Clinical Policy: Elapegademase-lvlr (Revcovi)

Reference Number: ERX.SPA.340
Effective Date: 09.01.19
Last Review Date: 05.20
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Elapegademase-lvlr (Revcovi®) is a recombinant adenosine deaminase.

FDA Approved Indication(s)
Revcovi is indicated for the treatment of adenosine deaminase severe combined immune deficiency disease (ADA-SCID) in pediatric and adult patients.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Revcovi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Adenosine Deaminase Severe Combined Immune Deficiency Disease (must meet all)**:**

1. Diagnosis of ADA-SCID confirmed by genetic testing;
2. Prescribed by or in consultation with an immunologist;
3. Dose does not exceed 0.4 mg/kg per week.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Adenosine Deaminase Severe Combined Immune Deficiency Disease (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy *(see Appendix D for examples);*
3. If request is for a dose increase, new dose does not exceed 0.4 mg/kg per week.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ADA-SCID: adenosine deaminase severe combined immune deficiency disease
dAXP: deoxyadenosine nucleotides
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information

- Examples of positive response to therapy include improvement in immune function (T cell, B cell, and natural killer lymphocytes), reduction in frequency/severity of opportunistic infections, and decrease from baseline or maintenance of normal red cell dATP levels.
- Once treatment with Revcovi has been initiated, a target trough plasma ADA activity should be at least 30 mmol/hr/L. In order to determine an effective dose of Revcovi, trough plasma ADA activity (pre-injection) should be determined every 2 weeks for Adagen®-naïve patients and every 4 weeks for patients previously receiving Adagen therapy, during the first 8 - 12 weeks of treatment, and every 3 - 6 months thereafter. A decrease of ADA activity below this level suggests noncompliance to treatment or a development of antibodies (anti-drug, anti-PEG, and neutralizing antibodies). Antibodies to Revcovi should be suspected if a persistent fall in pre-injection levels of trough plasma ADA activity below 15 mmol/hr/L occurs. In such patients, testing for antibodies to Revcovi should be performed. If a persistent decline in trough plasma ADA activity occurs, immune function and clinical status should be monitored closely and precautions should be taken to minimize the risk of infection. If antibodies to Revcovi are found to be the cause of a persistent fall in trough plasma ADA activity, then adjustment in the dosage of Revcovi and other measures may be taken to induce tolerance and restore adequate ADA activity.
- Two months after starting Revcovi treatment, trough erythrocyte dAXP levels should be maintained below 0.02 mmol/L, and monitored at least twice a year.
- The degree of immune function may vary from patient to patient. Each patient will require appropriate monitoring consistent with immunologic status. Total and subset lymphocytes should be monitored periodically as follows:
  - Adagen-naïve patients: every 4 - 8 weeks for up to 1 year, and every 3 - 6 months thereafter
  - Other patients: every 3 - 6 months
- Immune function, including the ability to produce antibodies, generally improves after 2 - 6 months of therapy, and matures over a longer period. In general, there is a lag between the correction of the metabolic abnormalities and improved immune function. Improvement in the general clinical status of the patient may be gradual (as evidenced by improvement in various clinical parameters) but should be apparent by the end of the first year of therapy.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ADA-SCID	Patients transitioning from Adagen to Revcovi: 0.2 mg/kg IM weekly. 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.	0.4 mg/kg/week

Indication	Dosing Regimen	Maximum Dose
	The total weekly dose may be divided into multiple IM administrations during a week. Adagen-naïve patients: 0.2 mg/kg IM twice a week. Dose may be gradually adjusted down 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.	

VI. Product Availability

Single-dose vial: 2.4 mg/1.5 mL (1.6 mg/mL)

VII. References

1. Revcovi Prescribing Information. Gaithersburg, MD: Leadiant Biosciences Inc.; October 2018. Available at: www.revcovi.com. Accessed February 13, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	06.25.19	08.19
2Q 2020 annual review: clarified diagnosis is confirmed by genetic testing; references reviewed and updated.	02.13.20	05.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.