



MEDICAL COVERAGE GUIDELINES
SECTION: DRUGS

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ADAGEN® (pegademase bovine)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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Description:

Adagen injection is a modified enzyme used for enzyme replacement therapy for the treatment of severe combined immunodeficiency disease (SCID) associated with a deficiency of adenosine deaminase (ADA).

SCID associated with a deficiency of ADA is a rare, inherited, and often fatal disease. In the absence of the ADA enzyme, the purine substrates adenosine and 2-deoxyadenosine accumulate, causing metabolic abnormalities that are directly toxic to lymphocytes.

ADAGEN (pegademase bovine) (cont.)

Criteria:

See Resources section for FDA-approved dosage.

- FDA-approved dosage for Adagen is considered **medically necessary** for infants from birth or children of any age at the time of diagnosis with documentation of **ALL** of the following:
 1. Severe combined immunodeficiency disease (SCID)
 2. Individual is not a suitable candidate for, or who has failed bone marrow transplantation
- Adagen for all other indications not previously listed or if above criteria not met is considered **experimental or investigational** based upon:
 1. Lack of final approval from the Food and Drug Administration, and
 2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
 3. Insufficient evidence to support improvement of the net health outcome, and
 4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
 5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to*:

- As a replacement for HLA identical bone marrow transplant therapy
- 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.

ADAGEN (pegademase bovine) (cont.)

Resources:

Adagen Package Insert:

FDA-approved indication and dosage:

Indications	Recommended dose
<p>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.</p> <p>Recommended for use in infants from birth or in children of any age at the time of diagnosis.</p>	<p>Plasma ADA activity and red cell dATP should be determined prior to treatment.</p> <p>Adagen should be administered every 7 days as an intramuscular injection. The dosage should be individualized.</p> <p>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.</p> <p>Once treatment has been initiated, a desirable range of plasma ADA activity (trough level before maintenance injection) should be 15–35 µmol/hr/mL. Plasma ADA activity (pre-injection) should be determined every 1-2 weeks during the first 8-12 weeks of treatment in order to establish an effective dose.</p> <p>After 2 months of maintenance treatment, red cell dATP levels should decrease to a range of ≤ 0.005 to 0.015 µmol/mL. The normal value of dATP is below 0.001 µmol/mL.</p> <p>Once the level of dATP has fallen adequately, it should be measured 2-4 times a year during the remainder of the first year and 2-3 times a year thereafter, assuming no interruption in therapy.</p> <p>Between 3 and 9 months, plasma ADA should be determined twice a month, then monthly until after 18 24 months of treatment.</p> <p>Individuals who have successfully been maintained on therapy for two years should continue to have plasma ADA measured every 2-4 months and red cell dATP measured twice yearly. More frequent monitoring would be necessary if therapy was interrupted or if an enhanced rate of clearance of plasma ADA activity develops.</p>