Avlayah™ (tividenofusp alfa-eknm)
(Intravenous)

Document Number: M-0848

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Dates Reviewed: 05/2026

I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 12 months (365 days).
- Renewal: Prior authorization validity may be renewed every 12 months (365 days) thereafter.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- 1,800 mg every 7 days

III. Initial Approval Criteria [1-5,11-13]

Prior authorization validity is provided in the following conditions:

- Member weighs at least 5 kg; **AND**
- Documented baseline age-appropriate values for one or more of the following have been obtained:
  - Members 5 years of age or greater: 6-minute walk test (6MWT), percent predicted forced vital capacity (FVC), joint range of motion, left ventricular hypertrophy, growth, quality of life measure (CHAQ/HAQ/MPS HAQ), and/or urinary glycosaminoglycan (uGAG)/urinary heparan sulfate (uHS); **OR**
  - Members less than 5 years of age: spleen volume, liver volume, FVC, 6-MWT, and/or urinary glycosaminoglycan (uGAG)/urinary heparan sulfate (uHS); **AND**

NOTE: *For very young members in which FVC or 6-MWT are not suitable for measuring, requests will be reviewed on a case-by-case basis.*

Universal Criteria [1-5]

- Will not be used in combination with other enzyme replacement therapies indicated for the treatment of Hunter Syndrome (e.g., idursulfase, etc.); **AND**
- Member hemoglobin levels will be obtained prior to initiation of therapy, at 3 months after initiation, and periodically thereafter, as clinically indicated; **AND**
- Member serum creatinine and urinary protein to creatinine ratio will be assessed and member will be monitored for the development of membranous nephropathy throughout therapy; **AND**

Hunter Syndrome (Mucopolysaccharidosis II; MPS II) † Φ [1,5]

- Member has a definitive diagnosis of MPS II as confirmed by one of the following:
  - Deficient or absent iduronate 2-sulfatase (I2S) enzyme activity in white cells, fibroblasts, or plasma in the presence of normal activity of at least one other sulfatase; **OR**
  - Detection of pathogenic (or likely pathogenic) variants in the *IDS* gene by molecular genetic testing; **AND**
- One of the following:
  - Clinical documentation of neurologic manifestations associated with MPS II; **OR**
  - Provider attestation that the member is presymptomatic and at risk for neurologic manifestations (e.g., genotype strongly associated with neuronopathic disease [large deletions, nonsense variants, severe splice-site variants]), family history (e.g., affected male relative with confirmed neuronopathic MPS II sharing the same IDS mutation), or metabolic genetics consultation confirming high probability of neuronopathic course; **AND**
- Provider attestation that the member does not have advanced neurological impairment

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1-5,11-13]

Prior authorization validity may be renewed based on the following criteria:

- Member continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe hypersensitivity reactions including anaphylaxis, severe infusion associated reactions (chills, angioedema, hypotension, tachycardia, urticaria, vomiting, wheezing, pyrexia, flushing, erythema, rash, cough, diarrhea, abdominal pain, retching, headache, irritability, papules, etc.), severe anemia, membranous nephropathy, etc.; **AND**
- Member has demonstrated a beneficial response to therapy compared to pretreatment age-appropriate baseline values in one or more of the following:
  - Members 5 years of age or greater: stabilization or improvement in percent predicted FVC and/or 6-MWT, increased joint range of motion, decreased left ventricular hypertrophy, improved growth, improved quality of life (clinically meaningful change in the CHAQ/HAQ/MPS HAQ disability index), and/or reduction in uGAG/uHS levels; **OR**
  - Members less than 5 years of age: reductions in spleen and/or liver volume, stabilization/improvement in FVC and/or 6-MWT, and/or reduction in uGAG/uHS levels

V. Dosage/Administration [1]

Indication	Dose

<table>
<tr>
<td>Hunter Syndrome; MPS II</td>
<td><u>Starting Dose for pediatric members weighing at least 5 kg</u>: 3 mg/kg administered once weekly via intravenous infusion.
<u>Maintenance Dose for pediatric members weighing at least 5 kg</u>: 15 mg/kg administered once weekly via intravenous infusion.
<u>NOTE</u>:
• Refer to the dosing table below for the appropriate dose escalation regimen and administer each dosage level for at least 4 weeks before escalating to the next dosage level.
• Do not escalate the dosage level if the current dosage level is not tolerated.
<table>
<tr><th>Dosing Week</th><th>Dosage Level</th></tr>
<tr><td>Week 1 to Week 4</td><td>3 mg/kg once weekly</td></tr>
<tr><td>Week 5 to Week 8</td><td>7.5 mg/kg once weekly</td></tr>
<tr><td>Week 9 and beyond</td><td>15 mg/kg once weekly</td></tr>
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VI. Billing Code/Availability Information

<u>HCPCS Code:</u>

- J3590 – Unclassified biologics

<u>NDC:</u>

- Avlayah 150 mg lyophilized powder for injection in a single-dose vial: 84976-0001-xx

VII. References

1. Avlayah [package insert]. San Francisco, CA; Denali Therapeutics, Inc.; March 2026. Accessed April 2026.
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11. Muenzer J, Wraith J, Beck M, *et al.* A phase II/III clinical study of enzyme replacement therapy with idursulfase in mucopolysaccharidosis II (Hunter syndrome). *Genet Med* **8,** 465–473 (2006) doi:10.1097/01.gim.0000232477.37660.fb
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14. Muenzer J, Burton Bk, Harmatz P, et al. An Intravenous Brain-Penetrant Enzyme Therapy for Mucopolysaccharidosis II. N Engl J Med 2026;394:39-50. DOI: 10.1056/NEJMoa2508681
15. McBride, K.L., Berry, S.A., Braverman, N. *et al.* Treatment of mucopolysaccharidosis type II (Hunter syndrome): a Delphi derived practice resource of the American College of Medical Genetics and Genomics (ACMG). *Genet Med* **22**, 1735–1742 (2020). https://doi.org/10.1038/s41436-020-0909-z

Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	Yes: Consider for PA
Potential for misuse/abuse	No: PA not a priority

Cost of drug	Yes: Consider for PA

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E76.1	Mucopolysaccharidosis, type II

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC