LifeWise
Health Plan of Washington

MEDICAL POLICY – 5.01.642

Gene Therapies for Rare Diseases

BCBSA Ref. Policy:	5.01.49
Effective Date:	Mar. 1, 2025
Last Revised:	Feb. 11, 2025
Replaces:	N/A

RELATED MEDICAL POLICIES:

2.04.144	Gene Therapy for Inherited Retinal Dystrophy
5.01.42	Gene Therapies for Thalassemia
5.01.634	Gene Therapies for Cerebral Adrenoleukodystrophy
5.01.570	Pharmacologic Treatment of Duchenne Muscular Dystrophy
5.01.574	Pharmacotherapy of Spinal Muscular Atrophy (SMA)
5.01.581	Pharmacologic Treatment of Hemophilia
5.01.635	Pharmacologic Treatment of Epidermolysis Bullosa
5.01.640	Pharmacologic Treatment of Sickle Cell Disease

Select a hyperlink below to be directed to that section.

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Gene therapy is a type of medical treatment that involves adding, removing, or changing a person's genetic material. Some gene therapies are already available for, and many gene therapies are being studied for individuals with serious or life-threatening rare diseases because they focus on correcting the root cause of the disease. This policy describes when gene therapies may be considered medically necessary for individuals with certain rare diseases.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Drug	Medical Necessity
Kebilidi (eladocagene exuparvovec-tneq)	**Kebilidi (eladocagene exuparvovec-tneq) may be considered medically necessary for the treatment of aromatic L-amino acid decarboxylase (AADC) deficiency when all the following criteria are met:** • The individual is aged 18 months or older **AND** • Has been diagnosed with AADC deficiency confirmed by the identification of biallelic mutations in the *DDC* gene **AND** • Has the severe phenotype of AADC deficiency defined as having no motor milestone achievement at baseline and no clinical response to standard of care therapies (e.g., dopamine receptor agonist or pyridoxine) **AND** • Kebilidi (eladocagene exuparvovec-tneq) is being prescribed by or in consultation with a specialist in pediatric neurology, a movement disorder specialist, or clinical geneticist specializing in the management of AADC deficiency **AND** • Has not previously received treatment with a gene therapy **AND** • Does not have neutralizing antibodies to adeno-associated virus serotype 2 (AAV2) **AND** • Kebilidi (eladocagene exuparvovec-tneq) will be administered as a one-time infusion
Lenmeldy (atidarsagene autotemcel)	**Lenmeldy (atidarsagene autotemcel) may be considered medically necessary for the treatment of metachromatic leukodystrophy (MLD) when all the following criteria are met:** • The individual has been diagnosed with MLD confirmed by ALL the following: ○ Arylsulfatase-A (ARSA) gene activity below the normal range in peripheral blood mononuclear cells or fibroblasts **AND** ○ Identification of two known or novel disease-causing ARSA alleles **AND**

Drug	Medical Necessity
	○ 24-hour urine collection shows elevated sulfatide levels **AND** • Was diagnosed with MLD when they were aged 6 years or younger **AND** • Currently has no clinical signs or symptoms related to their MLD diagnosis including but not limited to the following: ○ Delay in expected achievement of independent standing or independent walking ○ Documented normal neurological evaluation within the last 6 months **OR** • Has been diagnosed with MLD between 30 months and 6 years of age **AND** • Currently has a **Gross Motor Function Classification (GMFC-MLD)** level of 0 with ataxia or 1 **AND** • Currently has an intelligence quotient (IQ) of 85 or greater on age-appropriate neurodevelopmental testing **AND** • Lenmeldy (atidarsagene autotemcel) is being prescribed by or in consultation with a neurologist or a prescriber who specializes in MLD **AND** • Has not previously received treatment with a gene therapy **AND** • The individual has not previously received treatment with a hematopoietic stem cell transplant **AND** • Lenmeldy (atidarsagene autotemcel) will be administered as a one-time infusion

Drug	Investigational
• **Kebilidi (eladocagene exuparvovec-tneq)**	**Kebilidi (eladocagene exuparvovec-tneq) and Lenmeldy (atidarsagene autotemcel) are subject to the product's US**

Drug	Investigational
• **Lenmeldy (atidarsagene autotemcel)**	**Food and Drug Administration (FDA) dosage and administration prescribing information.** **All other uses of Kebilidi (eladocagene exuparvovec-tneq) and Lenmeldy (atidarsagene autotemcel) for conditions not outlined in this policy are considered investigational.** **Repeat treatment of Kebilidi (eladocagene exuparvovec-tneq) and Lenmeldy (atidarsagene autotemcel) is considered investigational.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**Non-formulary exception reviews for Kebilidi (eladocagene exuparvovec-tneq) and Lenmeldy (atidarsagene autotemcel) may be approved up to 12 months.** **All other reviews for Kebilidi (eladocagene exuparvovec-tneq) and Lenmeldy (atidarsagene autotemcel) may be approved as a one-time infusion.**
Re-authorization criteria	**Repeat treatment of Kebilidi (eladocagene exuparvovec-tneq) and Lenmeldy (atidarsagene autotemcel) is considered investigational.**

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the diagnosis, relevant history, genetic testing, physical evaluation, and medication history

Coding

Code	Description
CPT **HCPCS**	
J3590	Unclassified biologics (use to report Lenmeldy and Kebilidi)

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Gross Motor Function Classification in Metachromatic Leukodystrophy (GMFC-MLD)[1]

GMFC-MLD Level	
Level 0	Walking without support with quality of performance normal for age
Level 1	Walking without support but with reduced quality of performance, i.e. instability when standing or walking
Level 2	Walking with support. Walking without support not possible (fewer than five steps)
Level 3	Sitting without support and locomotion such as crawling or rolling. Walking with or without support not possible
Level 4	Sitting without support but no locomotion OR sitting without support not possible, but locomotion such as crawling or rolling
Level 5	No locomotion nor sitting without support, but head control is possible
Level 6	Loss of any locomotion as well as loss of any head and trunk control

Consideration of Age

The ages stated in this policy for which Kebilidi (eladocagene exuparvovec-tneq) and Lenmeldy (atidarsagene autotemcel) are considered medically necessary is based on the FDA prescribing information.

Benefit Application

Kebilidi (eladocagene exuparvovec-tneq) and Lenmeldy (atidarsagene autotemcel) are managed through the medical benefit.

Evidence Review

Kebilidi (eladocagene exuparvovec-tneq)

Kebilidi was granted an initial accelerated approval by the FDA based on safety and efficacy results from the Phase 2 PTC-AADC-GT-002 (NCT04903288) trial (referred to as Study 1 in the Kebilidi Prescribing Information), an ongoing, open-label, global study that enrolled 13 pediatric individuals with genetically confirmed, severe AADC deficiency who had achieved skull maturity assessed with neuroimaging. Individuals were compared to an external untreated natural history cohort of 43 pediatric individuals with severe AADC deficiency who had at least one motor milestone assessment after 2 years of age. The main efficacy outcome measure, gross motor milestone achievement evaluated at Week 48, was assessed using the Peabody Developmental Motor Scale, Second Edition (PDMS-2). The main efficacy outcome was evaluated in 12 of the 13 individuals treated in the study (one individual dropped out of the study prior to Week 48). Eight (67%) individuals achieved a new gross motor milestone at Week 48: three individuals achieved full head control, two individuals achieved sitting with or without assistance, two individuals achieved walking backward, and the individual with the "variant" severe phenotype was able to sit unassisted. The two individuals who achieved walking backward at Week 48 were treated before 2 years of age. The four individuals who were unable to achieve new gross motor milestones at Week 48 were treated between 2.8 and 10.8 years of age. In comparison, none of the 43 untreated control individuals with the severe phenotype had documented motor milestone achievement at last assessment at a median age of 7.2 years (range: 2–19 years). The median duration of follow-up was 72 weeks (range: 23–109 weeks). All reports of dyskinesia, the most common adverse reaction (AR), were reported within 3 months of Kebilidi administration, with two events requiring hospitalization. Though two reports of dyskinesia required hospitalization, most cases involved non-severe, involuntary movements of face, arm, leg, or entire body. The use of dopamine antagonists may be considered to control dyskinesia symptoms. One individual reported a worsening of oculogyric crisis (duration and frequency) during the hospitalization period post-Kebilidi administration. No other clinically significant ARs were reported.

Lenmeldy (atidarsagene autotemcel)

Metachromatic leukodystrophy (MLD) is a genetic condition that affects approximately 2500 individuals in the US and is caused by the accumulation of sulfatides, leading to myelin sheath destruction in the nerves of the central and peripheral nervous systems. Symptoms vary but include difficulty speaking, seizures, trouble walking, and behavioral and personality changes. Prior to the approval of Lenmeldy, the only treatment options for MLD were supportive care and stem cell transplant for pre-symptomatic or minimally symptomatic children. Lenmeldy is an ex vivo autologous hematopoietic stem cell gene therapy that uses a lentiviral vector (LVV) encoding the ARSA gene. The stem cells are collected from the individual, modified by adding a functional copy of the ARSA gene, and then transplanted back into the individual, where they engraft within the bone marrow. Lenmeldy is intended to be a one-time treatment, administered following conditioning with busulfan. The approval of Lenmeldy was supported by safety and efficacy data from a total of 39 children with PSLI, PSEJ, and ESEJ MLD who received the drug in two single-arm, open-label clinical trials and in an expanded access program (EAP). Data from children who received Lenmeldy were compared with data from 49 untreated natural history controls. For PSLI MLD, 14 treated children and 24 natural history children had sufficient follow-up to determine survival at 6 years from birth. At this time point, all individuals treated with Lenmeldy were alive, and 10 natural history children had died (42%). In addition, children with PSEJ MLD who received Lenmeldy showed slowing of motor and cognitive disease, and children with ESEJ MLD who received Lenmeldy showed slowing of cognitive disease. The most common side effects of Lenmeldy include fever and low white blood cell count, mouth sores, respiratory infections, rash, medical line infections, viral infections, fever, gastrointestinal infections, and enlarged liver. Treatment with Lenmeldy may be associated with the formation of blood clots or encephalitis. There is a potential risk of blood cancer associated with this treatment; however, no cases have been observed in individuals treated with Lenmeldy.

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History

Date	Comments
08/01/24	New policy, approved July 9, 2024. Added coverage criteria for Lenmeldy (atidarsagene autotemcel). Added drug name Lenmeldy to unlisted HCPCS code J3590.
03/01/25	Annual Review, approved February 11, 2025. Added coverage criteria for Kebilidi (eladocagene exuparvovec-tneq). Clarified that non-formulary exception review

Date	Comments
	authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.