment.

This guide was developed to help you understand the current recommendations and considerations for the delivery and monitoring of gene therapy and why they exist, empowering you and your family to make informed choices about gene therapy.



You will also find an overview of what gene therapy is, what to expect, and what questions to ask your healthcare provider. The guideline is based on clinical experience from experts who care for people living with DMD.

Recommendations may evolve as new research becomes available. Always consult with your medical team for guidance specific to you or your child and specific to a particular gene therapy program. While these guidelines are meant to apply to Duchenne gene therapies generally, each gene therapy (whether approved or investigational) will have its own specific eligibility criteria and treatment protocols that must be followed.

This guide is a family-friendly summary of a 2025 publication created by a work group coordinated by the Muscular Dystrophy Association (MDA) and Parent Project Muscular Dystrophy (PPMD). The workgroup included clinicians from fifteen gene therapy centers across the United States. They came together to create shared recommendations for how gene therapy for Duchenne muscular dystrophy (DMD) is given and monitored.

The original publication is titled Consensus Recommendations and Considerations for the Delivery and Monitoring of Gene Therapy in Patients with Duchenne Muscular Dystrophy (Wolff et al., 2025)[1]. That document was written for medical teams. This guide explains the same key points in language intended for families.

Many of the recommendations in this guide come from doctors' experience rather than peer-reviewed or published studies. This guide is meant to be a helpful starting point for you as you learn about gene therapy for people with DMD.

What is gene therapy for DMD?

Duchenne is caused by a missing or faulty dystrophin gene. Without it, muscle fibers break down over time. Gene therapy does not cure DMD or replace full-length dystrophin; it delivers a smaller, engineered version of "micro-dystrophin" designed to help slow progression using a viral vector called adeno-associated virus or AAV. Think of it as an 'envelope' to send instructions in the mail to specific areas of the body. In this case, the 'envelopes' are trillions of virus particles that help muscles produce dystrophin to stabilize muscle membranes and slow progressive damage.

Today, gene therapy is a one-time infusion. There is currently one FDA approved gene therapy for DMD, Elevidys (delandistrogene moxeparvovec-rokl). Other investigational gene replacement therapies are in clinical trials now. For approved gene therapies or gene therapies in clinical trials, each have specific criteria to determine who can receive therapy and what treatment protocols must be followed.

Once infused, the gene therapy treatment cannot be reversed. Following viral gene therapy, the body naturally develops antibodies to the viral envelope that was used, and these antibodies or immune cells are expected to stay in the body long term. For this reason, people who receive an AAV- based therapy are not yet eligible for another AAV-based therapy in the future.

It is important to understand that long term effects of gene therapy are still being studied and are currently unknown.

Eligibility

When deciding whether a person with DMD can receive gene therapy, clinicians are encouraged to engage in shared decision making with your family by discussing the following:

- **Genetic mutation:** Genetic testing is essential to confirm the diagnosis and identify risks. Some mutations in the dystrophin gene carry extra risk. For example, a person with deletions in exons 8 and/or 9 may develop dangerous immune reactions that impact muscle cells of the body and of the heart if the body rejects the new shortened dystrophin protein.

- **Antibody status:** Because gene therapy uses an AAV vector, people with existing antibodies against that virus may not qualify. This is because the antibodies in a person's body may clear out the gene therapy product before it has the opportunity to help, and this active immune response can cause other safety issues. A blood test is required to check for this. Even if a person has a negative test at first, antibody levels can change over time. Check with your doctor if you are unsure about your/your family member's antibody status or if repeat testing may be recommended prior to infusion.

- **Vaccination history:** A person considering gene therapy needs to be up to date on standard vaccines like Measles, Mumps, Rubella, Influenza, Pneumococcus, and COVID-19 before starting. This is important because with some treatments they will temporarily be on very high doses of steroids around the time of treatment, which weakens the immune system, potentially increasing the risk of getting sick.

- **Age and disease stage:** Most of the data we have today is from children (ages 4-7) who are still walking. Older or non-ambulatory people may qualify for treatment through a clinical trial, but evidence of benefit from gene therapy is limited, and risks may be higher depending on the age of the person and in cases of advanced progression.

- **Heart and liver function:** Gene therapy can stress the liver, sometimes severely. There can also be effects on the heart causing inflammation or abnormal heart rhythms. Those with serious heart or liver problems may not be good candidates for treatment. Before starting gene therapy, heart and liver testing will help your doctor understand whether gene therapy is a safe option.

Because of these factors, eligibility for treatment with gene therapy is not always simple. A careful evaluation at a specialized treatment center is required. You can expect careful screening. Safety considerations are paramount. The goal is always to minimize potential life-threatening complications and maximize potential benefits.

Choosing the right treatment provider

Gene therapy should only be given in hospitals or certified treatment centers with highly specialized teams that are experienced in the delivery of AAV-based gene therapy for DMD. Families should look for:

- **Experience in complex DMD care:** The center should already care for many individuals with DMD and have extensive experience managing steroids and gene therapy complications.

- **Multidisciplinary expertise:** A strong team includes a neurologist, cardiologist, pulmonologist, hepatologist (liver specialist), hematologist (a specialist in blood-related disorders), genetic counselor, endocrinologist, rehabilitation doctor, and specialized nurses. Additionally, this kind of treatment requires appropriate storage and preparation from a pharmacist or pharmacy.

- **Emergency capacity:** The hospital or treatment center must have access to intensive care (ICU) beds and lab testing on site since severe reactions can happen.

- **Insurance support:** Prior authorization requires medical records, test results, and letters of medical necessity. Approval can be a slow process. Families should plan for the process to take weeks to months before infusion is approved. Hospitals should have dedicated staff who handle prior authorizations and appeals.

- **Communication with local doctors:** If receiving the infusion far from home, the medical team at the treatment facility should coordinate with the family's local care team so that follow-up can be conducted safely.

You may need to stay near the treatment hospital for weeks after receiving gene therapy. It is important to ask how the hospital can facilitate housing and other support services.

WHY IT MATTERS

Gene therapy has known risks of lowered blood counts, allergic reactions, liver injury, heart or muscle inflammation, and immune system activation. Proper monitoring and emergency intervention can save lives.

Preparing for treatment

It is important to note that protocols may vary slightly between hospitals and/or gene therapy products. The purpose of this guide is to share recommendations for best practices.

Preparation should begin one to three months before infusion. The preparation phase is critical to safety and success. Here's what happens:

Testing: A full set of baseline assessments, including blood tests, heart scans, and detailed muscle function exams are recommended. These tests help doctors measure and assess the safety of delivering gene therapy to the person.

Steroid treatment: About a week before the infusion, it may be recommended that high-dose steroids (such as prednisone or prednisolone) begin. These medicines help reduce the chance of the immune system reacting against the gene therapy. Steroids may have side effects such as mood swings, weight gain, weaker bones, and upset stomach.

Medication review: Certain drugs, such as exon-skipping therapies or Duvyzat® (givinostat), are sometimes stopped before infusion. Doctors should carefully explain which medicines can continue and which need to be paused ahead and during treatment.

Family education: Your care team will meet with you to review risks, emergency plans, and what to expect in the weeks ahead. Some care teams ask families to complete a quiz or checklist to ensure everything is clearly understood and set expectations about the intensive follow-up required. Families should also consult any available FDA-approved Medication Guides.

Logistics: You may need to arrange for housing near the hospital, time off work, and care for siblings who may also require emotional support through the process.

WHY IT MATTERS:

The gene therapy product and the immune system interact in powerful, sometimes unpredictable ways. Good preparation, monitoring, and planning for possible complications reduces the chance of serious harm.

Infusion Day

On the day of infusion, plan to spend the entire day at the hospital. Any signs of fever or illness in the days prior to dosing must be brought to the attention of your medical team, who will determine whether it is safe to proceed with dosing or if there is a need to delay the infusion date for safety.

The gene therapy is delivered either through an intravenous (IV) infusion or via intrathecal (IT) administration, depending on the specific treatment. During the administration, the individual receiving treatment is closely monitored by the medical team for signs of allergic reaction: rash, fever, nausea, trouble breathing, or abdominal pain. Most facilities keep emergency medicines on hand to reduce or reverse severe reactions.

After the infusion, the person receiving treatment will be monitored for several hours. If the infusion is tolerated well, you may be able to go home or back to your temporary housing near the treatment center that same day. If there are concerns, a hospital stay may be recommended. You will be sent home with emergency contact numbers and instructions on signs and symptoms that may require immediate intervention.

WHY IT MATTERS:

Even though the infusion itself is short, allergic reactions can occur immediately or hours later. Make sure your care team is reachable by phone or nearby in case an unexpected reaction arises.

Aftercare and monitoring

The period immediately after the gene therapy infusion is the most critical due to the highest risk for serious side effects.

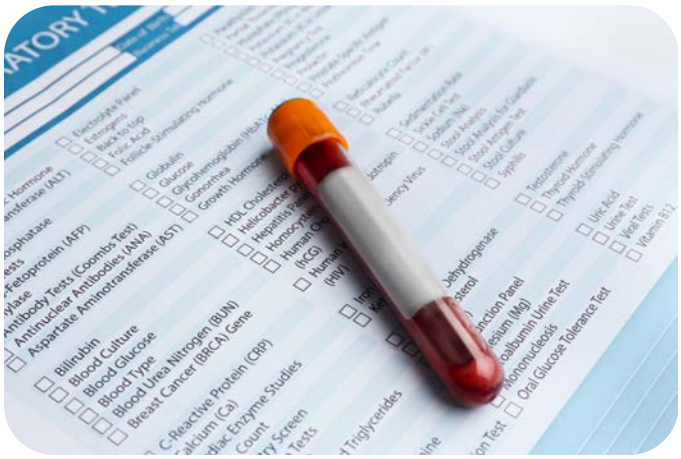
Families are usually asked to stay near the hospital or treatment center for a period of time, depending on the product's label or the clinical protocol. During this period, there are frequent blood tests and check-ups required to monitor how the body is responding. Fevers can happen, and any new symptoms should be reported to the care team right away.

High-dose daily steroids continue during this time and usually for at least two months after the infusion. After that, the dose is lowered slowly over time. Stopping steroids suddenly can be dangerous. If the person taking them is unable to take them for any reason, it is important to contact the care team immediately so another plan can be made. Side effects from daily high doses of steroids are expected and may include mood changes, trouble sleeping, and weight gain.

Because the AAV vector can be present in body fluids for a short time after treatment, families are advised to follow special precautions. This often includes wearing gloves during diaper changes or toileting, washing hands carefully, and double-bagging waste for about two months.

Using separate bathrooms or bedrooms can help reduce the chance of the viral vector coming into contact with other members of the household.

Long-term follow-up continues well past the infusion itself. After the first three months, families usually return for appointments every few months during the first year, then every six to twelve months after that. These visits help clinicians monitor safety and understand how well the therapy is working over time.



WHY IT MATTERS:

Many serious reactions start subtly—such as fever, nausea, weakness—and can escalate quickly. Being close to the hospital ensures rapid care is available if needed.

While long-term follow-up studies to measure efficacy and durability are being conducted, we do not yet know exactly how long benefits last or all the long-term risks. Continued care and monitoring is essential to keep individuals receiving gene therapy as safe and healthy as possible.

Risks families should know

While many people tolerate gene therapy well, serious complications can occur. These complications may include:

- **Liver injury:** After the gene therapy is delivered to the muscle, the viral vector is processed and broken down by the liver. In some cases, this has caused serious liver inflammation which can be severe and in rare cases, fatal. Regular blood tests are required to monitor liver enzyme levels.

- **Heart inflammation:** The immune system may attack the heart muscle. This can cause chest pain, fatigue, abnormal heart rhythms, or heart failure. Monitoring requires troponin blood tests and heart imaging.

- **Adrenal insufficiency:** Due to the daily high dose steroids, the adrenal glands of the body can be less active or 'sleepier' than normal in their activity. This means that during times of additional stress (illness, trauma, surgery) the body may not be able to make additional stress doses of cortisol when it is needed. Signs of adrenal crisis can include vomiting, change in mental status (seeming out of it or confused), abdominal pain, general weakness or fatigue, low blood sugar, or even lower blood pressure and shock. Talk to your care team about a stress dose steroid plan. See PJ Nicholoff Protocol for guidance (Ahmet & Kinnett, 2025)[2].

- **Muscle inflammation (myositis):** Rare but serious, myositis may appear weeks after the infusion causing weakness, swallowing problems, or breathing difficulties. Hospitalization and advanced immune therapies may be required.

- **Immune reactions:** Can happen during or soon after infusion. Rarely, reactions can affect multiple organs. This type of reaction requires emergency treatment.

- **Other side effects:** Fever, nausea, vomiting, kidney injury, or infusion reactions.

WHY IT MATTERS:

Because risks can be life-threatening, close monitoring helps catch problems early, when they are most treatable.

Talking to your care team

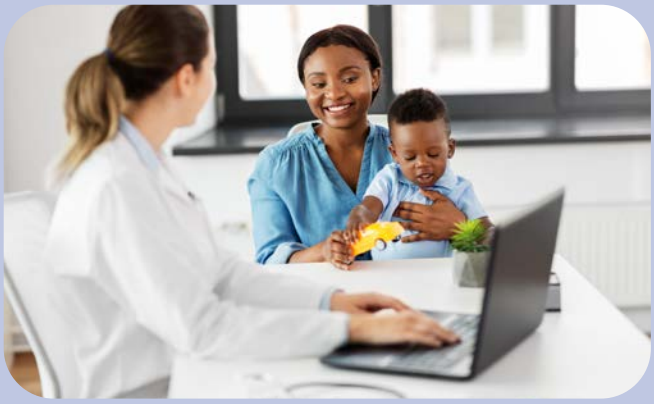
When considering gene therapy, it is normal to feel overwhelmed or frightened. Having a list of questions can help guide conversations with doctors and treatment centers.

Before deciding on gene therapy

- Is my/my loved one's genetic variant involved eligible for gene therapy?
- Does my/my loved one's age, heart health, or liver function change the risks of treatment?
- What benefits are realistic to expect? For example, could it help maintain strength or mobility for longer?
- Could gene therapy support more independence in daily life?
- How long might the benefits last?
- What are the main risks my family and I need to be prepared for?

Before deciding on gene therapy
(continued)

- Will the infusion interact with any medicines I am/my loved one is currently taking?
- What would happen if I/my loved one becomes very sick during or after the infusion?
- If gene therapy is not recommended, what other treatment or trial options are available now or in the near future?
- What should I know about long-term outcomes?



Questions for your care provider

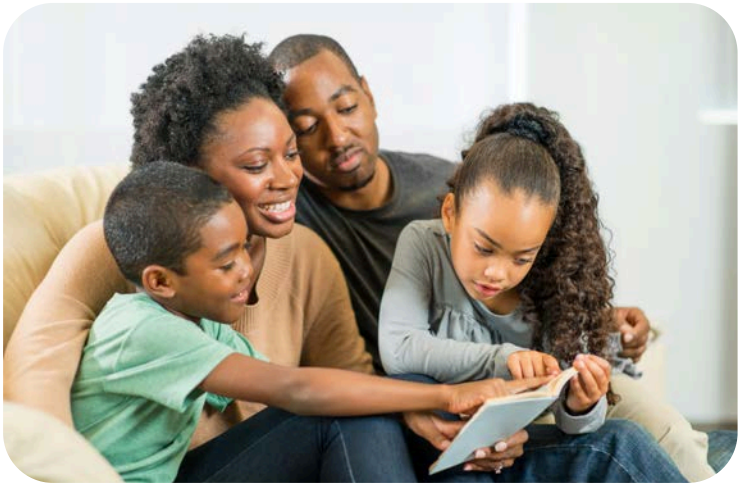
- How many people with DMD has this center treated with gene therapy?
- What side effects or complications have you seen here?
- How do you monitor people during and after infusion?
- How often will we need to return for visits in the first year? After that?

Questions for your care provider
(continued)

- How do you handle insurance approval and appeals? Who will help us with this?
- Will we need to relocate or stay near the hospital for follow-up? For how long?
- What housing or support services are available for families during this time?
- How do you coordinate care with our local neurologist or pediatrician?
- Who is on the care team, and how do we reach them after hours?
- What is your emergency plan if I/my loved one has a reaction during infusion?
- Do you provide an emergency card or instructions for local hospitals?
- What research or registry participation will be expected of us?
- If something goes wrong, what are your facility's capabilities for intensive care?
- How do you communicate results and next steps to my family and me?
- If there is more than one person in our family eligible for gene therapy, are there any special precautions that need to be taken to guard against antibody development in family members not treated at the same time?

Moving forward with confidence

Gene therapy for Duchenne muscular dystrophy represents both progress and complexity. It is not a simple treatment but rather a journey that involves careful preparation, monitoring, long-term follow-up, and risk. Gene therapy brings hope, but also important questions and responsibilities. Families should never feel rushed or pressured to make a decision. By asking questions, understanding the steps, and working with an experienced team, you can make the choice that feels right for you.



We invite you to contact MDA or PPMD for additional support:

MDA Resource Center Gene Therapy Specialists: for information, guidance and help facilitating access to novel therapies.

- Call: 1-833-ASK-MDA1 (1-833-275-6321)
- Email: ResourceCenter@mdausa.org.
- Schedule a time to connect: GTx Support Specialist Meeting

PPMD For You: to connect directly with a member of the PPMD with expertise in care, genetics, and approved therapies.

- Email: careteam@parentprojectmd.org
- Schedule a time to connect

For helpful resources, please visit:

- MDA Gene Therapy Support Network
- PPMD Gene Therapy Hub

References

1. Wolff, J. M., Capocci, N., Atas, E., Bharucha-Goebel, D. X., Brandsema, J. F., Butterfield, R. J., Chadwick, C. B., Corti, M., Crawford, T. O., Cripe, L., Day, J. W., Duong, T., ElMallah, M. K., Flanigan, K. M., George, L. A., … Byrne, B. J. (2025). Consensus recommendations and considerations for the delivery and monitoring of gene therapy in patients with Duchenne muscular dystrophy. Neuromuscular Disorders. Advance online publication. https://doi.org/10.1016/j.nmd.2025.106208
2. Ahmet, A., Kinnett, K., Lautatzis, M.-E., Lewis, L. M., & Cwik, V. A. (2025, April). The PJ Nicholoff Steroid Protocol. Parent Project Muscular Dystrophy. https://www.parentprojectmd.org/wp-content/uploads/2018/03/PJ-Nicholoff-Steroid-Protocol.pdf