ADVANCING MPS IIIA TREATMENT

The first and only FDA-approved therapy for MPS IIIA

(mucopolysaccharidosis type IIIA, Sanfilippo syndrome type A)

FAYUVI™
rebisufligene etisparvovec-hopf
suspension for IV infusion

Dosing and Administration Guide

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.
- 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.

Please see additional Important Safety Information throughout and the full Prescribing Information.

Getting started with FAYUVI

FAYUVI is administered as a single-dose intravenous (IV) infusion. The recommended dose of FAYUVI is 3.0 × 10^{13} vector genomes (vg)/kg body weight. FAYUVI is provided as a customized kit based on body weight.

The following tests and assessments should be performed prior to treatment with FAYUVI



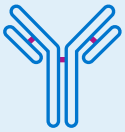
Due to the concern for potential hepatotoxicity, assess liver function (ALT, AST, GGT, and total bilirubin) and liver-related medical history



Due to the concern for potential thrombocytopenia, assess platelet counts, prothrombin time (PT), and activated partial thromboplastin time (aPTT)



Evaluate patients for conditions that may increase the risks associated with corticosteroid therapy. Delay treatment until clinically significant infections are adequately controlled



Perform testing for the presence of anti-AAV9 antibodies. FAYUVI administration is not recommended for patients with elevated anti-AAV9 total binding antibody titers (≥1:100)[a]

[a]An FDA authorized test for the detection of anti-AAV9 total binding antibodies is not currently available. For information regarding anti-AAV9 testing, contact Ultragenyx Pharmaceutical Inc. at 1-888-756-8657. Currently available tests may vary in accuracy and design.

AAV9, adeno-associated virus serotype 9; ALT, alanine aminotransferase; AST, aspartate aminotransferase; FDA, US Food and Drug Administration; GGT, gamma-glutamyl transferase.

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.

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Timing of other medications

Timing of other medications before and after FAYUVI infusion

APPROXIMATELY 1 MONTH BEFORE INFUSION	Vaccines should be avoided 30 days prior to treatment with FAYUVI (and use of corticosteroids) and while on corticosteroid therapy.
1 DAY BEFORE INFUSION	Administer oral corticosteroids (eg, prednisone or prednisolone) at 1.0 mg/kg/day.
POST-INFUSION	Continue oral corticosteroids at 1.0 mg/kg/day for 8 weeks post-dosing. Taper slowly for a minimum of 4 weeks. Refer to the *Management of Corticosteroid Regimen* section below.

Management of corticosteroid regimen

- Monitor ALT, AST, GGT, and total bilirubin levels closely during corticosteroid therapy. If liver enzymes are rising or remain elevated above baseline, the corticosteroid dose may be increased or prolonged. Taper corticosteroids after 8 weeks if liver enzymes are at or below baseline. If elevated liver enzymes persist despite the use of corticosteroids, promptly consult a pediatric gastroenterologist or hepatologist and/or immunologist to discuss additional immunosuppression
- Monitor for and manage adverse reactions secondary to corticosteroid use. Refer to the corticosteroid prescribing information for risks and required precautions

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

Important Safety Information (Cont.)

WARNINGS AND PRECAUTIONS (CONT.)

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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Supply, storage, and handling



FAYUVI is supplied as a sterile, preservative-free, clear to translucent, colorless suspension for intravenous infusion with a concentration of 1.0×10^{13} vg per mL

Each 8-mL glass vial of FAYUVI contains 2 mL of extractable volume. FAYUVI may contain small white to off-white particles

FAYUVI is provided in a kit containing 5 to 105 single-dose vials, with each kit constituting a dosage unit based on the patient's body weight

vg, vector genomes.

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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Supply, storage, and handling (cont.)

Storing FAYUVI



FAYUVI is shipped and stored frozen at ≤ -60 °C (-76 °F)



Store FAYUVI upright at ≤ -60 °C (-76 °F) in the original carton until ready to use



Thawed vials should not be punctured until immediately prior to use. Once drawn from the vial and prepared in syringes, FAYUVI can be stored at room temperature (20 °C – 25 °C [68 °F – 77 °F]) for up to 24 hours, including time for infusion



If necessary, an intact vial (stopper not yet punctured) that has been thawed can be stored refrigerated (2 °C – 8 °C [36 °F – 46 °F]) for up to 12 days, upright and protected from light (eg, in the original carton)



Once thawed, **do not refreeze** FAYUVI solution vials



Follow local guidelines on handling of biological waste

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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Preparing FAYUVI for infusion



The following equipment and materials are required for FAYUVI administration

- Flow rate-controlled syringe pump (prepare the syringe pump prior to administration)
- 20-mL or 50-mL polypropylene syringes for FAYUVI administration (prepare syringes prior to administration)
  - The number and size of syringes will depend on the patient's dose volume
- 21-gauge stainless steel needles
- 0.2-micrometer (µm) in-line infusion filter with maximum operating pressure adequate for the syringe pump or pump settings
- Sterile syringe of Lactated Ringer's solution, Hartmann's solution, or 0.9% sodium chloride injection for flushing the infusion line



General preparation precautions

- Prepare FAYUVI using aseptic technique. Wear gloves and safety glasses during preparation and administration
- Keep vials away from direct sunlight and in carton packaging prior to use
- Treat spills of FAYUVI with a virucidal agent with proven activity against non-enveloped viruses and blot using absorbent materials
- Dispose of unused medicinal product and materials that may have come in contact with FAYUVI in accordance with the local biosafety guidelines

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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Preparing FAYUVI for infusion (cont.)



Frozen FAYUVI vials must be inspected and thawed prior to preparation

- Verify the required dose of FAYUVI based on patient's body weight, and confirm the kit contains a sufficient number of vials to prepare the FAYUVI infusion
- Do not thaw or puncture vials until immediately prior to use. If the patient is not expected to be ready for same-day administration, store FAYUVI in a manner consistent with the recommended storage and handling
- Remove vials from the original packaging. Inspect vials for damage to the vial or cap. Do not use if damaged
- Allow vials to thaw at room temperature (20 °C – 25 °C [68 °F – 77 °F]) for a minimum of 30 minutes until there is no visible ice. Do not use a water bath or external heat sources. Do not shake the vials to avoid foaming. Do not thaw overnight
- Visually inspect the thawed vials. FAYUVI is a clear to translucent, colorless liquid that may contain small white to off-white particles. Do not use the vial if the solution is discolored or contains matter other than small white to off-white particles



The total FAYUVI dose must be withdrawn into syringes prior to administration

- Once thawed, withdraw FAYUVI from the vials into polypropylene syringes using 21-gauge stainless steel needles
- Multiple syringes may be needed. Prepare all syringes prior to administering FAYUVI. The contents of multiple vials may be combined into a single syringe
- Insert a 0.2-µm in-line filter between the syringe with FAYUVI and tubing
- Prime tubing and filter with FAYUVI
- Maintain syringes at room temperature prior to and during administration. FAYUVI is stable for up to 24 hours at room temperature 20 °C – 25 °C (68 °F – 77 °F)

Important Safety Information (Cont.)

WARNINGS AND PRECAUTIONS (CONT.)

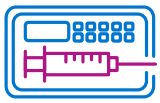
Risk of Malignancy

- 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.

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Administering FAYUVI



Administer FAYUVI **over approximately 1 hour** as a single-dose slow infusion through a peripheral vein using an IV catheter with a 0.2-µm in-line filter and a syringe pump

- Ensure personnel and equipment are immediately available to treat severe infusion and hypersensitivity reactions
  - Insertion of a second IV catheter is recommended to treat infusion reactions
- Administer FAYUVI as a single-dose **slow infusion over approximately 1 hour** through a peripheral vein using an IV catheter with a 0.2-µm in-line filter and a syringe pump
  - Do **not** administer FAYUVI as an IV push or bolus
  - Do **not** infuse FAYUVI in the same IV line with any other products
  - Do **not** use a central line or port
- **In the event of a severe infusion or hypersensitivity reaction, pause the infusion, and administer supportive care and medical treatment as appropriate. If the infusion is paused, the infusion may be restarted at a slower rate after symptoms are resolved, at the discretion of the treating healthcare provider**
- To ensure the patient receives the complete dose, after the content of the last FAYUVI-containing syringe is infused, infuse Lactated Ringer's solution, Hartmann's solution, or 0.9% sodium chloride injection at the same rate that was used for the last part of the infusion to clear FAYUVI from the tubing

IV, intravenous.

Important Safety Information (Cont.)

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%).

Please see additional Important Safety Information throughout and the full Prescribing Information.

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Post-infusion patient monitoring



Hypersensitivity and infusion reactions

- Closely monitor patients for clinical signs and symptoms of infusion reactions, including hypersensitivity reactions and anaphylaxis, and monitor vital signs during and after completion of FAYUVI infusion as clinically indicated
- Symptoms of hypersensitivity and infusion reactions may include but are not limited to hypotension, pyrexia, palpitation, nausea, vomiting, chills, or headache
- **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**



Liver function tests

- Closely monitor ALT, AST, GGT, and total bilirubin levels after FAYUVI administration once weekly **for the first 2 weeks, then every 2 weeks 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.
- **Note: Elevated liver enzyme levels occurred most often in the first 2 weeks after FAYUVI administration** (range: 2 days to 30.3 months). All liver enzyme elevations resolved within 6 days to 40.6 months of onset, except for 2 patients in whom slight elevations persisted



Platelet counts – thrombocytopenia and thrombotic microangiopathy (TMA)

- Monitor platelet counts **weekly for the first 4 weeks**, then monthly for 6 months following infusion. Continue monitoring as clinically indicated
- 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. **Monitor for signs and symptoms of TMA**, including, but 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

AAV, adeno-associated virus; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; IV, intravenous.

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.

Please see additional Important Safety Information throughout and the full Prescribing Information.

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Patient and caregiver education

It is important to educate caregivers on the symptoms associated with possible reactions their child may experience after FAYUVI infusion.

Hepatotoxicity

- Advise patients and/or caregivers to immediately contact their healthcare provider if the patient's skin and/or whites of their eyes appear yellowish or if the patient misses a dose of corticosteroid or vomits it up. Advise caregivers not to administer any medication, herbal product, or supplement to the patient without first confirming with a healthcare professional that they are not hepatotoxic. If use of a hepatotoxic agent appears unavoidable, instruct patients or caregivers that they or their healthcare professional contact you to discuss potential alternatives

Thrombocytopenia

- Advise patients and/or caregivers to seek medical attention if the patient experiences unexpected bruising or bleeding, as these may be signs of thrombocytopenia, a condition that has been reported to generally occur within the first 2 weeks after FAYUVI infusion

Thrombotic microangiopathy (TMA)

- Advise patients and/or caregivers to seek immediate medical attention if the patient experiences unexpected bruising or bleeding, seizures, or decreased urine output, as these may be signs of TMA, a condition that has been reported in association with AAV gene therapies

Hypersensitivity and infusion reactions

- Educate patients and/or caregivers on possible symptoms of infusion reactions, including hypersensitivity reactions, and advise them to immediately inform medical staff if they experience such a reaction

Remind patients and/or caregivers about the importance of continuing corticosteroid treatment as prescribed after FAYUVI infusion. Ensure they are also aware of the post-infusion monitoring schedule for liver enzymes and platelet levels.

AAV, adeno-associated virus.

Important Safety Information (Cont.)

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.

Please see additional Important Safety Information throughout and the full Prescribing Information.

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Patient and caregiver education (cont.)

It is also important to educate caregivers on the potential risks associated with FAYUVI treatment.

Risk of malignancy

- Malignancy may occur after AAV therapies such as FAYUVI. Advise patients and/or caregivers to contact their healthcare provider and Ultragenyx Pharmaceutical Inc. (1-888-756-8657) if the patient who received FAYUVI develops a malignancy

Vaccinations

- Advise patients and/or caregivers to consult with their healthcare provider to determine if adjustments to the patient's vaccination schedule are necessary prior to treatment with FAYUVI. Vaccines should be avoided 30 days prior to treatment with FAYUVI (and use of corticosteroids) and while on corticosteroid therapy

Vector shedding

- Temporary vector shedding of FAYUVI occurs primarily through bodily fluids and waste. Advise patients and/or caregivers on the proper handling of patient bodily fluids and waste, recommended procedures include sealing disposable diapers in disposable trash bags and then discarding into regular trash. Inform caregivers and family members regarding proper hand hygiene when coming into direct contact with patient bodily fluids and waste. These precautions should be followed for three months after FAYUVI infusion

AAV, adeno-associated virus.

Important Safety Information (Cont.)

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 additional Important Safety Information throughout and the full Prescribing Information.

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IMPORTANT POINTS TO REMEMBER

FAYUVI treatment checklist

CORTICOSTEROID REGIMEN (See page 3)

- ✓ Ensure a course of oral corticosteroids at 1.0 mg/kg/day is started 1 day before FAYUVI infusion. Continue corticosteroids at 1.0 mg/kg/day for 8 weeks post-dosing, then taper slowly for a minimum of 4 weeks
- ✓ **Monitor liver enzymes closely during corticosteroid therapy**. If liver enzymes are rising or remain elevated above baseline, the corticosteroid dose may be increased or prolonged
- ✓ Monitor for and manage adverse reactions secondary to corticosteroid use

FAYUVI INFUSION (See page 8)

- ✓ Administer FAYUVI as a **single-dose slow infusion over approximately 1 hour**
- ✓ **In the event of a severe infusion or hypersensitivity reaction, pause the infusion, and administer supportive care and medical treatment as appropriate**
- ✓ **If the infusion is paused, the infusion may be restarted at a slower rate after symptoms are resolved, at the discretion of the treating healthcare provider**

POST-INFUSION MONITORING (See page 9)

- ✓ **Liver enzymes:** monitor AST, ALT, GGT, and total bilirubin levels after FAYUVI administration once weekly **during the first 2 weeks, then every 2 weeks until 2 weeks after the corticosteroid taper period is complete** and as clinically indicated
- ✓ **Platelet count: obtain weekly for the first 4 weeks**, then monthly for 6 months following infusion. Continue monitoring as clinically indicated
- ✓ **Monitor for signs and symptoms of thrombotic microangiopathy**

UltraCare® Gene Therapy Guides are available to help provide educational support to your patient along their FAYUVI treatment journey

Scan or click to access UltraCare Patient Services for Gene Therapy

Scan or click to learn more about FAYUVI

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

Please see the full Prescribing Information for additional information on dosage and administration and Important Safety Information.

Reference: FAYUVI [Prescribing Information]. Novato, CA: Ultragenyx Pharmaceutical Inc; September 2026.

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