CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Mucopolysaccharidosis – Gene Therapy – Fayuvi Utilization Management Medical Policy
- Fayuvi™ (rebisufligene etisparvovec-hopf intravenous infusion – Ultragenyx)

REVIEW DATE: 09/30/2026

OVERVIEW

Fayuvi, an adeno-associated virus vector-based gene therapy, is indicated for the treatment of **neurologic manifestations of mucopolysaccharidosis type IIIA (MPS IIIA; Sanfilippo syndrome type A) in pediatric patients** with preserved neurodevelopmental function.[1]

Fayuvi is given as a one-time (per lifetime) single dose of 3.0×10^{13} genome copies per kg of body weight, as an intravenous infusion.[1]

Disease Overview

Sanfilippo syndrome is a group of lysosomal storage disorders.[2,3] The estimated prevalence of Sanfilippo syndrome (across all four subtypes) is between 1:50,000 and 1:250,000, depending on the population. It is estimated to affect fewer than 200,000 individuals in the US.[2,4] Sanfilippo syndrome type A is the most common and aggressive form of Sanfilippo syndrome and is caused by variants in the *N-sulfoglucosamine sulfohydrolase (SGSH)* gene.[2,3] The disease is characterized by early-onset, severe, and progressive degeneration of the central nervous system. In later stages, patients experience a progressive loss of motor function, develop seizures and dysphagia, and may become bedridden. Death usually occurs within the second decade of life in patients with Sanfilippo syndrome type A.

Clinical Efficacy

The efficacy of Fayuvi was evaluated in Transpher A (unpublished, n = 28), an open-label, single-dose, dose-escalation study, and a long-term follow-up study (which includes patients from Transpher A).[1,5] All of the patients in Transpher A were diagnosed with Sanfilippo syndrome type A and received one dose of Fayuvi. The modified intention-to-treat population, which was used to evaluate the efficacy endpoint, included patients who were either ≤ 2 years of age or > 2 years of age with a Bayley Scales of Infant and Toddler Development, Third Edition (commonly referred to as Bayley-III) Cognitive development quotient ≥ 60. The Bayley-III is a development assessment tool used to detect early developmental delay, such as cognitive delay, in early childhood. A higher score indicates higher skill level. Change in Bayley-III Cognitive raw score in patients 24 months to 60 months of age (chronological age) treated with Fayuvi (n = 17) was compared with that of an external, untreated natural history group (n = 27). The mean age of the patients in the Fayuvi group at treatment was 21.8 months (range 3.0 months to 32.9 months) and the mean Bayley-III Cognitive raw score at baseline was 47.6 (range 3 to 69). The mean age of the patients in the untreated natural history group was 38.3 months (range 12 months to 58 months) and the mean Bayley-III Cognitive raw score at baseline was 55.1 (range 24 to 76). Across Transpher A and the long-term study, the median duration of follow-up was 4.2 years (range 2.9 years to 7.8 years); 82% of patients (n = 14/17) were followed for 5 years. In the Fayuvi group, the change in the Bayley-III Cognitive raw score was an improvement of 16 points vs. a decline of 7.6 points in the natural history group; treatment resulted in a 23.5-point higher Bayley-III Cognitive raw score ($P < 0.0001$).

© Express Scripts Strategic Development, Inc., 2026. All Rights Reserved.
This document is confidential and proprietary to Express Scripts Strategic Development, Inc. Unauthorized use and distribution are prohibited.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Fayuvi. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Because of the specialized skills required for evaluation and diagnosis of patients treated with Fayuvi as well as the specialized training required for administration of Fayuvi, approval requires Fayuvi to be prescribed by a physician who specializes in the condition being treated. All approvals are provided for one time (per lifetime) as a single dose. The approval duration is 90 days to allow for an adequate timeframe to administer one dose of therapy. If claims history is available, verification is required for certain criteria as noted by **[verification in claims history required]**. For the dosing criteria, verification of the appropriate weight-based dosing is required by a Medical Director as noted by **[verification required]**. All reviews (approvals and denials) will be forwarded to the Medical Director for evaluation.

Documentation: Documentation is required for use of Fayuvi as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory results, medical test results, claims records, prescription receipts, and/or other information. All documentation must include patient-specific identifying information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Fayuvi is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Mucopolysaccharidosis Type IIIA.** Approve a one-time (per lifetime) single dose if the patient meets ALL of the following (A, B, C, D, E, and F):
   Note: Mucopolysaccharidosis type IIIA is also known as Sanfilippo syndrome type A.
   - **A)** Patient has not received Fayuvi in the past **[verification in claims history required]**; AND
     Note: If no claims for Fayuvi is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Fayuvi.
   - **B)** Diagnosis of mucopolysaccharidosis type IIIA was confirmed by ONE of the following (i or ii):
     - **i.** Molecular testing showing variants in the *N-sulfoglucosamine sulfohydrolase* (*SGSH*) gene **[documentation required]**; OR
     - **ii.** Enzyme testing showing deficient or absent lysosomal enzyme sulfamidase **[documentation required]**; AND
       Note: The sulfamidase enzyme is also known as heparan sulfate N-sulfatase, heparan N-sulfatase, N-sulfoglucosamine sulfohydrolase, or sulfoglucosamine sulfamidase.
   - **C)** Baseline anti-adeno-associated virus serotype 9 (AAV9) titers are less than 1:100 **[documentation required]**; AND
   - **D)** The medication is prescribed by a neurologist, medical geneticist, or metabolic disease specialist; AND
   - **E)** Current patient body weight has been obtained within the past 30 days **[documentation required]**; AND
   - **F)** If criteria A through E are met, approve one dose of Fayuvi to provide a one-time (per lifetime) single dose of 3.0×10^{13} genome copies per kg of body weight by intravenous infusion **[verification required]**.
     Note: Fayuvi is provided as a customized kit to meet dosing requirements for each patient per their weight (in kilograms). Fayuvi kit sizes (per the cited NDC) are in Table 1.

© Express Scripts Strategic Development, Inc., 2026. All Rights Reserved.
This document is confidential and proprietary to Express Scripts Strategic Development, Inc. Unauthorized use and distribution are prohibited.

Dosing. The recommended dose of Fayuvi is a one-time (per lifetime) single-dose intravenous infusion of 3.0×10^{13} genome copies per kg of body weight. Fayuvi is provided as a customized kit to meet dosing requirements for each patient per their weight (in kilograms). Refer to the appropriate NDC number below for approval.

Table 1. Fayuvi Kits.

Patient Body Weight Range	Total Dose Volume	Number of Vials	NDC Number
2.5 kg to 3.0 kg	10 mL	5	69794-301-05
3.1 kg to 4.0 kg	12 mL	6	69794-302-06
4.1 kg to 5.0 kg	16 mL	8	69794-303-08
5.1 kg to 6.0 kg	18 mL	9	69794-304-09
6.1 kg to 7.0 kg	22 mL	11	69794-305-11
7.1 kg to 8.0 kg	24 mL	12	69794-306-12
8.1 kg to 9.0 kg	28 mL	14	69794-307-14
9.1 kg to 10.0 kg	30 mL	15	69794-308-15
10.1 kg to 12.0 kg	36 mL	18	69794-309-18
12.1 kg to 14.0 kg	42 mL	21	69794-310-21
14.1 kg to 16.0 kg	48 mL	24	69794-311-24
16.1 kg to 18.0 kg	54 mL	27	69794-312-27
18.1 kg to 20.0 kg	60 mL	30	69794-313-30
20.1 kg to 22.0 kg	66 mL	33	69794-314-33
22.1 kg to 24.0 kg	72 mL	36	69794-315-36
24.1 kg to 26.0 kg	78 mL	39	69794-316-39
26.1 kg to 28.0 kg	84 mL	42	69794-317-42
28.1 kg to 30.0 kg	90 mL	45	69794-318-45
30.1 kg to 32.0 kg	96 mL	48	69794-319-48
32.1 kg to 34.0 kg	102 mL	51	69794-320-51
34.1 kg to 36.0 kg	108 mL	54	69794-321-54
36.1 kg to 38.0 kg	114 mL	57	69794-322-57
38.1 kg to 40.0 kg	120 mL	60	69794-323-60
40.1 kg to 42.0 kg	126 mL	63	69794-324-63
42.1 kg to 46.0 kg	138 mL	69	69794-325-69
46.1 kg to 50.0 kg	150 mL	75	69794-326-75
50.1 kg to 54.0 kg	162 mL	81	69794-327-81
54.1 kg to 58.0 kg	174 mL	87	69794-328-87
58.1 kg to 62.0 kg	186 mL	93	69794-329-93
62.1 kg to 66.0 kg	198 mL	99	69794-330-99
66.1 kg to 70.0 kg	210 mL	105	69794-331-05

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Fayuvi is not recommended in the following situations:

1. **Prior Receipt of Gene Therapy**. Fayuvi has not been studied in patients who have undergone prior gene therapy.[1,5]

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

© Express Scripts Strategic Development, Inc., 2026. All Rights Reserved.
This document is confidential and proprietary to Express Scripts Strategic Development, Inc. Unauthorized use and distribution are prohibited.

REFERENCES

1. Fayuvi™ intravenous infusion [prescribing information]. Novato, CA: Ultragenyx; September 2026.
2. Muschol N, Giugliani R, Jones SA, et al. Sanfilippo syndrome: consensus guidelines for clinical care. *Orphanet J Rare Diseases*. 2022;17:391.
3. Benetó N, Vilageliu L, Grinberg G, et al. Sanfilippo syndrome: molecular basis, disease models and therapeutic approaches. *Int J Mol Sci*. 2020;21:7819.
4. What is Sanfilippo syndrome. Last updated April 17, 2026. Available at: https://curesanfilippofoundation.org/what-is-sanfilippo/. Accessed on September 23, 2026.
5. Fayuvi – Data on File, from Ultragenyx. Received on September 24, 2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	09/30/2026

© Express Scripts Strategic Development, Inc., 2026. All Rights Reserved.
This document is confidential and proprietary to Express Scripts Strategic Development, Inc. Unauthorized use and distribution are prohibited.