

Clinical Policy: Sutimlimab-jome (Enjaymo)

Reference Number: CP.PHAR.503

Effective Date: 02.04.22

Last Review Date: 05.22

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 to decrease the need for red blood cell transfusion due to 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 \geq 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 \geq 64 at 4 degrees Celsius;
6. Hemoglobin \leq 10 g/dL;
7. History of at least one documented blood transfusion within 6 months prior to initiating Enjaymo therapy;
8. Enjaymo is not prescribed concurrently with rituximab or rituximab-based regimens (i.e., rituximab with bendamustine or fludarabine);
9. 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 \geq 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

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by both of the following since initiation of Enjaymo therapy (a and b):
 - a. Increase in hemoglobin $>$ 2 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 \geq 75 kg: 7,500 mg (7 vials) every 2 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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: <ul style="list-style-type: none"> • 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); February 2022. Available at <https://www.enjaymohcp.com/>. Accessed March 8, 2022.
2. FDA grants priority review of sutimlimab, potential first approved treatment of hemolysis in adult patients with Cold Agglutinin Disease. Sanofi Press Release. May 14, 2020. Available at <https://www.sanofi.com/-/media/Project/One-Sanofi-Web/Websites/Global/Sanofi-COM/Home/media-room/press-releases/2020/2020-05-14-07-00-00-2033186-en.pdf>. Accessed March 23, 2021.

3. Positive results presented from pivotal Phase 3 trial of sutimlimab in people with cold agglutinin disease. Presented at the Late Breaking Abstracts Session of the 61st Annual Meeting of the American Society of Hematology in Orlando, FL. Sanofi Press Release. December 10, 2019. Press release available at <https://www.sanofi.com/-/media/Project/One-Sanofi-Web/Websites/Global/Sanofi-COM/Home/media-room/press-releases/2019/2019-12-10-13-30-00-1958469-en.pdf>. Accessed March 23, 2021.
4. 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?term=NCT03347396&rank=1>. Accessed March 23, 2021.
5. Ulrich J, D'Sa S, Schorogenhofer 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.
6. 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>.
7. 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.
8. Berentsen S. How I manage patients with cold agglutinin disease. *British Journal of Haematology*. 2018;181:320-330.
9. 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.
10. 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.

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
J3590	Unclassified biologics
C9094	Inj, 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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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 [C9094].	06.30.22	

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.

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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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