FAYUVI™
rebisufligene etisparvovec-hopf
suspension for IV infusion

ADVANCING MPS IIIA TREATMENT

The first and only FDA-approved therapy for MPS IIIA

(mucopolysaccharidosis type IIIA, Sanfilippo syndrome type A)

FDA, US Food and Drug Administration.

Indication

FAYUVI™ (rebisufligene etisparvovec-hopf) is an adeno-associated virus (AAV) vector-based gene therapy indicated for the treatment of neurologic manifestations of mucopolysaccharidosis type IIIA (MPS IIIA, Sanfilippo syndrome type A) in pediatric patients with preserved neurodevelopmental function.

Important Safety Information

WARNINGS AND PRECAUTIONS

Hepatotoxicity

- Elevated liver enzymes (ALT, AST, and GGT) were observed in clinical studies of FAYUVI. Prior to FAYUVI infusion, assess liver function by clinical examination and laboratory testing (ALT, AST, GGT, and total bilirubin), and evaluate liver-related medical history. Administer corticosteroids to all patients before and after the FAYUVI infusion. If abnormalities are observed, adjust the corticosteroid treatment regimen, including increasing the dose and/or prolonging the corticosteroid taper period.

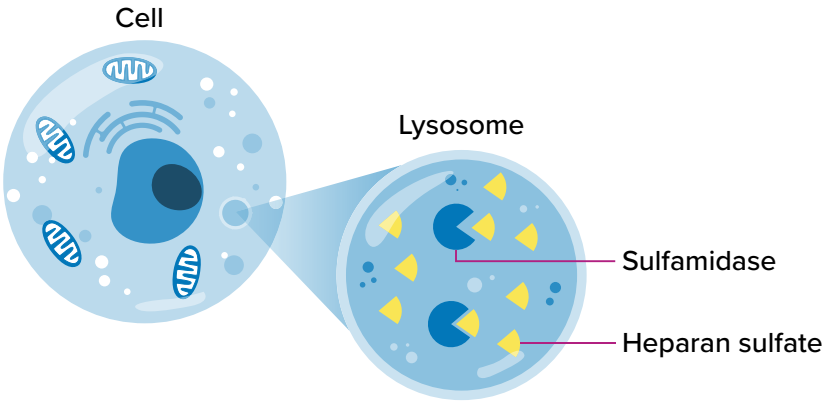
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Mechanism of action

FAYUVI is a single-dose intravenous therapy designed to address MPS IIIA at the genetic level[1]

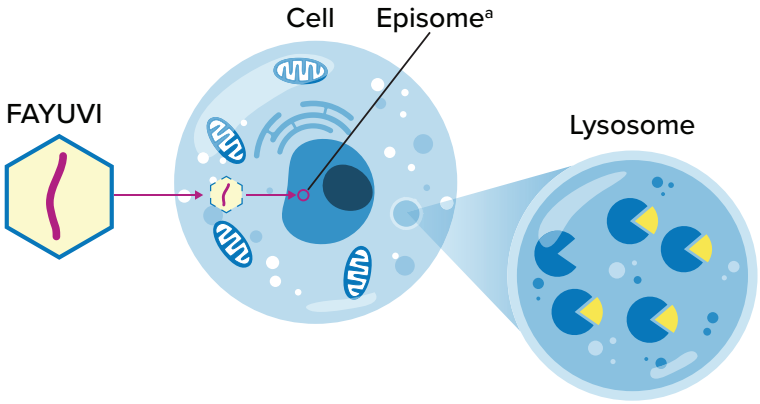
MPS IIIA Pathophysiology[2,3]

- Pathogenic variants of the *SGSH* gene lead to a deficiency in sulfamidase, a lysosomal enzyme necessary for the metabolism of heparan sulfate
- Lack of functional sulfamidase causes toxic heparan sulfate buildup, leading to cell damage and multisystemic MPS IIIA manifestations



How FAYUVI Is Designed to Work[1,4]

- AAV9-based gene therapy designed to deliver a functional copy of the human *SGSH* gene to cells. The *SGSH* gene encodes N-sulfoglucosamine sulfohydrolase, also known as sulfamidase
- Intravenous infusion of FAYUVI results in production of the lysosomal enzyme sulfamidase in target tissues, with subsequent breakdown of heparan sulfate in lysosomes



[a]Exogenous DNA that remains separate from the cell's endogenous chromosomes.[5]

AAV9, adeno-associated virus serotype 9; MPS IIIA, mucopolysaccharidosis type IIIA; *SGSH*, N-sulfoglucosamine sulfohydrolase.

Important Safety Information (Cont.)

WARNINGS AND PRECAUTIONS (CONT.)

Hepatotoxicity (Cont.)

- Closely monitor ALT, AST, GGT, and total bilirubin levels after FAYUVI administration until 2 weeks after the corticosteroid taper is complete and as clinically indicated. Continue to monitor liver function in all patients who develop elevated liver enzymes until levels return to baseline.

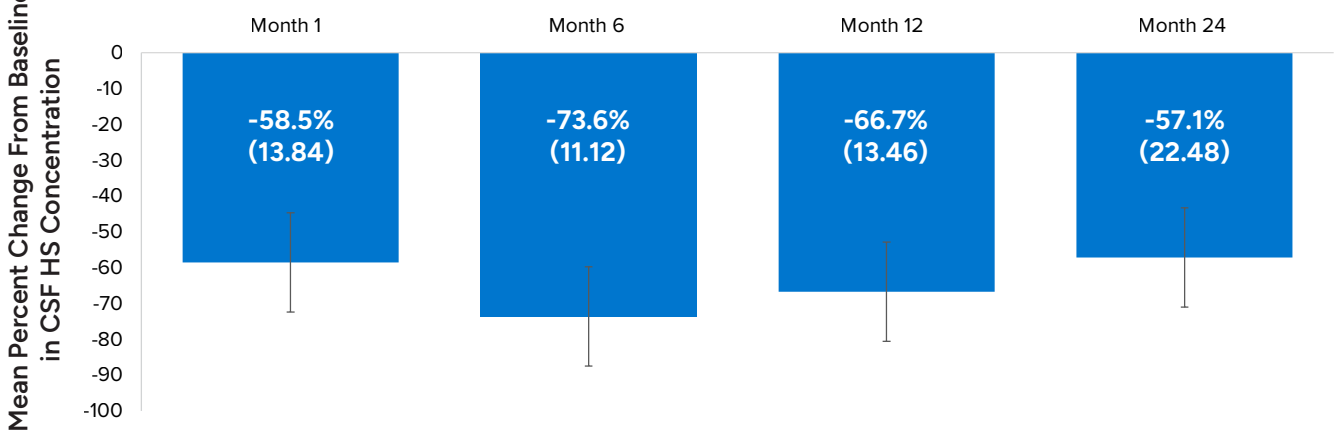
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Pharmacodynamics: FAYUVI reduces CSF HS levels[1]

FAYUVI-treated patients (mITT, n=16) experienced a reduction in CSF HS levels at Month 1 and sustained through Month 24[1]

MEAN (SD) PERCENT CHANGE FROM BASELINE[a] IN CSF HS CONCENTRATION IN mITT POPULATION



CSF HS EXPOSURE[b] AT MONTH 24 (mITT population)

-63.78% (11.56)
Mean (SD) percent change from baseline (N=17)

93.8%
of patients (15 of 16) **maintained a reduction of at least 50%**

[a]In Study 1, the mean (SD) baseline CSF HS concentration in the mITT population (N=17) was 335.3 (156.9) nmol/L.
[b]CSF HS exposure represents the time-normalized AUC of the percent change from baseline in CSF HS concentration. In Study 1, the mean (SD) change from baseline in CSF HS exposure was -29.25% (6.92) at Month 1, -60.17 (9.43) at Month 6, -65.02 (9.42) at Month 12, and -63.78% (11.56) at Month 24 in the mITT population (N=17).

AUC, area under the curve; CSF, cerebrospinal fluid; HS, heparan sulfate; mITT, modified intention-to-treat; SD, standard deviation.

Important Safety Information (Cont.)

WARNINGS AND PRECAUTIONS (CONT.)

Thrombocytopenia

- Decreased platelet counts were observed in clinical studies of FAYUVI.
- Prior to FAYUVI infusion, assess platelet counts. Monitor platelet counts weekly for the first 4 weeks, then monthly for 6 months following infusion. Continue monitoring as clinically indicated.

Thrombotic Microangiopathy

- Thrombotic microangiopathy (TMA) has been reported in association with AAV gene therapies. While there have been no cases of TMA associated with FAYUVI in clinical studies, laboratory and clinical monitoring for TMA following FAYUVI infusion is recommended.

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Efficacy was evaluated in 2 clinical studies[1]

Overview of clinical studies[1,6]

STUDY 1

Multicenter, open-label, single-arm, single-dose, dose-escalation (NCT02716246)

17 patients with MPS IIIA administered a 3.0 × 10^{13} vg/kg dose of FAYUVI and observed for 24 months (mITT population)

STUDY 2

Long-term follow-up of patients from Study 1 (NCT04360265)

Continued observation after FAYUVI administration

Primary efficacy population[1]

The primary efficacy population was the modified intention-to-treat (mITT) population,[a] which included 17 pediatric patients from Study 1 who received the recommended dose of FAYUVI 3.0 × 10^{13} vg/kg and were:

- ≤2 years of age at treatment, or
- >2 years of age with a cognitive developmental quotient (DQ) of ≥60[b] at treatment calculated by the Bayley Scales of Infant and Toddler Development – Third Edition (Bayley-III) or the Mullen Scales of Early Learning

Efficacy endpoint[1]

EFFICACY ENDPOINT

The difference in mean change in Bayley-III Cognitive Scale raw score between 24 to 60 months of chronologic age between FAYUVI-treated patients in mITT population and untreated natural history patients[c]

What is Bayley-III?

The Bayley-III Cognitive subtest assesses sensorimotor development, exploration and manipulation, object relatedness, concept formation, memory, and other aspects of cognitive processing.

Each item is scored 0 or 1, and scores range from 0 to 91 with higher scores indicating higher skill level.

[a]Mean age (range) at time of treatment was 21.8 months (3.0 to 32.9 months); mean weight (range) at baseline was 13.1 kg (3.9 to 17.5 kg); mean Bayley-III Cognitive raw score (range) at baseline was 47.6 (3 to 69) (population size was n=14 for mean Bayley-III Cognitive raw score).
[b]Indicative of mild or moderate neurodevelopmental impairment.
[c]FAYUVI-treated patients from the mITT population (N=17) were compared to untreated patients with MPS IIIA from an external, natural history control (N=27).

mITT, modified intention-to-treat; MPS IIIA, mucopolysaccharidosis type IIIA; vg/kg, vector genomes per kilogram.

Important Safety Information (Cont.)

WARNINGS AND PRECAUTIONS (CONT.)

Thrombotic Microangiopathy (Cont.)

- Monitor platelet counts closely within the first 4 weeks following FAYUVI infusion. Signs and symptoms of TMA may include, but are not limited to, thrombocytopenia, hemolytic anemia, easy bruising, hypertension, seizures, decreased urine output, and renal dysfunction. If TMA is suspected, immediately consult a pediatric hematologist and/or nephrologist for further evaluation and management as clinically indicated.

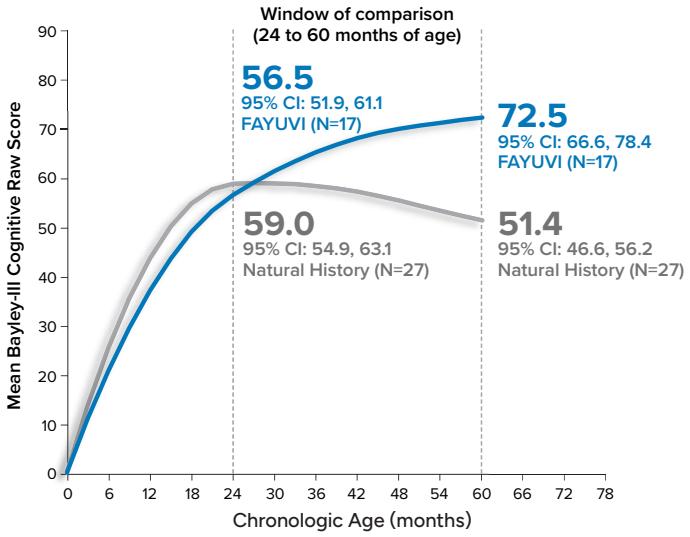
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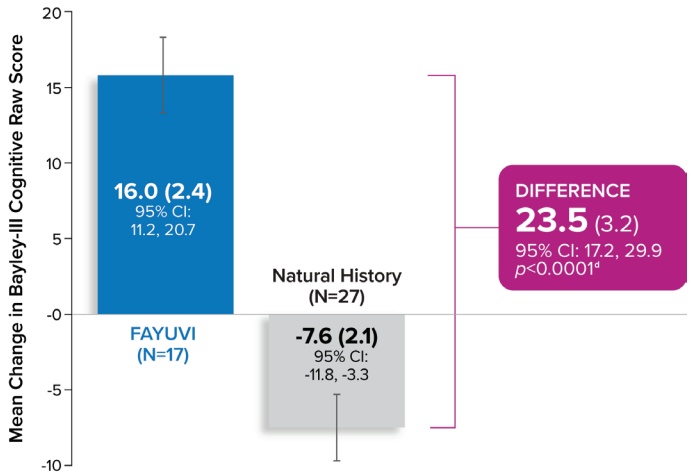
FAYUVI significantly improved Bayley-III Cognitive raw score vs natural history cohort[1]

FAYUVI-treated patients (mITT, N=17) demonstrated a statistically significant mean change in Bayley-III Cognitive raw score from 24 to 60 months of age vs untreated patients in the natural history cohort (N=27)[1a]

PREDICTED MEAN BAYLEY-III COGNITIVE RAW SCORES VERSUS AGE[7b]



MEAN CHANGE[c] (SE) IN BAYLEY-III COGNITIVE RAW SCORE FROM 24 TO 60 MONTHS OF AGE[1]



[a]Data from Study 1 and Study 2.
[b]Individual patients were weighted based on their propensity scores using baseline age (age at treatment for mITT and age at consent for Natural History Analysis Sets) using Stabilized Inverse Probability of Treatment Weighting method.
[c]Least squares mean changes were based on a non-linear mixed effects model adjusted for chronologic age (months).
[d]*p*-value is based on a non-linear mixed effects model with response variable Bayley-III Cognitive raw score and with chronologic age (months) as a covariate.

FAYUVI-treated patients gained or maintained developmental skills, while untreated patients in the natural history population experienced a loss of developmental skills

Bayley-III, Bayley Scales of Infant and Toddler Development – Third Edition; CI, confidence interval; mITT, modified intention-to-treat; SE, standard error.

Important Safety Information (Cont.)

WARNINGS AND PRECAUTIONS (CONT.)

Hypersensitivity and Infusion Reactions

- Infusion reactions, including hypersensitivity reactions and anaphylaxis, may occur with infusion of FAYUVI. Symptoms may include, but are not limited to, hypotension, pyrexia, palpitation, nausea, vomiting, chills, or headache.

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Adverse reactions

Adverse reactions following treatment with FAYUVI[1]

- Safety was evaluated in 33 pediatric patients with MPS IIIA who received a single intravenous infusion of FAYUVI in 3 clinical studies: 2 open-label, single-arm studies (Study 1 and Study 3) and 1 long-term follow-up study (Study 2) that enrolled patients who participated in one of the prior studies.
- 27 patients received the recommended dose of 3.0×10^{13} vg/kg.
- The mean age at the time of treatment was 38.5 months (range: 3.0 months to 9.2 years) and the mean weight was 17.1 kg (range: 3.9 to 31.2 kg).
- The median duration of follow-up after FAYUVI infusion was 4.1 years (range: 7.0 months to 7.8 years).

ADVERSE REACTIONS OCCURRING IN ≥5% OF PATIENTS FOLLOWING TREATMENT WITH FAYUVI 3.0×10^{13} vg/kg (N=27)[1]

Adverse Reactions	Number of Patients (%)	Adverse Reactions	Number of Patients (%)
Liver enzyme increased[a]	23 (85%)	**Constipation**[b]	4 (15%)
Vomiting[b]	18 (67%)	**Nausea**[b]	3 (11%)
Abnormal behavior[b,c]	15 (56%)	**Amylase increased**[b]	3 (11%)
Diarrhea[b]	13 (48%)	**Alkaline phosphatase increased**[b]	3 (11%)
Pyrexia[b]	11 (41%)	**Seizure**[f]	3 (11%)
White cell count decreased[d]	8 (30%)	**Hepatomegaly**[b]	3 (11%)
Cushingoid features[b]	8 (30%)	**Muscle spasticity**[b]	2 (7%)
Decreased appetite[b]	6 (22%)	**Hypokalemia**[b]	2 (7%)
Platelet count decreased[b,e]	5 (19%)	**Gait disturbance**	2 (7%)
Anemia[b]	5 (19%)	**Adrenal insufficiency**[b]	2 (7%)

[a]Includes aspartate aminotransferase (AST) increased, alanine aminotransferase (ALT) increased, and gamma-glutamyl transferase (GGT) increased.
[b]All adverse reactions were of Grade 1 or Grade 2 severity.
[c]Includes abnormal behavior, affect lability, aggression, agitation, irritability, nervousness, anxiety, attention-deficit/hyperactivity disorder, behavior disorder, insomnia, mental status changes, and related behavioral terms.
[d]Includes white blood cell count decreased, leukopenia, lymphocyte count decreased, lymphopenia, and neutropenia.
[e]Includes platelet count decreased and thrombocytopenia.
[f]Includes seizure, epilepsy, status epilepticus, partial seizures.

MPS IIIA, mucopolysaccharidosis type IIIA; vg/kg, vector genomes per kilogram.

Important Safety Information (Cont.)

WARNINGS AND PRECAUTIONS (CONT.)

Hypersensitivity and Infusion Reactions (Cont.)

- Closely monitor patients for clinical signs and symptoms of infusion reactions, including hypersensitivity reactions, and monitor vital signs during and after completion of FAYUVI infusion as clinically indicated. In the event of an infusion reaction during administration, pause the infusion and provide supportive care according to clinical practice. If the infusion is paused and continued administration is appropriate, restart at a slower rate after the infusion reaction has resolved.

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Adverse reactions (cont.)



Hepatotoxicity[1]

In clinical trials, 85% (23/27) of patients receiving the recommended dose of FAYUVI experienced adverse reactions associated with liver enzyme elevations (AST, ALT, and/or GGT).

- Most liver enzyme elevations were less than Grade 3 in severity, and none were associated with elevations of total bilirubin.
- A single Grade 3 ALT elevation in one patient occurred in the setting of gastroenteritis 62 days following FAYUVI infusion and resolved spontaneously within 8 days.
- The time to first onset was most frequently within the first 14 days and ranged from 2 days to 30.3 months following FAYUVI infusion.
- All liver enzyme elevations resolved within 6 days to 40.6 months of onset, except in 2 patients where slight elevations persisted.



Neutropenia[1]

In clinical trials, 22% (6/27) of patients receiving the recommended dose of FAYUVI experienced neutropenia.

- One patient experienced Grade 3 neutropenia, and the remaining events were of Grade 1 or 2 severity.

For more information, scan or click for FAYUVI full Prescribing Information

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase.

Important Safety Information (Cont.)

WARNINGS AND PRECAUTIONS (CONT.)

Risk of Malignancy

- Malignancy may occur following treatment with FAYUVI due to potential integration of AAV vector DNA into the genome.
- In the event of a malignancy, contact Ultragenyx Pharmaceutical Inc. at 1-888-756-8657.

ADVERSE REACTIONS

- The most common adverse reactions are (≥5%): liver enzyme increased (85%), vomiting (67%), abnormal behavior (56%), diarrhea (48%), pyrexia (41%), white cell count decreased (30%), Cushingoid features (30%), decreased appetite (22%), platelet count decreased (19%), anemia (19%), constipation (15%), nausea (11%), amylase increased (11%), alkaline phosphatase increase (11%), seizure (11%), hepatomegaly (11%), muscle spasticity (7%), hypokalemia (7%), gait disturbance (7%), and adrenal insufficiency (7%).

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FAYUVI is the first and only FDA-approved therapy for MPS IIIA

Once enrolled, UltraCare® Gene Therapy Guides are available to help support your patient along their FAYUVI treatment journey

Scan or click to enroll a patient in UltraCare Patient Services for Gene Therapy

Scan or click to learn more about FAYUVI

FDA, US Food and Drug Administration; MPS IIIA, mucopolysaccharidosis type IIIA.

Indication

FAYUVI™ (rebisufligene etisparvovec-hopf) is an adeno-associated virus (AAV) vector-based gene therapy indicated for the treatment of neurologic manifestations of mucopolysaccharidosis type IIIA (MPS IIIA, Sanfilippo syndrome type A) in pediatric patients with preserved neurodevelopmental function.

Important Safety Information (Cont.)

VACCINATIONS

- Prior to FAYUVI administration, consider the patient's vaccination status. Vaccines should be avoided 30 days prior to treatment with FAYUVI (and use of corticosteroids) and while on corticosteroid therapy.

PREGNANCY

- There are no data on the use of FAYUVI in pregnant women. Women who are pregnant or desire to become pregnant should not be treated with FAYUVI. A negative serum pregnancy test must be confirmed before administration of FAYUVI in females of childbearing potential.

VECTOR SHEDDING

- Temporary vector shedding of FAYUVI occurs primarily through bodily fluids and waste. Advise patients and/or caregivers on proper handling of patient bodily fluids and waste, including hand hygiene after direct contact. These precautions should be followed for 3 months after FAYUVI infusion.

Report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088. You may also report side effects to Ultragenyx Pharmaceutical Inc. at 1-888-756-8657.

Please see the full Prescribing Information for FAYUVI.

References: 1. FAYUVI [Prescribing Information]. Novato, CA: Ultragenyx Pharmaceutical Inc; October 2026. **2.** Seker Yilmaz B, Davison J, Jones SA, Baruteau J. Novel therapies for mucopolysaccharidosis type III. *J Inherit Metab Dis*. 2021;44(1):129-147. **3.** Sidhu NS, Schreiber K, Pröpper K, et al. Structure of sulfamidase provides insight into the molecular pathology of mucopolysaccharidosis IIIA. *Acta Crystallogr D Biol Crystallogr*. 2014;70(Pt 5):1321-1335. **4.** National Center for Biotechnology Information. *SGSH* N-sulfoglucosamine sulfohydrolase [Homo sapiens (human)]. Gene. National Library of Medicine. Accessed October 20, 2026. https://www.ncbi.nlm.nih.gov/gene/6448#bibliography **5.** NEJM Illustrated Glossary. Episome. Accessed October 10, 2026. https://illustrated-glossary.nejm.org/term/episome **6.** ClinicalTrials.gov. NCT04360265. Accessed October 20, 2026. https://clinicaltrials.gov/study/NCT04360265?cond=mpsiiia&viewType=Card&page=2&rank=11 **7.** Ultragenyx Pharmaceutical Inc. Data on file.

ultragenyx

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