Clinical Policy: Sutimlimab-jome (Enjaymo)

Reference Number: ERX.SPA.411
Effective Date: 02.04.22
Last Review Date: 05.22
Line of Business: Commercial, Medicaid

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 is strongly positive;
      ii. IgG DAT is negative or weakly positive;
   d. Cold agglutinin titer ≥ 64 at 4 degrees Celsius;
6. Hemoglobin ≤ 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 ≥ 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 ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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 ≥ 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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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); 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, 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.
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.

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 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;	03.08.22	05.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
added criteria that Enjaymo is not prescribed concurrently with rituximab or rituximab-based regimens; adjusted dosing weight cut-off; references reviewed and updated.		

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.