BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 08/17/23**
SECTION: SPECIALTY MEDICAL DRUGS	**LAST REVIEW DATE: 08/15/24**
	CURRENT EFFECTIVE DATE: 10/14/24
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ENJAYMO™ (sutimlimab-jome)

Non-Discrimination Statement is located at the end of this document.

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

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

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.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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Criteria:

Refer to FDA website for current indications and dosage.

- **Criteria for initial therapy:** Enjaymo (sutimlimab-jome) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Hematologist

2. Individual is 18 years of age or older and weighs at least 39 kilograms

3. Individual has a confirmed diagnosis of cold agglutinin disease for the treatment of hemolysis confirmed by **ALL** of the following:

   - Evidence of hemolysis demonstrated by **BOTH** of the following:

     a. Elevated lactate dehydrogenase (LDH) above the upper limit of normal
     b. Decreased haptoglobin level below the lower limit of normal

   - Positive polyspecific direct antiglobulin test (DAT)
   - Monospecific DAT strongly positive for C3d
   - Cold agglutinin titer 1:64 or higher measured at 4^{o} Celsius
   - DAT result for Immunoglobulin G (IgG) is negative or weakly positive (≤ 1+)

4. Individual has documented failure, contraindication per FDA label or intolerance to rituximab

5. Individual meets **ALL** of the following:

   - Evidence of at least one sign or symptoms associated with cold agglutinin disease (see Definitions Section)
   - Hemoglobin ≤ 10 g/dL
   - Elevated total bilirubin above upper limit of normal
   - Has been immunized against encapsulated bacteria (e.g., Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae) at least 2 weeks prior to first dose of Enjaymo

6. Individual does **NOT** have **ANY** of the following:

   - Secondary causes of cold agglutinin syndrome (e.g., infection, rheumatologic diseases, active hematologic malignancies)
   - Concomitant use of other immunosuppressants (e.g., rituximab), chemotherapy or complement inhibitors (e.g., eculizumab, pegcetacoplan, ravulizumab)

Initial approval duration: 6 months

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- **Criteria for continuation of coverage (renewal request):** Enjaymo (sutimlimab-jome) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by physician specializing in the patient's diagnosis or is in consultation with a Hematologist

  2. Individual has a confirmed diagnosis of cold agglutinin disease for the treatment of hemolysis confirmed by **ALL** of the following (at baseline):

     - Evidence of hemolysis demonstrated by **BOTH** of the following:

       a. Elevated lactate dehydrogenase (LDH) above the upper limit of normal
       b. Decreased haptoglobin level below the lower limit of normal

     - Positive polyspecific direct antiglobulin test (DAT)
     - Monospecific DAT strongly positive for C3d
     - Cold agglutinin titer 1:64 or higher measured at 4^{o} Celsius
     - DAT result for Immunoglobulin G (IgG) is negative or weakly positive (≤ 1+)

  3. Individual's condition has responded while on therapy with response defined as **THREE** of the following:

     - Decrease in requirement for red blood cell transfusions compared to baseline
     - Increase in hemoglobin by 1.5 g/dL from baseline or hemoglobin 12 g/dL or greater
     - Improvement in markers of hemolysis (decreased total bilirubin, decreased LDH, increased haptoglobin)
     - Improvement in symptoms of CAD (see Definitions Section)

  4. Individual has been adherent with the medication

  5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use, including:

     - Infusion-related reactions
     - Serious infections
     - Autoimmune disease

  Renewal duration: 12 months

- Enjaymo (sutimlimab-jome) for all other indications not previously listed is considered ***experimental or investigational*** and will not be covered when any **ONE** or more of the following criteria are met:

  1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or

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2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but not limited to:*

- Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, or duration.

Description:

Cold agglutinin disease (CAD) is one form of autoimmune hemolytic anemia (AIHA) in which caused by autoantibodies that bind to red blood cells antigens at low temperatures and cause agglutination or clumping. This antigen-antibody complex triggers the classic complement pathway and triggers hemolysis and other related symptoms.

The primary treatment for anemia has been red blood cell transfusions. Rituximab (off-label) monotherapy and rituximab-containing regimens are first-line for CAD disease modification and treatment of hemolysis. Enjaymo (sutimlimab-jome) is the first FDA approved treatment for CAD.

Enjaymo (sutimlimab-jome) is a classical complement inhibitor indicated for the treatment of hemolysis in adults with CAD. Sutimlimab-jome is an immunoglobulin G (IgG), subclass 4 (IgG4) monoclonal antibody (mAb) that specifically binds to complement protein component 1, s subcomponent (C1s), a serine protease which cleaves C4. 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.

Enjaymo has been studied in primary CAD, whereas those with secondary causes such as infection, rheumatologic disease, systemic lupus erythematosus, or overt hematologic malignancy. Patients with a history of or concomitant low-grade lymphoproliferative disease were allowed. Enjaymo was found to have a significant improvement in hemoglobin and reduction in blood transfusions, fatigue, and other lab parameters corresponding with a decrease in hemolysis.

Definitions:

Symptoms of CAD:

- Symptomatic anemia (fatigue, weakness, shortness of breath, heart palpitations, lightheadedness, chest pain)
- Acrocyanosis (blue-colored fingers or toes, cold and sweaty hands and feet, low skin temperatures, slow blood flow, swelling in hands and feet)

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- Raynaud's syndrome (cold fingers or toes, areas of skin that turn white then blue, numb or prickly feeling or stinging pain when warming)
- Disabling circulatory symptoms
- Hemoglobinuria
- Major adverse vascular event (thrombosis, etc.)

History:	**Date**:	**Activity**:
Pharmacy and Therapeutics Committee	08/15/24	Review with revision: criteria (effective 10/14/24)
Pharmacy and Therapeutics Committee	08/17/23	Approved guideline
Clinical Pharmacist	08/02/23	Development

Coding:

HCPCS: J1302

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Resources:

Literature reviewed 08/15/24. We do not include marketing materials, poster boards and non-published literature in our review.

1. Berentsen S, Brugnara C. Cold agglutinin disease. In: UpToDate, Brodsky RA, Tirnauer JS (Eds). UpToDate, Waltham, MA.: Available at http://uptodate.com. Topic last updated April 1, 2024. Accessed May 17, 2024.

2. Enjaymo (sutimlimab-jome). Prescribing information. Bioverativ Therapeutics Inc.; February 2024 at DailyMed http://dailymed.nlm.nih.gov. Accessed May 17, 2024.

3. Jäger, U, Barcellini W, Broome CM. Diagnosis and treatment of autoimmune hemolytic anemia in adults: Recommendations from the First International Consensus Meeting. *Blood Reviews* 2020; 41: 1006-1048.

4. Röth A, Barcellini W, D'Sa S, et al. Sutimlimab in cold agglutinin disease. *N Engl J Med* 2021; 384: 1323-1334.

5. Röth A, Berentsen S, Barcellini W, et al. Sutimlimab in patients with cold agglutinin disease: results of the randomized placebo-controlled phase 3 CADENZA trial. *Blood* 2022; 140(9): 980-991.

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Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html