Medical Drug Clinical Criteria

Subject:	Avlayah (tividenofusp alfa-eknm)		
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Overview

This document addresses Avlayah (tividenofusp alfa-eknm), an enzyme replacement therapy approved by the Food and Drug Administration (FDA) to treat neurologic manifestations of Mucopolysaccharidosis II (Hunter syndrome) when initiated in presymptomatic or symptomatic pediatric individuals 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 observed in individuals treated with Avlayah. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial.

The mucopolysaccharidoses are a group of inherited metabolic diseases caused by the deficiency of lysosomal enzymes needed to breakdown mucopolysaccharides or glycosaminoglycan (GAGs). The progressive accumulation of GAGs in lysosomes leads to respiratory, cardiac, skeletal and connectivity, neurologic and ophthalmologic complications. There are seven distinct types of mucopolysaccharidosis (I, II, III, IV, VI, VII, and IX). Accurate diagnosis is important to provide disease-specific enzyme replacement therapy. Diagnosis is confirmed through urinary GAG concentration measurement, enzymatic activity measurement or genetic testing.

Avlayah has a boxed warning for hypersensitivity reactions including anaphylaxis. Reactions have occurred during the early course of enzyme replacement therapy and after extended duration of therapy. Appropriate medical support should be available during Avlayah administration. If a severe hypersensitivity reaction occurs, Avlayah should be discontinued and treatment initiated immediately. Individuals should be educated on the signs and symptoms of anaphylaxis and to seek immediate medical care should they occur.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Avlayah (tividenofusp alfa-eknm)

Initial requests for Avlayah (tividenofusp alfa-eknm) may be approved if the following criteria are met:

I. Individual is less than 18 years of age AND weighs at least 5 kg; **AND**
II. Individual has a diagnosis of Mucopolysaccharidosis II (MPS II, Hunter syndrome) demonstrated by (Scarpa 2011, Wraith 2008):
    A. Deficiency in iduronate 2-sulfatase enzyme activity as measured in fibroblasts or leukocytes combined with normal enzyme activity level of another sulfatase, and documentation is provided;
    OR
    B. Pathologic iduronate 2-sulfatase gene mutation, and documentation is provided**;**

AND

III. Individual is requesting Avlayah for the treatment of neurologic manifestations of MPS II (Hunter syndrome);

AND

IV. Individual does not have advanced neurologic impairment.

Continuation requests for Avlayah (tividenofusp alfa-eknm) may be approved if the following criterion is met:

I. Documentation is provided that there is clinically significant improvement or stabilization in clinical signs and symptoms of disease (including but not limited to reduction in cerebrospinal fluid heparan sulfate (HS), improvement in neurologic function) compared to the predicted natural history trajectory of disease.

Avlayah (tividenofusp alfa-eknm) may not be approved for the following:

I. Individual using in combination with Elaprase; **OR**
II. When the above criteria are not met and for all other indications.

Quantity Limits

Avlayah (tividenofusp alfa-eknm) Quantity Limit

Drug	Limit
Avlayah (tividenofusp alfa-eknm) 150 mg vial	15 mg/kg once weekly

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J1757	Injection, tividenofusp alfa-eknm, 1 mg [Avlayah]
S9357	Home infusion therapy, enzyme replacement intravenous therapy, (e.g., Imiglucerase); administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem

ICD-10 Diagnosis

E76.1	Mucopolysaccharidosis, type II [Hunter's syndrome]

Document History

Reviewed: 9/14/2026
Document History:

- 9/14/2026 – Annual Review: No changes. Coding Reviewed: No changes.
- 09/08/2026 – Coding Update: Removed HCPCS NOC C9399, J3590 effective 9/30/26 and added J1757 effective 10/1/26.
- 5/15/2026 – Select Review: New clinical criteria and quantity limit for Avlayah. Coding Reviewed: Added HCPCS NOC C9399, J3590, HCPCS S9357, and ICD-10-CM E76.1.

References

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Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.

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