



## Drug Coverage Policy

Effective Date .....3/15/2025

Coverage Policy Number.....IP0399

# Enzyme Replacement Therapy – Rencovi

- Rencovi® (elapegedemase-lvlr intramuscular injection – Chiesi)

### 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.

## Medical Necessity Criteria

**Rencovi is considered medically necessary when the following criteria are met:**

1. **Adenosine Deaminase Severe Combined Immunodeficiency (ADA-SCID).** Individual meets **ALL** of the following criteria:
  - A. Diagnosis of ADA-SCID confirmed by documentation of **ONE** of the following:
    - i. At baseline, individual has had absent or very low (<1% of normal) adenosine deaminase (ADA) catalytic activity
    - ii. Molecular genetic testing confirming bi-allelic pathogenic variants in the ADA gene

- B. Medication is prescribed by, or in consultation with, with an immunologist, hematologist/oncologist or physician who specializes in ADA-SCID or related disorders

**Dosing.** Up to a maximum weekly dose of 0.4 mg/kg by intramuscular route (Doses may be divided into multiple injections as long as weekly cumulative maximum of 0.4 mg/kg is not exceeded)

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.

## Reauthorization Criteria

Continuation of elapegamase-ivlr (Revcovi) is considered medically necessary for the treatment of ADA-SCID when the above medical necessity criteria are met AND there is documentation of beneficial response.

## Authorization Duration

Initial approval duration: up to 12 months

Reauthorization approval duration: up to 12 months

## Conditions Not Covered

Any other use is considered experimental, investigational, or unproven.

## Background

### OVERVIEW

Revcovi, a recombinant adenosine deaminase, is indicated for the treatment of **adenosine deaminase severe combined immune deficiency (ADA-SCID)** in pediatric and adult patients.<sup>1</sup>

### Disease Overview

ADA-SCID is an ultra-rare, autosomal recessive genetic disorder of purine metabolism affecting lymphocyte development, viability, and function.<sup>1,2</sup> It is estimated to occur in 1:200,000 to 1:1,000,000 live births. ADA is a purine salvage enzyme which metabolizes deoxyadenosine (dAdo) and adenosine (Ado) into deoxyinosine and inosine, respectively.<sup>3</sup> When ADA is deficient, dAdo accumulates in intracellular and extracellular compartments, along with its metabolite, deoxyadenosinetriphosphate (dATP). The buildup of both dAdo and dATP negatively impacts lymphocyte development and function by impeding DNA replication and repair, inducing apoptosis, and inhibiting lymphocyte activation.

There are a variety of phenotypes of ADA deficiency; ADA-SCID is the most severe and typically diagnosed before 1 year of age.<sup>2</sup> Infants with typical ADA-SCID have failure to thrive and opportunistic infections associated with marked depletion of B, T, and NK lymphocytes. Manifestations include persistent diarrhea, extensive dermatitis, recurrent pneumonia, and other

life-threatening illnesses caused by opportunistic infections. Growth failure and other physical manifestations, including hepatic and neurologic abnormalities, may also be present. Without treatment, patients with ADA-SCID rarely survive beyond 1 to 2 years of age.

### Guidelines

According to a consensus statement for management of ADA-SCID (2018) and updated guidelines in 2023, diagnosis is usually established by demonstrating absent or very low (< 1 % of normal) ADA catalytic activity, accompanied by elevated Ado or dAdo in plasma, urine, or dried blood spots.<sup>3,4</sup> This should be followed by genetic testing to confirm bi-allelic mutations in the *ADA* gene. Enzyme replacement therapy (ERT) is recommended by the consensus panel for all patients newly diagnosed with ADA-SCID as an immediate stabilizing measure. The ideal duration of ERT has not been established. The consensus recommends that most patients use ERT as a “bridge” for a few months to approximately 2 years, prior to undergoing curative therapy with a hematopoietic stem cell transplant (HSCT) or hematopoietic stem cell gene therapy. Long-term use of ERT has declined in the past 30 years and has not been systematically studied. Lymphocyte counts and function may deteriorate over time, contributing to increased risk of infections and malignancy. Therefore, ERT longer than 5 to 8 years should be avoided and employed on a continuous basis only when neither HSCT nor gene therapy have been available or effective. The consensus also suggests ERT use for patients with later-onset phenotypes who may not be ideal candidates for curative processes.

### Dosing Considerations

Dosing is provided in the Prescribing Information for patients who are naïve to Adagen® (pegademase bovine injection for intramuscular use), as well as for patients who are Adagen-experienced.<sup>1</sup> For Adagen-naïve patients, the starting weekly dose of Revcovi is 0.4 mg/kg (divided into two doses) by the intramuscular route. This dose is continued for at least 12 to 24 weeks until immune reconstitution is achieved. Thereafter, the dose may be gradually adjusted down for maintenance (adjusted based on laboratory values). Lower starting doses are generally recommended for Adagen-experienced patients; the Prescribing Information provides a conversion factor for calculating the Revcovi dose based on the prior Adagen dose. The Prescribing Information notes that the optimal long-term dose and schedule of administration are individualized; total weekly doses may be divided into multiple intramuscular injections during a week. The dosing provided in this policy is intended to provide a sufficient maximum weekly dose for the majority of patients; exceptions will be reviewed by a clinician on a case-by-case basis.

## References

1. Revcovi® injection [prescribing information]. Cary, NC: Chiesi; August 2022.
2. Hershfield M. GeneReviews [Internet]. Updated March 7, 2024. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK1483/>. Accessed on December 6, 2024.
3. Kohn DB, Hershfield MS, Puck JM, et al. Consensus approach for the management of severe combined immune deficiency caused by adenosine deaminase deficiency. *J Allergy Clin Immunol*. 2019;143(3):852-863.
4. Grunebaum E, Booth C, Cuvelier GDE, et al. Updated Management Guidelines for Adenosine Deaminase Deficiency. *J Allergy Clin Immunol Pract*. 2023 Jun;11(6):1665-1675.

## Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	No criteria changes.	4/15/2024

Annual Revision	No criteria changes.	3/15/2025
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The policy effective date is in force until updated or retired.

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