Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 04/10/2025

Enjaymo™ (sutimlimab)

HCPCS: J1302

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. Diagnosis of cold agglutin disease confirmed by a cold agglutinin titer level of ≥ 64
   b. FDA approved age
   c. Hemoglobin level ≤ 10.0 g/dL
   d. Prescence of one or more symptoms associated with CAD (including but not limited tosymptomatic anemia, acrocyanosis, Raynaud's phenomenon, hemoglobinuria)
   e. Trial and failure, contraindication, OR intolerance to:
      i. Rituximab in combination with bendamustine
         OR
      ii. Rituximab monotherapy if the patient is not a candidate for bendamustine
   f. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: One year at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are metand that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Enjaymo is a classical complement inhibitor indicated to decrease the need for red blood cell (RBC) transfusion due to hemolysis in adults with cold agglutinin disease (CAD).

- CAD is a type of autoimmune hemolytic anemia characterized by the premature destruction of RBCs. The antibodies that cause CAD activate hemolysis at cold temperatures, usually 37 to 39° Fahrenheit. Most cases of CAD are due to immunoglobulin M (IgM) antibodies. CAD affects approximately one person per million every year and is prevalent in about 16 people per million. CAD typically develops between the ages of 40 to 80 years. In the United States, the estimated prevalence of primary CAD is around 5,000 cases. Symptoms include fatigue, weakness, pallor, dizziness, palpitations, dyspnea, jaundice, and discoloration of digits, ankles, or wrists.

- Enjaymo is an immunoglobulin G 4 (IgG4) monoclonal antibody that inhibits the classical complement pathway. Inhibition of the classical complement pathway prevents deposition of complement opsonins (extracelluarl proteins that induce phagocytosis) on the surface of RBCs, resulting in inhibition of hemolysis in patients with CAD.

- The First International Consensus Group of experts representing autoimmune hemolytic anemia (AIHA) centers, registries, and study groups have developed recommendations for the diagnosis and management of AIHA (2020). Recommendations includes, but is not limited to, the following:

    - A diagnosis of CAD is defined by chronic hemolysis and a cold agglutinin titer level of ≥64.

    - Patients whose Hgb is >10 g/dL are usually not recommended treatment, except in the presence of significant comorbidities such as ischemic cardiomyopathy and chronic obstructive pulmonary disease that would reduce oxygen delivery to the tissues unrelated to the oxygen-carrying capacity of the blood.

    - For asymptomatic patients, watchful waiting with supportive care only is recommended.

    - For symptomatic patients:

        - First-line treatment: rituximab alone or in combination with bendamustine depending on the severity of CAD and the presence of contraindications to cytotoxic therapies.

        - Second-line treatment: rituximab + bendamustine (if not administered in the first line or if ≥2 years have passed since response to prior combination treatment), rituximab monotherapy (if patient previously responded for ≥1 year) as repeat courses is often effective in relapsed disease.

        - Although there are no randomized trials and no formal approval of any chemoimmunotherapy in CAD, remission after B cell–directed treatment has been confirmed in several systematic studies.

        - Treatment with rituximab + fludarabine or botezomib alone are listed as alternative treatment options. However, use is limited due to toxicity or limited evidence.

    - Treatment goals include, but are not limited to, an increase in hemoglobin levels in patients with symptom-producing anemia, decrease in transfusions or achievement of transfusion independency, resolution of disabling cold-induced circulatory symptoms. All treatment should aim at an improved quality of life.

- Enjaymo was approved in February 2022 based on positive results from a 26-week open label, single arm Phase III study (CARDINAL; NCT03347396) in 24 patients with CAD with a recent history of transfusion. The results showed 54% of participants responded to Enjaymo, defined in the study as a hemoglobin ≥ 12 g/dL or an increase of at least 2 g/dL; patients remaining transfusion-free after week five, and patients did not use other CAD-related treatments.

- As of February 2023, there are now 2.5 years of data available to inform the safety and efficacy of Enjaymo. After completion of the initial 26-week study period in the CARDINAL trial (Part A), participants were allowed to enter the two-year extension period (Part B). 19 out of the 22 original trial participants completed Part B of the open-label study. Results demonstrated that Enjaymo maintained hemoglobin levels higher than 11 g/dL and led to a sustained normalization of hemolysis markers thoughout the study. Additionally, 68% of patients enrolled in Part B remained transfusion-free through the two-year treatment period.

- Enjaymo received an expanded indication in January 2023 to treat hemolysis in adults with CAD without a recent history of transfusion, in addition to its original indication to treat hemolysis in adults with CAD with a recent history of transfusion. Approval of the expanded indication was based on positive results from a 26-week, randomized, placebo controlled Phase III study (CADENZA, NCT03347422) in 42 patients with CAD without a recent history of transfusion. The results showed that 73% and 15% of participants who received Enjaymo and the placebo, respectively, achieved the primary endpoint, defined as an increase in hemoglobin from baseline by at least 1.5 g/dL at Weeks 23, 25 and 26, and the absence of blood transfusions and avoidance of CAD medications from Week 5 to Week 26 of the study.

- Enjaymo offers a novel mechanism of action, substantial efficacy, and a favorable safety profile for adults with CAD. Without long term data and data comparing it to use of the guideline-recommended options with an established track record of safety and efficacy along with the probable need for indefinite treatment duration, it is unknown whether Enjaymo is a superior treatment option at this time.

References:

1. Enjaymo [prescribing information]. Waltham, MA: Bioverativ; February 2024.
2. Drug manufacturer press release. Available at: FDA approves Enjaymo™ (sutimlimab-jome), first treatment for use in patients with cold agglutinin disease - Sanofi. Accessed February 5, 2022.
3. Jäger, U., Barcellini, W., et al. (2020). "Diagnosis and treatment of autoimmune hemolytic anemia in adults: Recommendations from the First International Consensus Meeting." Blood Rev 41: 100648
4. Röth A, Barcellini W, D'Sa S, et al. Inhibition of complement C1s with sutimlimab in patients with cold agglutinin disease (CAD): interim results of the phase 3 CARDINAL study long-term follow-up. Blood. 2020;136(Suppl 1):24-25.
5. Röth A, Barcellini W, D'Sa S, et al. Complement C1s inhibition with sutimlimab results in durable response in cold agglutinin disease: CARDINAL study 1-year interim follow-up results. Haematologica. 2022 Feb 17.
6. Express Scripts Drug Evaluation: Enjaymo™ (sutimlimab-jome intravenous infusion – Bioverativ/Sanofi). March 2022.
7. IPD Analytics. Enjaymo (sutimlimab-jome). New Drug Approval Review. March 2022. Accessed March 8, 2022. https://www.ipdanalytics.com.
8. Berentsen S. How I treat cold agglutinin disease. Blood. 2021;137(10):1295-1303.
9. Berentsen S, Randen U, Oksman M, et al. Bendamustine plus rituximab for chronic cold agglutinin disease: results of a Nordic prospective multicenter trial. Blood. 2017;130(4):537-541.
10. Berentsen S, Fattizzo B, Barcellini W. The choice of new treatments in autoimmune hemolytic anemia: how to pick from the basket? Front Immunol. 2023 Apr 24;14:1180509. doi: 10.3389/fimmu.2023.1180509. PMID: 37168855; PMCID: PMC10165002.

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<tr><td>1.6</td><td>Effective Date: 04/11/2024</td><td>Annual review – No changes made to existing criteria</td></tr>
<tr><td>1.5</td><td>Effective Date: 04/06/2023</td><td>Annual review – No changes made to existing criteria</td></tr>
<tr><td>1.4</td><td>Effective Date: 04/14/2022</td><td>New policy</td></tr>
<tr><td>1.3</td><td>Effective Date: 03/17/2022</td><td>UM medical management system update for BCBSM and BCN
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.2</td><td>Effective Date: 03/07/2022</td><td>UM medical management system update for MAPPO and BCNA
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>No</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.1</td><td>Effective Date: 10/07/2021</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.0</td><td>Effective Date: 10/08/2020</td><td>Preliminary drug review</td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*