

Clinical Policy: Pegademase Bovine (Adagen)

Reference Number: CP.PHAR.392

Effective Date: 08.28.18

Last Review Date: 11.19

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Pegademase bovine (Adagen[®]) is a modified enzyme.

FDA Approved Indication(s)

Adagen is indicated for enzyme replacement therapy for adenosine deaminase (ADA) deficiency in patients with severe combined immunodeficiency disease (SCID) who are not suitable candidates for, or who have failed, bone marrow transplantation.

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.

It is the policy of health plans affiliated with Centene Corporation[®] that Adagen is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Adenosine Deaminase Deficient Severe Combined Immunodeficiency Disease (must meet all):

1. Diagnosis of ADA deficiency in SCID;
2. Prescribed by or in consultation with an immunologist;
3. Member has failed bone marrow transplantation or is not a candidate for bone marrow transplantation;
4. Dose does not exceed:
 - a. Initial: 10 units/kg per week on Week 1, 15 units/kg per week on Week 2, and 20 units/kg per week on Week 3;
 - b. Maintenance: 30 units/kg per week.

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Adenosine Deaminase Deficient Severe Combined Immunodeficiency Disease (must meet all):

1. Currently receiving medication via Centene benefit 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 30 units/kg per week.

Approval duration:

Medicaid/HIM – 12 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ADA: adenosine deaminase deficiency

FDA: Food and Drug Administration

SCID: severe combined immunodeficiency disease

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): use of Adagen as preparatory or support therapy for bone marrow transplantation, severe thrombocytopenia
- Boxed warning(s): 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.

- Immune function, including the ability to produce antibodies generally improves after 2 to 6 months of therapy and matures over a longer period. The lag between the correction of metabolic abnormalities and improved immune function ranges from a few weeks to approximately 6 months.
- After 2 months of maintenance treatment with Adagen, red cell dATP levels should decrease to a range of ≤ 0.005 to $0.015 \mu\text{mol/mL}$. Normal dATP levels are below $0.001 \mu\text{mol/mL}$. Once the level of dATP levels has fallen adequately, it should be measured two to four times per year for the first year, and then two to three times a year thereafter assuming no interruption in therapy.
- Plasma ADA activity should be measured at the trough level pre-injection to ensure that plasma ADA level is maintained above the level of total erythrocyte ADA activity in the blood of normal individuals and to establish the effective dose of Adagen. Desirable range of plasma ADA activity (trough level before maintenance injection): 15 to $35 \mu\text{mol/hr/mL}$.
 - Plasma ADA should be determined twice a month between 3 and 9 months, then monthly until after 18 to 24 months of treatment.
 - If plasma ADA levels fall to $< 10 \mu\text{mol/hr/mL}$, antibody development should be suspected. However, other causes of decreasing plasma ADA levels may include improper storage of Adagen vials, or improper handling of plasma samples. A specific assay for antibody to ADA and Adagen should be performed.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ADA in SCID	Administer IM every 7 days: <ul style="list-style-type: none"> • Week 1: 10 units/kg • Week 2: 15 units/kg • Week 3: 20 units/kg • Maintenance: 20 units/kg/week (dose may be adjusted by 5 units/kg/week) 	30 units/kg/dose (1 dose/week)

VI. Product Availability

Single-use vial: 375 units/1.5 mL

VII. References

1. Adagen Prescribing Information. Indianapolis, IN: Exelead, Inc., November 2017. Available at: <https://leadiant.com/wp-content/uploads/2019/06/AdagenPI.pdf> . Accessed August 8, 2019.
2. Bonilla FA, Khan DA, Ballas ZK, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol 2015; 136(5): 1186-1205.e78. Available at: <https://www.allergyparameters.org/published-practice-parameters/alphabetical-listing/immunodeficiency-download/>.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-

date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2504	Injection, pegademase bovine, 25 IU

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.28.18	11.18
4Q 2019 annual review: no significant changes; references reviewed and updated.	08.08.19	11.19

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.

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