



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Effective Date 8/15/2011
Next Review Date..... 8/15/2012
Coverage Policy Number 5005

Subject **Pegademase (Adagen™)**

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Hyperlink to Related Coverage Policies

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), 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 supercedes** 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. 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. Proprietary information of CIGNA. Copyright ©2011 CIGNA

Coverage Policy

CIGNA covers pegademase (Adagen™) as medically necessary as enzyme replacement therapy for adenosine deaminase (ADA) deficiency in an individual with severe combined immunodeficiency disease (SCID) who is not a suitable candidate for or who has failed bone marrow transplantation.

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

FDA Approved Indications

Adagen injection 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. Adagen is recommended for use in infants from birth or in children of any age at the time of diagnosis. Adagen is not intended as a replacement for HLA identical bone marrow transplant therapy. Adagen is also not intended to replace continued close medical supervision and the initiation of appropriate diagnostic tests and therapy (e.g., antibiotics, nutrition, oxygen, gammaglobulin) as indicated for intercurrent illnesses.

FDA Recommended Dosing

Adagen is recommended for use in infants from birth or in children of any age at the time of diagnosis. Adagen should be administered every 7 days as an intramuscular injection. The dosage should be individualized. The recommended dosing schedule is 10 U/kg for the first dose, 15 U/kg for the second dose, and 20 U/kg for the third dose. The usual maintenance dose is 20 U/kg per week. Further increases of 5 U/kg/week may be necessary, but a maximum single dose of 30 U/kg should not be exceeded. The optimal dosage and schedule of administration should be established for each patient based on monitoring of plasma ADA activity levels (trough levels before maintenance injection) and biochemical markers of ADA deficiency (primarily red cell dATP content). Since improvement in immune function follows correction of metabolic abnormalities, maintenance dosage in individual patients should be aimed at achieving the following biochemical goals: 1) maintain plasma ADA activity (trough levels before maintenance injection) in the range of 15-35 $\mu\text{mol/hr/mL}$ (assayed at 37°C); and 2) decline in erythrocyte dATP to $\leq 0.005\text{-}0.015 \mu\text{mol/mL}$ packed erythrocytes, or $\leq 1\%$ of the total erythrocyte adenine nucleotide (ATP + dATP) content, with a normal ATP level, as measured in a pre-injection sample.

Drug Availability

Adagen is a clear, colorless, preservative free solution for intramuscular injection. Each vial contains 250 units/mL and is supplied as a 1.5 mL single-use vial, in boxes of 4 vials.

General Background

Pharmacology

Pegademase is a modified enzyme of ADA attached to numerous strands of monomethoxypolyethylene glycol (PEG), which permits prolonged circulation of ADA in the blood. The ADA enzyme is derived from bovine intestines. Pegademase is used as enzyme replacement therapy for ADA deficiency in patients with SCID who are not suitable candidates for, or who have failed, bone marrow transplantation. In the absence of ADA, purine substrates and their metabolites, adenosine and 2'-deoxyadenosine, accumulate. These are toxic to lymphocytes, causing severe immunodeficiency. Replacing the ADA corrects the metabolic abnormality, leading to improved immune function, decreased frequency of opportunistic infections and fewer complications of infections. After treatment with pegademase, onset of metabolic deficiency correction and initial improvement in immune function is within 2–6 months. Improvement in overall clinical function is usually seen after the completion of one year of therapy.

Adverse Reactions

Headache in one patient and pain at the injection site in two patients were reported during clinical trials. Hemolytic anemia, auto-immune hemolytic anemia, thrombocytopenia, injection site erythema, and urticaria have been identified during post-approval use of Adagen (pegademase bovine) injection. Because these reactions are reported voluntarily from a very small population, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. There is no evidence to support the safety and efficacy of pegademase as preparatory or support therapy for bone marrow transplantation.

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

Covered when medically necessary:

HCPCS Codes	Description
J2504	Injection, pegademase bovine, 25 IU

ICD-9-CM Diagnosis Codes	Description
279.2	Combined immunity disease

References

1. Kaufman, DA, Hershfield, MS, Bocchini JA, et al. Cerebral Lymphoma in an Adenosine Deaminase-Deficient Patient with Severe Combined Immunodeficiency Receiving Polyethylene Glycol-Conjugate Adenosine Deaminase. *Pediatrics*. December 2005; 116(6): 876–79.
2. Malacarne, F, Benicchi, T, Notarangelo, LD, et al. Reduced thymic output, increased spontaneous apoptosis and oligoclonal B cells in polyethylene glycol-adenosine deaminase treated patients. *European Journal of Immunology*. November 2005; 35(11):3376–86.
3. McEvoy GK, ed. AHFS 2011 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2011.
4. Sigma-Tau Pharmaceuticals, Inc. Adagen (pegademase bovine) injection package insert. Gaithersburg, MD: Sigma-Tau Pharmaceuticals, Inc. May 2010.

Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare Great-West Healthcare	8/15/2008	5005	Pegademase (Adagen™)

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