Enjaymo (sutimlimab-jome)
PAM – 053

Iowa Medicaid Program	Prior Authorization	**Effective Date**	07/01/2022
Revision Number	3	**Last Reviewed**	04/18/2025
Reviewed By	Medicaid Medical Director	**Next Review**	04/17/2026
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	04/01/2023

Overview

Medication: [1]	sutimlimab-jome
Brand Name:	Enjaymo™
Pharmacologic Category:	Immunoglobulin G, subclass 4 (IgG4) monoclonal antibody (classical complement inhibitor)
FDA-Approved Indication(s):	Indicated for the treatment of hemolysis in adults with cold agglutinin disease (CAD)
How Supplied:	Single-dose vial: 1,100 mg/22 mL (50 mg/mL)
Dosage and Administration:	• Vaccinate against encapsulated bacteria at least 2 weeks prior to treatment (ACIP recommendation) • Intravenous administration: once weekly for 2 weeks, then every 2 weeks thereafter • Dosage is based on body weight: ○ 39 kg to less than 75 kg: 6,500 mg ○ 75 kg or more: 7,500 mg
Benefit Category:	Medical

WARNINGS AND PRECAUTIONS

- **Serious infection.** Enjaymo™ may increase susceptibility to serious infections, including infections caused by encapsulated bacteria such as *Neisseria meningitidis* (any serogroup), *Streptococcus pneumoniae*, and *Haemophilus influenzae*.
  - Vaccinate patients for encapsulated bacteria according to the most current ACIP recommendations for patients with persistent complement deficiencies. Revaccinate patients in accordance with ACIP recommendations. Immunize patients without a history of vaccination against encapsulated bacteria at least two weeks prior to receiving the first dose of Enjaymo™. If urgent Enjaymo™ therapy is indicated in an unvaccinated patient, administer vaccine(s) as soon as possible.
  - Vaccination reduces, but does not eliminate, the risk of encapsulated bacterial infections.
- **Infusion-related reactions.** Administration of Enjaymo™ may result in infusion-related reactions (in the two phase 3 studies, 29% of patients experienced infusion-related reactions (e.g., shortness of breath (SOB), rapid heartbeat, nausea, flushing, headache, injection site reaction, etc.).
- **Risk of autoimmune disease.** Based on its mechanism of action, Enjaymo™ may potentially increase the risk for developing autoimmune diseases such as systemic lupus erythematosus (SLE). Development of SLE has been associated with inherited classical component deficiency. Patients with SLE or autoimmune disease with positive anti-nuclear antibody were excluded from the Enjaymo™ clinical trials.

Descriptive Narrative

Autoimmune hemolytic anemia (AIHA) occurs when the host's immune system makes antibodies that attack the red blood cells. AIHA can be due to warm or cold autoantibody types (and rarely, by mixed types). Cold-type AIHA accounts for 16-32% of AIHA cases.[2]

There are three major types of cold-sensitive antibodies that can cause clinical manifestations:

1. Cold agglutinins – antibodies that recognize antigens on red blood cells (RBCs) at temperatures below normal core body temperature. They can cause agglutination of the RBCs and extravascular hemolysis, resulting in anemia, typically without hemoglobinuria.
2. Donath-Landsteiner antibodies – antibodies that recognize RBC antigens at cold temperatures, but unlike cold agglutinins, these antibodies fix complement and cause hemolysis in the circulation (intravascular hemolysis). Patients have symptoms associated with hemoglobinemia and hemoglobinuria, a condition called paroxysmal cold hemoglobinuria.
3. Cryoglobulins – antibodies that form immune complexes in the cold and generally do not interact with RBCs. Cryoglobulins can cause a systemic vasculitis, a systemic inflammatory syndrome, or vascular occlusion). [3]

Cold agglutinin disease (CAD) is a rare disease, affecting an estimated 5,000 people in the United States. Patients with cold agglutinin disease may experience complement-mediated symptoms, including chronic hemolysis resulting in anemia, profound fatigue, jaundice.[4] Non-complement-mediated symptoms include transient, cold-induced agglutination-mediated circulatory symptoms, such as acrocyanosis and Raynaud phenomenon. Patients with CAD also have an increased risk of thromboembolism and early mortality.[5]

There are two types of the disease:

1. CAD: Chronic cold agglutinin disease, the most common form, is a B-cell lymphoproliferative disorder with production of a monoclonal hemagglutinin. Most patients suffer from mild or moderate anemia, with exacerbation at cold temperature. Circulatory symptoms resulting from erythrocyte agglutination may also be present.
2. CAS: Cold agglutinin syndrome is also referred to as secondary CAD. It is attributable to production of a hemagglutinin as a by-product of infection, cancer, or other diseases. Hemolysis may be severe, but, in most instances, the disorder is transient subsiding when the underlying cause is eliminated.[6]

Enjaymo™ (sutimlimab-jome) is an immunoglobulin G, subclass 4 (IgG4) monoclonal antibody that inhibits the classical complement pathway (CP) and specifically binds to complement protein component 1, s subcomponent (C1s), a serine protease which cleaves C4. Enjaymo™ does not inhibit the lectin and alternative pathways. Inhibition of the classical complement pathway at the level of C1s prevents deposition of complement opsonins on the surface of RBCs, resulting in inhibition of hemolysis in patients with CAD.[1]

Guidelines

In November 2017, an international consensus meeting convened with the aim of providing an international consensus for the diagnosis and management of all major forms of autoimmune hemolytic anemia (AIHA) (additional meetings were held in June 2018, December 2018, and June 2019 before the manuscript was finalized). Goals from these meetings included the following:

- Review published data on epidemiology, pathophysiology, classification, diagnostics, transfusion policies, as well as standard and novel treatment options in AIHA.
- Provide international guidelines for the diagnosis of AIHA.
- Create a framework for current treatment of AIHA.
- Establish standardized criteria for diagnosis and outcomes that will instruct clinical studies and provide an overview of novel treatment approaches.

Abbreviations

- **AIHA:** autoimmune hemolytic anemia
- **CAD:** cold agglutinin disease
- **DAT:** direct antiglobulin testing
- **IAT:** indirect antiglobulin testing
- **IgG:** immunoglobulin G
- **RBCs:** red blood cells

Antiglobulin Testing (also known as Coombs test)

Antiglobulin testing, also known as Coombs test, is an immunology laboratory procedure used to detect the presence of antibodies against circulating red blood cells (RBCs) in the body, which then induce hemolysis. The destruction of these RBCs by antibodies directed against them is described diagnostically as autoimmune hemolytic anemia (AIHA).[7]

- Direct antiglobulin testing (DAT)
  - Used to detect the presence of antibodies attached directly to the RBCs. Blood sample is washed in saline to isolate the patient's RBCs.
  - A monospecific or polyspecific reagent is then added to the washed RBCs to detect bound IgG and/or complement C3.
  - In practice, many laboratories will first use the polyspecific reagent that can detect both IgG and C3; a positive result will then be followed with monospecific testing to characterize the antibody further.
- Indirect antiglobulin testing (IAT)
  - Used to detect unbound antibodies to RBCs, which may be present in patient's serum.
  - Serum from a blood sample gets isolated, and native RBCs removed. The isolated serum sample is then incubated with foreign RBCs of known antigenicity. Antiglobulin reagent is then added, and the presence of agglutination indicates a positive result.

Criteria

Prior authorization is required.

Enjaymo™ is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of primary cold agglutinin disease (CAD); **AND**
2. Documentation supports **ALL** of the following for the member:
    a. Presence of chronic hemolysis; **AND**
    b. Polyspecific direct antiglobulin (i.e., Coombs test) test result is positive; **AND**
    c. Monospecific direct antiglobulin test result is strongly specific for C3d; **AND**
    d. Cold agglutinin titer of 64 or less at 4 degrees Celsius; **AND**
    e. Direct antiglobulin test result for IgG of 1+ or less; **AND**
    f. Hemoglobin level of 10 g/dL or less; **AND**
3. Secondary cold agglutinin syndrome has been ruled out (e.g., CAD secondary to infection, rheumatologic disease, or active hematologic malignancy); **AND**
4. History of at least one blood transfusion in the past 6 months; **AND**
5. Member is 18 years of age or older; **AND**
6. Presence of one or more symptoms associated with CAD (i.e., symptomatic anemia, acrocyanosis, Raynaud's phenomenon, hemoglobinuria, disabling circulatory symptoms, or a major adverse vascular event); **AND**
7. Enjaymo™ is not prescribed concurrently with rituximab or rituximab-based regimens (i.e., rituximab with bendamustine or fludarabine); **AND**
8. Prescribed by, or in consultation with, a hematologist; **AND**
9. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed (i or ii):
        i. For patient weight 39 kg to less than 75 kg: 6,500 mg once weekly for the first two weeks, then 6,500 mg once every 2 weeks thereafter; or
        ii. For patient weight 75 kg or greater: 7,500 mg once weekly for the first two weeks, then 7,500 mg once every 2 weeks thereafter; **OR**
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Enjaymo™ is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as evidenced by both of the following since the initiation of treatment:
    a. Increase in hemoglobin > 2 g/dL or hemoglobin level > 12 g/dL; **AND**
    b. Transfusion-free or decreased number of transfusions/blood units; **AND**
3. Prescribed by, or in consultation with, a hematologist; **AND**
4. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed (i or ii):
        i. For patient weight 39 kg to less than 75 kg: 6,500 mg once every 2 weeks; or
        ii. For patient weight 75 kg or greater: 7,500 mg once every 2 weeks; **OR**
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	Up to 12 months
Quantity Limits	• IV infusion once weekly for 2 weeks, then every 2 weeks thereafter • Dosage is based on member weight: ○ 39 kg to < 75 kg: 6,500 mg ○ 75 kg or more: 7,500 mg	

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
~~C9094~~	~~Injection, sutimlimab-jome, 10 mg~~ *(effective 07/01/2022 to 09/30/2022)*
J1302	Injection, sutimlimab-jome, 10 mg *(effective 10/01/2022)*

ICD-10	Description
D59.12	Cold autoimmune hemolytic anemia

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/ Pkg
80203-0347-01 (1,100 mg/22 mL [50 mg/mL] single-dose vial)	Bioverativ USA, Inc. (80203)	10 mg	1	EA	110

Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Enjaymo™ prescribing information (02/2024). Bioverativ USA, Inc.: Waltham, MA. Available online: www.enjaymohcp.com. Accessed February 26, 2025.

[2] Cold agglutinin disease (ORPHA:56425). Orphanet portal for rare diseases and orphan drugs. www.orpha.net. Accessed February 26, 2025.

[3] Berentsen S, Brugnara C. Cold agglutinin disease. Tirnauer JS, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed February 26, 2025.

[4] Röth A, et al. Sutimlimab in Cold Agglutinin Disease. N Engl J Med. 2021 Apr 8;384(14):1323-1334. PMID: 33826820.

[5] Röth A, et al. Sutimlimab in patients with cold agglutinin disease: results of the randomized placebo-controlled phase 3 CADENZA trial. Blood. 2022 Sep 1;140(9):980-991. PMID: 35687757.

[6] Röth A, et al. Eculizumab in cold agglutinin disease (DECADE): an open-label, prospective, bicentric, nonrandomized phase 2 trial. Blood Adv. 2018 Oct 9;2(19):2543-2549. PMID: 30291112.

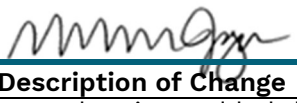
[7] Theis SR, Hashmi MF. Coombs Test. [Updated 2022 Sep 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: www.ncbi.nlm.nih.gov/books/NBK547707. Accessed February 27, 2025.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
04/18/2025	CAC	Annual review. Updated references. Added information in Overview table regarding new ACIP recommendation to vaccinate against encapsulated bacteria at least 2 weeks prior to treatment. Removed paragraph in Guidelines regarding Enjaymo™ approval. Added package description in Coding and Product Information.	3
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
04/19/2024	CAC	Annual review. Added dosing information into criteria.	2
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
04/21/2023	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee