PHARMACY POLICY STATEMENT
TRICARE

DRUG NAME	Avlayah (tividenofusp alfa-eknm)
BENEFIT TYPE	Medical
STATUS	Prior Authorization Required

Avlayah, approved by the FDA in 2026, is a hydrolytic lysosomal glycosaminoglycan (GAG)-specific enzyme replacement therapy indicated for the treatment of neurologic manifestations of Hunter syndrome (Mucopolysaccharidosis type II, MPS II) when initiated in presymptomatic or symptomatic pediatric patients weighing at least 5 kg prior to advanced neurologic impairment. This indication is approved under accelerated approval based on reduction of cerebrospinal fluid heparan sulfate. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial(s).
MPS II is a rare, X-linked lysosomal storage disease also known as Hunter syndrome, which can be classified as either severe or attenuated. Pathogenic mutations of the iduronate 2-sulfatase (IDS or I2S) gene cause the enzyme iduronate 2-sulfatase to be deficient or absent. Normally this lysosomal enzyme breaks down glycosaminoglycans (GAGs) (previously known as mucopolysaccharides) but when reduced in MPS II, the GAG substrates heparan sulfate (HS) and dermatan sulfate (DS) accumulate throughout the body causing chronic progressive damage. Unlike Elaprase (idursulfase), Avlayah is designed to cross the blood-brain barrier (BBB) to deliver the IDS enzyme to the brain and address CNS symptoms.

Avlayah (tividenofusp alfa-eknm) will be considered for coverage when the following criteria are met:

Mucopolysaccharidosis II (MPS II; Hunter Syndrome)

For **initial** authorization:

1. Member is male, weighs at least 5 kg, and is less than 18 years of age; AND
2. Medication must be prescribed by or in consultation with a geneticist, metabolic specialist, neurologist, or pediatrician experienced with managing mucopolysaccharidoses; AND
3. Member has a diagnosis of MPS II confirmed by at least one of the following
   a) Low iduronate 2-sulfatase (IDS) enzyme activity AND normal activity of a second sulfatase enzyme (to exclude Multiple Sulfatase Deficiency), and/or
   b) Molecular genetic testing identifies pathogenic IDS gene mutation; AND
4. Documentation of baseline cerebrospinal fluid (CSF) heparan sulfate level; AND
5. Documentation of baseline hemoglobin level; AND
6. Member does NOT have advanced neurologic impairment per the clinical judgement of the specialist; AND
7. Avlayah is NOT being used in combination with other enzyme replacement therapies.
8. **Dosage allowed/Quantity limit:** Titrate up to 15 mg/kg once weekly via IV infusion, per prescribing information.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Chart notes must show improvement or stabilized signs and symptoms of disease (neurologic and/or somatic); AND
2. Documentation of reduced CSF heparan sulfate level from baseline.

If all the above requirements are met, the medication will be approved for an additional 6 months.

TRICARE Prime® Demo by CareSource Military & Veterans™ considers Avlayah (tividenofusp alfa-eknm) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
04/13/2026	New policy for Avlayah created.

References:

1. Avlayah [prescribing information]. Denali Therapeutics Inc.; 2026.
2. Muenzer J, Burton BK, Harmatz P, et al. An Intravenous Brain-Penetrant Enzyme Therapy for Mucopolysaccharidosis II. *N Engl J Med*. 2026;394(1):39-50. doi:10.1056/NEJMoa2508681
3. Scarpa M, Lampe C. Mucopolysaccharidosis Type II. 2007 Nov 6 [Updated 2025 Jan 16]. In: Adam MP, Bick S, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2026. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1274/
4. McBride KL, Berry SA, Braverman N; ACMG Therapeutics Committee. Treatment of mucopolysaccharidosis type II (Hunter syndrome): a Delphi derived practice resource of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2020;22(11):1735-1742. doi:10.1038/s41436-020-0909-z
5. Wang RY, Bodamer OA, Watson MS, Wilcox WR; ACMG Work Group on Diagnostic Confirmation of Lysosomal Storage Diseases. Lysosomal storage diseases: diagnostic confirmation and management of presymptomatic individuals. *Genet Med*. 2011;13(5):457-484. doi:10.1097/GIM.0b013e318211a7e1
6. Scarpa M, Almássy Z, Beck M, et al. Mucopolysaccharidosis type II: European recommendations for the diagnosis and multidisciplinary management of a rare disease. *Orphanet J Rare Dis*. 2011;6:72. Published 2011 Nov 7. doi:10.1186/1750-1172-6-72

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