Clinical Policy: Sutimlimab-jome (Enjaymo)

Reference Number: CP.PHAR.503
Effective Date: 02.04.22
Last Review Date: 05.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Sutimlimab-jome (Enjaymo®) is a classical complement inhibitor.

FDA Approved Indication(s)

Enjaymo is indicated for the treatment of hemolysis in adults with cold agglutinin disease (CAD).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Enjaymo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cold Agglutinin Disease (must meet all)**:**

1. Diagnosis of primary CAD;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 18 years;
4. Secondary CAD has been ruled out (i.e., cold agglutinin syndrome secondary to infection, rheumatologic disease, or active hematologic malignancy);
5. Member meets all of the following (a, b, c, and d):
   a. Active hemolysis as evidenced by elevated total bilirubin;
   b. Polyspecific direct antiglobulin test (DAT) (i.e., Coombs test) is positive;
   c. Monospecific DAT shows both of the following (i and ii):
      i. C3d DAT: strongly positive;
      ii. IgG DAT: negative or weakly positive;
   d. Cold agglutinin titer ≥ 64 at 4 degrees Celsius;
6. Hemoglobin ≤ 10 g/dL;
7. Enjaymo is not prescribed concurrently with rituximab or rituximab-based regimens (i.e., rituximab with bendamustine or fludarabine);
8. Dose does not exceed one of the following (a or b):
   a. For body weight 39 kg to < 75 kg: 6,500 mg (6 vials) on Day 0, Day 7, then every 2 weeks thereafter;
   b. For body weight ≥ 75 kg: 7,500 mg (7 vials) on Day 0, Day 7, then every 2 weeks thereafter.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Cold Agglutinin Disease (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by one of the following since initiation of Enjaymo therapy (a or b):
   a. Increase in hemoglobin ≥ 1.5 g/dL or hemoglobin level ≥ 12 g/dL;
   b. Transfusion free or decreased number of transfusions/blood units;
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. For body weight 39 kg to < 75 kg: 6,500 mg (6 vials) every 2 weeks;
   b. For body weight ≥ 75 kg: 7,500 mg (7 vials) every 2 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid

Approval duration: Duration of request or 6 months (whichever is less)

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CAD: cold agglutinin disease
DAT: direct antiglobulin test
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): known hypersensitivity to sutimlimab-jome or any inactive ingredients
- Boxed warning(s): none reported

Appendix D: Cold Agglutinins
- During passage through acral parts of the body, cooling of the blood allows cold agglutinins (CA) to bind to erythrocytes and cause agglutination.
- The antigen-IgM complex binds complement protein 1q (C1q) on the cell surface and initiates the classical complement pathway.
- C1 esterase activates C2 and C4, generating C3 convertase which results in the cleavage of C3 to C3a and C3b.
- Upon warming to 37°C in the central circulation, the CA detach from the cells, allowing agglutinated erythrocytes to separate, while C3b remains bound.
- C3b-opsonized cells are prone to phagocytosis by the mononuclear phagocytic system, mainly in the liver, a process known as extravascular hemolysis.
- On the surface of the surviving erythrocytes, C3b is cleaved, leaving high numbers of C3d molecules that can be detected by the DAT.

Berentsen S. How I manage patients with cold agglutinin disease. British Journal of Haematology. 2018;181:320–330.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CAD	Weight-based dose IV weekly for 2 weeks then every 2 weeks thereafter: • 39 kg to < 75 kg: 6,500 mg (6 vials) • ≥ 75 kg: 7,500 mg (7 vials) Must be administered at the recommended dosage regimen time points or within 2 days of these time points	39 kg to < 75 kg: 6,500 mg/dose ≥ 75 kg: 7,500 mg/dose

VI. Product Availability

Solution for injection in single-dose vial: 1,100 mg/22 mL (50 mg/mL)

VII. References

1. Enjaymo Prescribing Information. Waltham, MA: Bioverativ USA Inc (A Sanofi Company); March 2023. Available at https://www.enjaymohcp.com/. Accessed January 12, 2024.
2. A study to assess the efficacy and safety of BIVV009 (sutimlimab) in participants with primary cold agglutinin disease who have a recent history of blood transfusion (Cardinal Study). NCT03347396. ClinicalTrials.gov. Available at https://www.clinicaltrials.gov/ct2/show/NCT03347396. Accessed February 8, 2024.
3. A study to assess the efficacy and safety of BIVV009 (sutimlimab) in participants with primary cold agglutinin disease without a recent history of blood transfusion (Cadenza). NCT03347422. ClinicalTrials.gov. Available at https://clinicaltrials.gov/ct2/show/NCT03347422. Accessed February 8, 2024.
4. Ulrich J, D'Sa S, Schorgenhofer C et al. Inhibition of complement C1s improves severe hemolytic anemia in cold agglutinin disease: a first-in-human trial. Blood. February 28, 2019;133(9):893-901.
5. Hill QA, Stamps R, Massey E, et al. The diagnosis and management of primary autoimmune haemolytic anaemia. British Journal of Haematology. 2017;176:395-411. https://doi.org/10.1111/bjh.14478.
6. Bylsma LC, Ording AG, Rosenthal A, et al. Occurrence, thromboembolic risk, and mortality in Danish patients with cold agglutinin disease. Blood Adv. 2019 Oct 22;3(20):2980-2985. DOI:10.1182/bloodadvances.2019000476.
7. Berentsen S. How I manage patients with cold agglutinin disease. British Journal of Haematology. 2018;181:320-330.
8. Berentsen S, Ulvestad E, Langholm R, et al. Primary chronic cold agglutinin disease: a population based clinical study of 86 patients. Haematologica. 2006;91:460-466.
9. Röth A, Barcellini W, D'Sa S, et al. Sutimlimab in cold agglutinin disease. N Engl J Med. 2021;384(14):1323-1334. doi:10.1056/NEJMoa2027760.
10. Roth 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. doi: 10.1182/blood.2021014955.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1302	Injection, sutimlimab-jome, 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	07.07.20	08.20
3Q 2021 annual review: no significant changes as drug is not yet FDA-approved; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	03.23.21	08.21
RT4: Drug is now FDA approved - criteria updated per FDA labeling: adjusted hemoglobin level criteria for continued therapy from 11 to 12 g/dL; added criteria that Enjaymo is not prescribed concurrently with rituximab or rituximab-based regimens; adjusted dosing weight cut-off; references reviewed and updated.	03.08.22	05.22
Added HCPCS code [J1302]. Template changes applied to other diagnoses/indications and continued therapy section.	09.09.22	
2Q 2023 annual review: RT4: removed requirement for history of at least one documented blood transfusion within 6 months (initial criteria), revised required increase in hemoglobin level from 2 to 1.5 g/dL (continued criteria), and modified evidence of positive response from being both of the following to just one of the following per revised FDA indication and new data from the CADENZA study; corrected hemoglobin-related continued criteria from > to ≥ per pivotal trial design; removed inactive HCPCS codes; references reviewed and updated.	01.26.23	05.23
2Q 2024 annual review: no significant changes; references reviewed and updated.	02.08.24	05.24

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health

plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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