Original Effective Date: 04/28/2022
Current Effective Date: 04/11/2025
Last P&T Approval/Version: 01/29/2025
Next Review Due By: 01/2026
Policy Number: C22996-A

Enjaymo (sutimlimab-jome)

PRODUCTS AFFECTED

Enjaymo (sutimlimab-jome)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline 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 Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Cold agglutinin disease (CAD)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. COLD AGGLUTININ DISEASE (CAD):
1. Documentation of confirmed diagnosis of primary cold agglutinin disease (CAD)
   AND
2. Documentation member has the presence of one or more symptoms associated with CAD such

as symptomatic anemia, acrocyanosis, Raynaud's phenomenon, hemoglobinuria, disabling circulatory symptoms, or a major adverse vascular event
AND

3. Prescriber attests member has been vaccinated at least within the past two weeks or has history of vaccination against encapsulated bacteria
MOLINA REVIEWER NOTE: Examples of encapsulated bacteria: Neisseria meningitides (any serogroup), Streptococcus pneumoniae, and Haemophilus influenzae.
AND
4. (a) Documentation of an inadequate response, serious side effects, or contraindication to a rituximab-containing regimen (i.e., Rituximab monotherapy: 4 weeks; Rituximab combination: 4 cycles)
OR
(b) Documentation member is utilizing Enjaymo (sutimlimab-jome) for a rapid response and who are awaiting definitive effects from rituximab
OR
(c) Documentation member is undergoing cardiac surgery within the next 30 days and a dose of Enjaymo (sutimlimab-jome) is needed preoperatively.
AND
5. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Enjaymo (sutimlimab-jome) include: known hypersensitivity to sutimlimab-jome or any of the inactive ingredients]

CONTINUATION OF THERAPY:

A. COLD AGGLUTININ DISEASE (CAD):

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms [DOCUMENTATION REQUIRED]

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months
MOLINA REVIEWER NOTE: For Texas Marketplace, please see Appendix.

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified hematologist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

For members weighing 39 kg to < 75 kg, the recommended dose is 6,500 mg
For members weighing ≥ 75 kg, the recommended dose is 7,500 mg.
Administer once weekly for 2 doses then administer every two weeks thereafter.

PLACE OF ADMINISTRATION:

The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-inpatient hospital facility-based location as per

Note: Site of Care Utilization Management Policy applies for Enjaymo (sutimlimab). For information on site of care, see Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous

DRUG CLASS:
Complement C1 inhibitor

FDA-APPROVED USES:
Indicated for the treatment of hemolysis in adults with cold agglutinin disease (CAD)

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Reserved for State specific information. Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.

State Specific Information
State Marketplace
Texas (Source: Texas Statutes, Insurance Code)
"Sec. 1369.654. PROHIBITION ON MULTIPLE PRIOR AUTHORIZATIONS.
(a) A health benefit plan issuer that provides prescription drug benefits *may not require an enrollee to receive more than one prior authorization annually* of the prescription drug benefit for *a prescription drug prescribed to treat an autoimmune disease, hemophilia, or Von Willebrand disease*.
(b) This section does not apply to:
(1) opioids, benzodiazepines, barbiturates, or carisoprodol;
(2) prescription drugs that have a typical treatment period of less than 12 months;
(3) drugs that:
(A) have a boxed warning assigned by the United States Food and Drug Administration for use; and
(B) must have specific provider assessment; or
(4) the use of a drug approved for use by the United States Food and Drug Administration in a manner other than the approved use."

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Cold agglutinin disease (CAD) is a form of autoimmune hemolytic anemia (AIHA) in which cold agglutinins (IgM autoantibodies against red blood cell [RBC] antigens with an optimum temperature of 3 to 4°C) can cause clinical symptoms related to RBC agglutination in cooler parts of the body and hemolytic anemia. Cold agglutinins trigger hemolysis when they are exposed to temperatures below normal core body temperature. Once a red blood cell (RBC) is recognized by the cold-induced antibody, it will cause agglutination, or clumping, of RBCs. The RBCs then become bound to complement. Once the RBCs are bound to complement, they can be attacked and destroyed by other immune cells (e.g. macrophages). This results in a hemolytic anemia.
Most cases of CAD are due to immunoglobulin M (IgM) antibodies. CAD can be primary (meaning the cause is unknown) or secondary (due to another condition, most commonly an infectious disease [especially M.

pneumoniae and Epstein-Barr virus infection] or immunoproliferative disease [e.g. non- Hodgkin's lymphoma, chronic lymphocytic leukemia]).
Cold agglutinins have also been observed in patients with other viral infections such as HIV, influenza, and COVID-19 infection.
The symptoms associated with CAD are generally triggered by exposure to cold temperatures and can be classified into hemolytic and circulatory symptoms.

- Hemolytic symptoms: Characterized by paleness of the skin, fatigue, shortness of breath, dizziness, and palpitations; severe hemolysis may lead to chest pain, deregulation of heart rate and blood pressure, jaundice, and dark-pigmented urine.
- Circulatory (or cold-induced) symptoms: Characterized by coldness of the fingers and/or toes (digits) and painful bluish or reddish discoloration of the skin of the digits, ankles, and wrists (acrocyanosis or Raynaud phenomenon). In severe cases, ulcers may develop on the extremities of digits.

According to a retrospective review of over 200 patients with CAD, the most common symptoms of the disease include anemia (median hemoglobin [Hgb] level of 9.5 g/dL), affecting about 90% of patients; increased lactate dehydrogenase (LDH) and bilirubin, each present in about 90% of patients; and cold-induced symptoms (most commonly acrocyanosis), in about 50% of patients.

Enjaymo (sutimlimab-jome)
Sutimlimab is an immunoglobulin G subclass 4 (IgG4) monoclonal antibody that inhibits the classical complement pathway and specifically binds to complement protein component 1. This inhibition prevents deposition of complement opsonins on the surface of RBCs, resulting in inhibition of hemolysis in patients with CAD. Enjaymo™ (sutimlimab-jome) is indicated to decrease the need for red blood cell (RBC) transfusion due to hemolysis in adults with cold agglutinin disease (CAD).
The FDA approval was based on data from the open-label, single-arm phase 3 CARDINAL study, which evaluated the efficacy and safety of sutimlimab in 24 patients with primary CAD who had a recent blood transfusion. Patients received an intravenous infusion of sutimlimab through week 26. The primary end point was the proportion of patients with a response, defined by an increase in hemoglobin (Hgb) of at least 2g/dL from baseline or reaching a Hgb level of at least 12g/dL at the 26- week treatment assessment timepoint, as well as the absence of blood transfusions from weeks 5 to 26 or any other CAD-related treatments.
Results showed that 54% (n=13) of patients achieved the composite endpoint. Sixty-three percent (n=15) of patients had an increase in Hgb of at least 2g/dL or reached an Hgb of at least 12g/dL, while 71% (n=17) did not receive RBC transfusion after week 5 and 92% (n=22) did not use other CAD- related treatments. Treatment with sutimlimab was also associated with improvements in total bilirubin (mean reduction in bilirubin levels [n=14]: -2.23mg/dL [95% CI, -2.49, -1.98]) and lactate dehydrogenase (least squared mean change: -126 [95% CI, -218, -35]). At week 3, the mean increase in Hgb level was observed to be 2.29g/dL (SE: 0.308). At the 26-week treatment assessment timepoint, the mean increase in Hgb was 3.18g/dL (SE: 0.476).
The most common adverse reactions reported with sutimlimab included respiratory tract infection, viral infection, diarrhea, dyspepsia, cough, arthralgia, arthritis, and peripheral edema.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Enjaymo (sutimlimab-jome) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Enjaymo (sutimlimab-jome) include: patients with known hypersensitivity to sutimlimab-jome or any of the inactive ingredients.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device*

code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.

HCPCS CODE	DESCRIPTION
J1302	Injection, sutimlimab-jome, 10 mg

AVAILABLE DOSAGE FORMS:
Enjaymo SOLN 1100MG/22MLsingle-dose vial

REFERENCES

1. Enjaymo (sutimlimab) [prescribing information]. Waltham, MA: Bioverativ USA Inc; February 2024.
2. Berentsen S. How I treat cold agglutinin disease. Blood 2021; 137:1295.
3. Röth A, Barcellini W, D'Sa S, et al. Sutimlimab in Cold Agglutinin Disease. N Engl J Med 2021; 384:1323.
4. Berentsen S, Tjønnfjord GE. Diagnosis and treatment of cold agglutinin mediated autoimmune hemolytic anemia. Blood Rev 2012; 26:107.
5. Schöllkopf C, Kjeldsen L, Bjerrum OW, et al. Rituximab in chronic cold agglutinin disease: a prospective study of 20 patients. Leuk Lymphoma 2006; 47:253.
6. Berentsen S, Ulvestad E, Gjertsen BT, et al. Rituximab for primary chronic cold agglutinin disease: a prospective study of 37 courses of therapy in 27 patients. Blood 2004; 103:2925.
7. Gueli A, Gottardi D, Hu H, et al. Efficacy of rituximab-bendamustine in cold agglutinin haemolytic anaemia refractory to previous chemo-immunotherapy: a case report. Blood Transfus 2013; 11:311.
8. Fattizzo B, Zaninoni A, Pettine L, et al. Low-dose rituximab in autoimmune hemolytic anemia: 10 years after. Blood 2019; 133:996.
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; 130:537.
10. Jäger, U., Barcellini, W., Broome, C. M., Gertz, M. A., Hill, A., Hill, Q. A., … Berentsen, S. (2020). Diagnosis and treatment of autoimmune hemolytic anemia in adults: Recommendations from the First International Consensus Meeting. Blood Reviews, 41(1), 100648. https://doi.org/10.1016/j.blre.2019.100648

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: References	Q1 2025
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Place of Administration FDA-Approved Uses References	Q1 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Route of Administration Coding/Billing Information	Q1 2023
NEW DEVELOPMENT	Q2 2022