09-J3000-40

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Reviewed: 11/09/22

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Subject: Elapegademase-lvlr (Revcovi) injection

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Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Adenosine deaminase (ADA) deficient severe combined immune deficiency (SCID) is a rare, autosomal recessive primary immunodeficiency caused by mutations in the ADA gene. Deficient ADA results in the accumulation of toxic metabolites that disrupt cell function particularly in lymphocytes. The majority of patients are diagnosed prior to 6 months of age and experience recurrent opportunistic infections, lymphopenia, failure to thrive, and metabolic abnormalities. If left undiagnosed, the disease can be fatal by 2 years of age. Some patients develop disease later in life an may exhibit a milder form of the disease while others have a partial ADA deficiency and have no symptoms. Hematopoietic stem cell transplant from a human leukocyte antigen (HLA)-identical sibling donor is the preferred treatment. Enzyme replacement with ADA is typically utilized prior to transplant or until a donor is available. A bovine-derived form of ADA (Adagen) has been the only available form of enzyme replacement for ADA-SCID.

Elapegedamase-lvlr (Revcovi®) is a recombinant adenosine deaminase (rADA) Food and Drug Adminstration (FDA) approved for the treatment of ADA-SCID in pediatric and adult patients. Two prospective, single arm, open-label studies were conducted in a total of 10 patients to evaluate the safety and efficacy of elapegadamase. The first study evaluated 6 patients (age 8 to 37) with ADA-SCID who were receiving bovine-derived ADA and crossed over to receive recombinant ADA. The efficacy was assessed by trough deoxyadenosine nucleotides (dAXP) level equal to or below 0.02 mmol/L, trough plasma ADA activity above 15 mmol/hr/L, and immune status (lymphocyte and B-,T-, and NK-lymphocyte subset counts, and quantitative immunoglobulin concentration [IgG, IgA, IgM]). Five of six patients reached the 21-week endpoint, and three of six patients received treatment over 125 weeks. Erythrocyte dAXP concentrations were equal to or below 0.2 mmol/L in all but one value at week 47. Trough plasma ADA activity was equal to or above 15 mmol/hr/L at 88/89 timepoints and metabolic detoxification was maintained for at least 2 years. Trough plasma ADA activity was above 30 mmol/hr/L by week 5. Lymphocyte and subset counts increased above initial levels. The second trial was a single-

arm prospective study in 4 patients (age 3.4 months to 25 years). Three patients had previously received bovine-derived ADA and one patient was treatment naïve. All patients maintained trough dAXP less than or equal to 0.02 mmol/L throughout the 21 week study. Serum ADA activity increased in all patients and three patients achieved a trough over 15 mmol/hr/L during the dose maintenance period. Total lymphocyte counts and B-/T-/NK-lymphocyte subset counts for 3 patients increased from screening to day 15 and were stable or increasing with treatment. The most common adverse reactions with treatment were cough and vomiting.

POSITION STATEMENT:

Initiation of elapegademase-lvlr (Revcovi®) **meets the definition of medical necessity** for the treatment of adenosine deaminase (ADA)-deficient severe combined immunodeficiency (SCID) when ALL of the following are met:

1. The member is diagnosed with ADA-SCID and meets **ONE** of the following: - documentation must be submitted
    a. Mutation of both alleles of the ADA gene
    b. Positive screening by T cell receptor excision circles (TRECs)
    c. The member has absent or low trough plasma ADA activity (<1% of normal)
2. **ONE** of the following:
    a. The member will receive treatment while awaiting a hematopoietic stem cell transplant
    b. The member has failed a hematopoietic stem cell transplant
    c. The member is not a candidate for hematopoietic stem cell transplant
3. The initial dose does not exceed FDA label recommendations and will be titrated to the minimum number of vials to achieve the total weekly dose to sustain clinical response

Approval duration: 6 months

Continuation of elapegademase-lvlr (Revcovi®) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. An authorization or reauthorization for elapegademase-lvlr has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of ADA-SCID **OR** the member has previously met **ALL** indication-specific criteria.
2. In the past 12 weeks, the member has evidence of improved or stable trough plasma ADA activity– documentation must be submitted
3. In the past 12 weeks, the member has evidence of improved or stable trough erythrocyte dAXP level– documentation must be submitted
4. The member has a beneficial response to therapy (e.g., improved immune function, lymphocyte counts)
5. **ONE** of the following:
    a. The member will receive treatment while awaiting a hematopoietic stem cell transplant

b. The member has failed a hematopoietic stem cell transplant

c. The member is not a candidate for hematopoietic stem cell transplant

6. The dose is titrated to the minimum number of vials to achieve the total weekly dose to sustain clinical response

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Elapegademase-lvlr injection is a recombinant adenosine deaminase indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.
    - **For transition from Adagen:** 0.2 mg/kg weekly intramuscularly if the weekly Adagen dose is at or lower than 30 units per kg. If the weekly Adagen dose is above 30 units per kg, calculate the dose of Revcovi using the following conversion formula:

$$\text{Revcovi dose in mg/kg} = \frac{\text{Adagen dose in units per kg}}{150}$$

    - Subsequent doses may be increased by increments of 0.033 mg/kg weekly if trough ADA activity is under 30 mmol/hr/L, trough deoxyadenosine nucleotides (dAXP) are above 0.02 mmol/L, and/or the immune reconstitution is inadequate based on the clinical assessment of the patient. The total weekly dose may be divided into multiple IM adminstrations during a week.
    - **For Adagen naïve:** 0.4 mg/kg weekly based on ideal body weight or actual weight (whichever is greater), divided into two doses (0.2 mg/kg twice a week), intramuscularly, for a minimum of 12 to 24 weeks until immune reconstitution is achieved. Subsequently, adjust the dose down gradually to maintain trough ADA activity over 30 mmol/hr/L, trough dAXP level under 0.02 mmol/L, and/or to maintain adequate immune reconstitution based on clinical assessment of the patient.
- See prescribing information for the therapeutic monitoring schedule of trough plasma ADA activity, trough erythrocyte dAXP levels, total lymphocyte counts and neutralizing antibodies.
- Immune function generally improves after 2 to 6 months. There is a lag between correction of metabolic abnormalities and improved immune function. Improvement of clinical status may be gradual but apparent by the end of the first year of treatment.

Dose Adjustments

- The dose may be adjusted based on trough plasma ADA activity, trough erythrocyte dAXP levels, total lymphocyte counts, neutralizing antibodies and clinical status of the patient.

Drug Availability

- 2.4 mg/1.5 mL (1.6 mg/mL) in a single-dose vial

PRECAUTIONS:

Boxed Warning

- none

Contraindications

- none

Precautions/Warnings

- Injection site bleeding in patients with thrombocytopenia: Increased risk of local bleeding in patients with thrombocytopenia; should not use if thrombocytopenia is severe.
- Delay in improvement of immune function: Protect immune deficient patients from infections until improvement in immune function.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

C9399	Unclassified drugs and biologicals (Hospital Outpatient Use ONLY)
J3590	Unclassified biologics

ICD-10 Diagnosis Codes That Support Medical Necessity

D81.31	Severe combined immunodeficience due to adenosine deaminase [ADA] deficiency

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Bradford KL, Moretti FA, Carbonaro-Sarracino DA et al. Adenosine Deaminase (ADA)-Deficient Severe Combined Immune Deficiency (SCID): Molecular Pathogenesis and Clinical Manifestations. J Clin Immunol. 2017. 37: 626 – 637.
2. Cagdas D, Cetinkaya PG, Karaatmaca B et al. ADA Deficiency: Evaluation of the Clinical and Laboratory Features and the Outcome. J Clin Immunol. 2018. 38: 484-493.
3. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2022 [cited 2022 October 26]. Available from: http://www.clinicalpharmacology.com/.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2022 October 26]. Available from: http://www.thomsonhc.com/
5. NCT01420627: EZN-2279 in patients with ADA-SCID. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT01420627
6. Revcovi® (elapegadamase-lvlr) [package insert]. Leadiant Biosciences, Inc. Gaithersburg, MD. December 2020.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/09/22.

GUIDELINE UPDATE INFORMATION:

09/15/19	New Medical Coverage Guideline.
12/15/21	Review and revision to guideline; consisting of updating dosing and references.
12/15/22	Review and revision to guideline; consisting of updating the references.
08/15/23	Update to ICD-10 code.