Oscar Clinical Guideline: Elevidys (delandistrogene moxeparvovec-rokl) (PG160, Ver. 2)

Elevidys (delandistrogene moxeparvovec-rokl)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Duchenne muscular dystrophy (DMD) is an X-linked genetic disorder characterized by progressive muscle weakness and wasting due to lack of dystrophin protein. It primarily affects males, with onset around 2-5 years old. As the disease progresses, patients experience loss of ambulation, respiratory and cardiac complications, and premature death. There is no cure for DMD. Current management focuses on glucocorticoids to slow progression, supportive care, and emerging gene targeted therapies.

Elevidys (delandistrogene moxeparvovec-rokl) is an adeno-associated virus (AAV)-based gene therapy designed to deliver a micro-dystrophin transgene to muscle cells. It is FDA-approved under the accelerated approval pathway for:

- Ambulatory pediatric patients aged 4-5 years with confirmed DMD gene mutations.
- Non-ambulatory patients aged 4 years and older with confirmed DMD gene mutations (approval contingent on confirmatory trials).

While Elevidys (delandistrogene moxeparvovec-rokl) shows promise in increasing micro-dystrophin expression, its clinical efficacy in improving functional outcomes remains under investigation.

Definitions

"**Accelerated approval**" is a pathway by the FDA to allow earlier approval of drugs that treat serious conditions and fill an unmet medical need, based on surrogate or intermediate endpoints.

"**Adeno-associated virus (AAV)**" is a type of virus that can be used to deliver genetic material into cells during gene therapy.

"**Ambulation**" refers to the ability to walk without assistance.

"**Anti-AAV antibodies**" are proteins produced by the immune system in response to the AAV vector used in some gene therapies. These can potentially limit the effectiveness of future AAV-based gene therapies.

"**Biomarkers**" are measurable indicators of the severity or presence of a disease.

"**Blinded studies**" are clinical trials in which participants do not know whether they are receiving the experimental treatment or a placebo.

"**Duchenne muscular dystrophy (DMD)**" is a genetic disorder characterized by progressive muscle degeneration and weakness. It is caused by an absence of dystrophin, a protein that helps keep muscle cells intact.

"**Dystrophin**" is a protein necessary for muscle strength and function. Its absence or dysfunction leads to the muscle degeneration seen in DMD.

"**Gene therapy**" is a technique that aims to treat or prevent disease by replacing, adding, or editing genes within an individual's cells.

"**Glucocorticoids**" is a class of steroid hormones that can reduce inflammation and alter the immune response. They are used in DMD to slow the progression of the disease.

"**Micro-dystrophin**" is a smaller but functional form of the dystrophin protein, which gene therapies like Elevidys aim to introduce to patients' muscles.

"**North Star Ambulatory Assessment (NSAA)**" is a validated measure to assess ambulatory function in DMD patients.

"**Open-label**" is a type of clinical trial where both the researchers and the participants know which treatment is being administered.

"**Placebo-controlled trial**" is a study where the effect of a drug is compared with a placebo (a substance with no therapeutic effect).

"**Primary & Secondary endpoints**" are specific outcomes that a clinical trial is designed to measure, determining the effectiveness and side effects of a treatment.

"**Randomized controlled trials**" are clinical studies where participants are assigned to groups randomly, with one group receiving the treatment and the other a control (like a placebo).

"**X-linked**" is a mode of inheritance where the gene causing the condition is located on the X chromosome.

Policy Statement on Elevidys (delandistrogene moxeparvovec-rokl) Efficacy Information

There is insufficient evidence to indicate that Elevidys (delandistrogene moxeparvovec-rokl) provides clinically meaningful benefits that outweigh the potential risks for patients with Duchenne muscular dystrophy (DMD). The Plan considers Elevidys (delandistrogene moxeparvovec-rokl) to be not medically necessary for DMD at this time, as it is deemed to be experimental, investigational, or unproven.

- The clinical trials for Elevidys (delandistrogene moxeparvovec-rokl) (e.g., SRP-9001-101, SRP-9001-102, SRP-9001-103) have not demonstrated consistent, statistically significant improvements in functional outcomes, such as the North Star Ambulatory Assessment (NSAA), which is a key measure of efficacy in Duchenne muscular dystrophy (DMD).
    - Trial #1: SRP-9001-101 (Study 101, NCT03375164) is an open-label study with small sample size, showing numerical improvements in NSAA scores but lacking robust statistical significance.

    - Trial #2: SRP-9001-102 (Study 102, NCT03769116) failed to demonstrate statistically significant improvement in NSAA scores at 48 weeks compared to placebo. Subgroup analyses suggested potential benefit in patients aged 4-5 years.
    - Trial #3: SRP-9001-103 (Study 103, NCT04626674) is an ongoing open-label study showing increased micro-dystrophin expression but limited functional data.
- While Elevidys (delandistrogene moxeparvovec-rokl) has shown an increase in micro-dystrophin expression (a surrogate biomarker), there is no established correlation between this biomarker and clinically meaningful functional improvements in patients with DMD.
- Subgroup analyses suggest potential benefits in younger patients (ages 4-5 years), but these findings are exploratory and not prespecified, limiting their reliability.
- Safety Considerations
    - Serious adverse events, including acute liver injury, immune-mediated myositis, and myocarditis, have been observed in clinical trials.
    - The long-term safety profile of Elevidys (delandistrogene moxeparvovec-rokl) remains uncertain, particularly regarding the implications of high anti-AAVrh74 antibody titers, which may limit future gene therapy options.
- Elevidys (delandistrogene moxeparvovec-rokl) was initially approved under the accelerated approval pathway based on micro-dystrophin expression as a surrogate endpoint. For ambulatory pediatric patients aged 4-5 years, the FDA has granted traditional approval based on evidence of clinical benefit. However, for non-ambulatory patients aged 4 years and older, the approval remains under the accelerated pathway, contingent on confirmatory trials demonstrating clinical efficacy.

Medical Necessity Criteria for Elevidys (delandistrogene moxeparvovec-rokl)

Elevidys (delandistrogene moxeparvovec-rokl) is considered not medically necessary for any indication, including for the treatment of Duchenne muscular dystrophy (DMD).

Experimental or Investigational / Not Medically Necessary

Elevidys (delandistrogene moxeparvovec-rokl) is considered not medically necessary for any indication, including for the treatment of Duchenne muscular dystrophy (DMD) at this time. The available data are insufficient to demonstrate that Elevidys (delandistrogene moxeparvovec-rokl) provides clinically meaningful benefits that outweigh its risks.

The Plan will continue to monitor ongoing and future clinical trials, particularly confirmatory studies required by the FDA, to reassess its position as new evidence emerges. Individual coverage requests for Elevidys (delandistrogene moxeparvovec-rokl) may be considered on a case-by-case basis, particularly for members who meet the FDA-approved criteria. Until then, we encourage our members to explore alternative treatment options with their healthcare providers.

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
96367	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); additional sequential infusion of a new drug/substance, up to 1 hour (List separately in addition to code for primary procedure)
96368	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); concurrent infusion (List separately in addition to code for primary procedure)
J1413	Injection, delandistrogene moxeparvovec-rokl, per therapeutic dose
ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
G71.01	Duchenne or Becker muscular dystrophy

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