

sutimlimab-jome (Enjaymo™)

Medicare Advantage Medical Policy #MNG-035

Original Effective Date: 01/01/2025

Current Effective Date: 01/01/2025

Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Health Plan may consider the use of sutimlimab-jome (Enjaymo™)‡ for the treatment of cold agglutinin disease to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for sutimlimab-jome (Enjaymo) will be considered when the following criteria are met for the requested drug:

- Initial
 - Patient has a diagnosis of primary cold agglutinin disease confirmed by ALL of the following:
 - Direct antibody test strongly positive for C3d and negative or only weakly positive for immunoglobulin G; AND
 - Cold agglutinin antibody titer ≥ 64 at 4 degrees Celsius (approximately 40 degrees Fahrenheit); AND
 - Total bilirubin level is above the reference range; AND
 - Provider attests that patient does NOT have cold agglutinin syndrome secondary to infection, rheumatologic disease, systemic lupus erythematosus, or overt hematologic malignancy; AND
 - Patient is ≥ 18 years of age; AND
 - Patient has a history of at least one sign or symptom associated with cold agglutinin disease (examples include symptomatic anemia [e.g., anemia associated with fatigue, weakness, shortness of breath, heart palpitations, lightheadedness, chest pain], acrocyanosis, Raynaud's syndrome, hemoglobinuria, disabling circulatory symptoms, or a major adverse vascular event [e.g., thrombosis]); AND
 - Patient's hemoglobin level (prior to treatment with Enjaymo) is ≤ 10 g/dL; AND
 - Enjaymo will not be used in combination with rituximab; AND
 - Patient has been vaccinated against encapsulated bacteria (e.g., *Neisseria meningitides*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*) at least two weeks prior to initiation of Enjaymo; AND
 - Dose will not exceed the following:
 - If weight 39 to <75 kg: 6,500 mg on day 1 and 8, then every 2 weeks maintenance
 - If weight ≥ 75 kg: 7,500 mg on day 1 and 8, then every 2 weeks maintenance

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- Continuation:
 - Patient has received an initial authorization for Enjaymo from the plan OR has provided documentation of authorization from previous Medicare Advantage plan; AND
 - Patient has experienced improvement on therapy as evidenced by at least ONE of the following:
 - Increase in hemoglobin of at least 2 g/dL from baseline; OR
 - Hemoglobin level ≥ 12 g/dL; OR
 - Decrease in number of transfusions needed from baseline; AND
 - Enjaymo will not be used in combination with rituximab; AND
 - Dose of Enjaymo will not exceed the following:
 - If weight 39 to <75 kg: 6,500 mg every 2 weeks
 - If weight ≥ 75 kg: 7,500 mg every 2 weeks

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of sutimlimab-jome (Enjaymo) in patients who do not have a history of at least one sign or symptom of cold agglutinin disease, who have a hemoglobin level greater than 10 g/dL, or who will be using the drug in combination with rituximab to be **not medically necessary**.**

Based on review of available data, the Health Plan considers the continued use of sutimlimab-jome (Enjaymo) when the patient has not demonstrated improvement in hemoglobin level or number of transfusions needed while on therapy to be **not medically necessary**.**

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of sutimlimab-jome (Enjaymo) when patient selection criteria are not met (except those noted to be **not medically necessary*****) to be **investigational**.*

Background/Overview

Enjaymo is a complement inhibitor indicated to treat hemolysis in adults with cold agglutinin disease (CAD). It is administered intravenously with the first two doses being given one week apart and subsequent doses given every two weeks. The dose is weight-based up to a maximum of 7,500 mg. As with other complement inhibitors, Enjaymo increases the risk of infection with encapsulated bacteria and patients should be vaccinated at least two weeks prior to the first dose of Enjaymo according to current recommendations for patients with persistent complement deficiencies.

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CAD is a rare condition in which autoantibodies are produced against antigens on the surface of red blood cells. These antibodies are termed cold agglutinins and optimally bind at temperatures of 3 to 4 degrees Celsius. The binding of the cold agglutinins ultimately leads to hemolytic anemia and cold-induced symptoms ranging from slight acrocyanosis to severe Raynaud phenomena. It should be noted that primary cold agglutinin disease is distinct from secondary disease, termed cold agglutinin syndrome, which can occur with underlying conditions such as malignancy, infection, and autoimmune diseases. Primary CAD is estimated to affect approximately 16 patients per million persons with a higher incidence in females and a higher prevalence in colder climates. The median age of onset is 67 years. Prior to the availability of Enjaymo, treatment for CAD included non-pharmacologic management with cold-avoidance and increased use of warm clothing as well as transfusions for severe anemia. There are no other medications approved specifically for cold agglutinin disease, but rituximab has been studied and is often used either alone or in combination with fludarabine or bendamustine. However, rituximab regimens are limited by toxicities and delay of response.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Enjaymo was approved in February 2022 to decrease the need for red blood cell transfusion due to hemolysis in adults with cold agglutinin disease. In January 2023, the label was updated to indicate that Enjaymo can be used for the treatment of hemolysis in patients with CAD regardless of prior transfusion need.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Enjaymo in patients with a recent blood transfusion was assessed in the CARDINAL study, an open-label, single-arm, 6-month trial in 24 patients. Following the completion of the 6-month treatment period, patients continued to receive Enjaymo in a long-term safety and durability of response extension phase for an additional 24 months. Included patients had a confirmed diagnosis of cold agglutinin disease (CAD) based on chronic hemolysis, polyspecific direct antiglobulin test (DAT), monospecific DAT specific for C3d, cold agglutinin titer ≥ 64 at 4 degrees Celsius, and IgG DAT $\leq 1+$, and a recent blood transfusion in the 6 months prior to enrollment. All participants were administered 6.5 g or 7.5 g Enjaymo (based on body weight) intravenously over approximately 60 minutes on Day 0, Day 7, and every 14 days thereafter through Week 25. Patients with CAD secondary to infection, rheumatologic disease, systemic lupus erythematosus, or overt hematologic malignancy were excluded, whereas patients with a history of or concomitant low-grade lymphoproliferative disease were not excluded.

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Last Reviewed: 10/15/2024

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Efficacy was based on the proportion of patients who met the following criteria: an increase from baseline in Hgb level ≥ 2 g/dL or a Hgb level ≥ 12 g/dL at the treatment assessment time point, no blood transfusion from Week 5 through Week 26, and no treatment for CAD beyond what was permitted per protocol from Week 5 through Week 26. Based on this definition, 54% of participants (13/24) were considered responders at Week 26. It should be noted that varying numbers of patients met some (but not all) of the response criteria with 92% not receiving protocol-prohibited CAD medications from Weeks 5 through 26.

The efficacy of Enjaymo in patients without a recent blood transfusion was assessed in the CADENZA study, a placebo-controlled, 6-month trial in 42 patients. Following the completion of the 6-month treatment period in which 22 patients received Enjaymo and 20 patients received placebo, 39 patients continued to receive Enjaymo in a long-term safety and durability of response extension phase for an additional 12 months. Included patients had a confirmed diagnosis of CAD based on chronic hemolysis, polyspecific DAT test, monospecific DAT specific for C3d, cold agglutinin titer ≥ 64 at 4 degrees C, an IgG dAT $\leq 1+$, no history of transfusion within 6 months of screening, and less than or equal to 1 blood transfusion within 12 months of screening. Patients with CAD secondary to infection, rheumatologic disease, systemic lupus erythematosus, or overt hematologic malignancy were excluded. All participants were administered 6.5 g or 7.5 g Enjaymo (based on body weight) intravenously over approximately 60 minutes on Day 0, Day 7, and every 14 days thereafter; or placebo.

Efficacy was based on the proportion of patients who met the following criteria: an increase from baseline in Hgb level ≥ 1.5 g/dL at the treatment assessment time point, no blood transfusion from Week 5 through Week 26, and no treatment for CAD beyond what was permitted per protocol from Week 5 through Week 26. There was a statistically significant treatment effect in the Enjaymo group compared with placebo. At the treatment assessment timepoint, 16 of the 22 patients on Enjaymo (72.7%; 95% CI: 49.8% to 89.3%) and 3 of 20 patients on placebo (15%; 95% CI: 3.2% to 37.9%) met the efficacy criteria.

References

1. Enjaymo [package insert]. Bioverative U.S. LLC. Waltham, MA. Updated May 2023.
2. Enjaymo Drug Evaluation. Express Scripts. Updated February 2022.

Policy History

Original Effective Date: 01/01/2025

Current Effective Date: 01/01/2025

10/15/2024 UM Committee review

Next Scheduled Review Date: 10/2025

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Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of the Health Plan Medical Policy Coverage Guidelines is with the Health Plan and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in the Health Plan Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of the Health Plan Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No code
HCPCS	J1302
ICD-10 Diagnosis	D59.12

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

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- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

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Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: <https://www.cms.gov/medicare-coverage-database/search.aspx>. You may wish to review the Guide to the MCD Search here: <https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx>.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.