Drug Coverage Policy

Effective Date..... 5/15/2026
Coverage Policy Number IP0449
Policy Title..... Mepsevii

Enzyme Replacement Therapy – Mepsevii

- Mepsevii® (vestronidase alfa-vjbk intravenous infusion – Ultragenyx)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW
Mepsevii, a lysosomal beta glucuronidase (GUS), is indicated for the treatment of **Mucopolysaccharidosis type VII** ([MPS VII], Sly syndrome).[1] It is produced in a Chinese hamster ovary cell line via recombinant DNA technology. It has the same amino acid sequence as human GUS and catabolizes accumulated glycosaminoglycans in lysosomes in affected tissues.

Disease Overview
MPS VII or Sly syndrome is an extremely rare lysosomal storage disorder characterized by deficient GUS activity.[2] In MPS VII, the partially catabolized glycosaminoglycans, chondroitin sulfate, dermatan sulfate, and heparin sulfate accumulate in the lysosomes, ultimately leading to the signs and symptoms of the disease.[2,3] The onset, severity, and rate of progression of MPS VII is heterogeneous. Patients may present at birth with hydrops fetalis and only survive a few months

while others may have milder disease and survive into their 40s.[2] However, most patients have mental retardation, hepatosplenomegaly, and musculoskeletal issues including short stature, course facial features, loss of range of motion, restricted mobility, scoliosis, and kyphosis. The diagnosis of MPS VII is established by demonstrating deficient GUS activity in leukocytes, fibroblasts, or serum; or by genetic testing.[3] Treatment for MPS VII includes enzyme replacement therapy with Mepsevii and hematopoietic stem cell transplantation.[2]

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POLICY STATEMENT
Prior Authorization is required for benefit coverage of Mepsevii. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Mepsevii as well as the monitoring required for adverse events and long-term efficacy, approval requires Mepsevii to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Mepsevii is considered medically necessary when the following criteria are met:

FDA-Approved Indication
1. Mucopolysaccharidosis Type VII (Sly Syndrome). Approve for 1 year if the patient meets BOTH of the following (A and B):
    A) The diagnosis is established by ONE of the following (i or ii):
        i. Patient has a laboratory test demonstrating deficient beta-glucuronidase activity in leukocytes, fibroblasts, or serum; OR
        ii. Patient has a molecular genetic test demonstrating biallelic pathogenic or likely pathogenic glucuronidase (GUS) gene variants; AND
    B) Mepsevii is prescribed by or in consultation with a geneticist, endocrinologist, a metabolic disorder sub-specialist, or a physician who specializes in the treatment of lysosomal storage disorders.

Dosing
Each dose must not exceed 4 mg/kg administered intravenously no more frequently than once every 2 weeks.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Mepsevii for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

Coding Information

Note: 1) This list of codes may not be all-inclusive.

2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J3397	Injection, vestronidase alfa-vjbk, 1 mg

References

1. Mepsevii® intravenous infusion [prescribing information]. Novato, CA: Ultragenyx; December 2020.
2. Montano AM, Lock-Hock N, Steiner RD, et al. Clinical course of sly syndrome (mucopolysaccharidosis type VII). J Med Genet. 2016;53:403-418.
3. Tomatsu S, Montano AM, Dung VC, et al. Mutations and polymorphisms in GUSB gene in mucopolysaccharidosis VII (Sly syndrome). Hum Mutat. 2009;30:511-51

Revision Details

Summary of Changes	Review Date	Effective Date
Updated coverage policy title from *Vestronidase Alfa-vjbk* to *Enzyme Replacement Therapy - Mepsevii*. **<u>Mucopolysaccharidosis Type VII (Sly Syndrome):</u>** **Added** dosing.	6/20/2024	8/1/2024
No criteria changes.	5/8/2025	7/15/2025
No criteria changes	4/23/2026	5/15/2026

The policy effective date is in force until updated or retired.