09-J4000-25

Original Effective Date: 06/15/22

Reviewed: 09/11/24

Revised: 10/15/24

Subject: Sutimlimab-jome (Enjaymo) Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Cold agglutinin disease is a rare disease in which following exposure to cold temperatures, IgM antibodies attach to red blood cells and form clumps. The clumps bind to complement and result in premature hemolysis of red blood cells. Symptoms depend on the severity of hemolysis but include pale skin, fatigue, shortness of breath, dizziness, palpitations, dark urine, jaundice, painful bluish or reddish coloration of the extremities. The disease also results in low hemoglobin (Hgb) levels and increased lactacte dehydrogenase (LDH) and bilirubin. Sutimlimab-jome (Enjaymo™) is a monoclonal antibody that inhibits the classical complement pathway by binding to complement protein component 1 subcomponent s (C1s). This inhibition ultimately prevents hemolysis in patients with cold agglutinin disease (CAD). Sutimlimab-jome (Enjaymo) is FDA-approved for the treatment of hemolysis in adults with cold agglutinin disease (CAD).

In an open-label, single-arm trial in 24 patients, patients with confirmed CAD were administered sutimlimab-jome for 6 months and then permitted to continue an extension for an additional 24 months. CAD was confirmed based on chronic hemolysis, polyspecific direct antiglobulin test (DAT), monospecific DAT specific for C3d, cold agglutinin titer greater than or equal to 64 at 4 degree Celsius and IgG DAT less than or equal to 1+. Patients had a recent blood transfusion in the 6 months prior to enrollment. Patients were excluded with cold agglutinin syndrome secondary to infection, rheumatologic disease, systemic lupus erythematosus, or overt hematologic malignancy. Patients with a history of or concomitant low-grade lymphoproliferative disease were not excluded. The efficacy of sutimlimab-jome was evaluated based on the proportion of patients meeting target hemoglobin levels, avoidance of transfusion and treatment with CAD medications. There were 15 patients or 63% who had an increase from baseline in the Hgb level greater than or equal to 2 g/dL or a Hgb level greater than or equal to 12 g/dL at the end of the study. There were 17 patients or 71% that did not require blood transfusion and 22 patients or 92% who did not require CAD treatment with rituximab alone or in combination with cytotoxic agents between week 5 through week 26. The overall response was

achieved in 13 patients or 54% of those receiving treatment. There was a reduction in bilirubin and LDH values and an increase in mean hemoglobin from baseline to the end of treatment. The most common adverse reactions included respiratory tract infections, viral infection, diarrhea, dyspepsia, cough, arthralgia, arthritis, and peripheral edema. Serious reactions included streptococcal sepsis and staphylococcal wound infection, arthralgia, and respiratory tract infection.

POSITION STATEMENT:

I. Initiation of sutimlimab-jome (Enjaymo) **meets the definition of medical necessity** when used to treat the following indications when the specific criteria are met:

A. Cold Agglutinin Disease (CAD)

i. Diagnosis is confirmed by ALL of the following – lab documentation must be submitted:

a. Chronic hemolysis

b. Polyspecific direct antiglobulin test (DAT)

c. Monospecific DAT specific for C3d

d. Cold agglutinin titer greater than or equal to 64 at 4 degree Celsius

e. IgG DAT less than or equal to 1+

ii. Member has anemia with a hemoglobin less than the lower limit of normal – lab documentation must be provided

iii. The member had an inadequate response, intolerance, or is not a candidate for rituximab – documentation must be provided

iv. **ONE** of the following:

a. Member has been vaccinated against encapsulated bacteria (e.g., Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae type B) at least 2 weeks prior to therapy initiation

b. Member has been vaccinated against encapsulated bacteria less than 2 weeks prior to therapy initiation and will receive prophylactic antibiotics for at least 2 weeks following vaccination

v. The member does not have cold agglutinin syndrome secondary to infection, rheumatologic conditions, systemic lupus erythematosus, or hematologic malignancy

vi. The member will not receive an additional complement inhibitor (eculizumab, ravulizumab, pegcetacoplan) or rituximab

vii. The dose does not exceed the following:

a. 39 kg to less than 75 kg: 6,500 mg on day 1 and 8, then every 2 weeks maintenance

b. 75 kg or more: 7,500 mg on day 1 and 8, then every 2 weeks maintenance

Approval duration: 6 months

II. Continuation of sutimlimab-jome meets the definition of medical necessity for CAD when ALL of the following are met

A. The member has been previously approved for sutimlimab-jome in the treatment of CAD by Florida Blue or another health plan in the past 2 years, OR the member has previously met all indication-specific criteria for coverage

B. Member has a history of beneficial response to sutimlimab-jome therapy–examples of beneficial response include absence of or decreased requirement for red blood cell transfusion compared to baseline, improvement in hemoglobin by 2 g/dL from baseline, hemoglobin greater than or equal to 12 g/dL – documentation must be provided

C. Member has been revaccinated against encapsulated bacteria (e.g., Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae type B) according to current medical guidelines for vaccination while receiving sutimlimab-jome therapy

D. The member will not receive an additional complement inhibitor (eculizumab, ravulizumab, pegcetacoplan) or rituximab

E. The dose does not exceed the following:

i. 39 kg to less than 75 kg: 6,500 mg every 2 weeks maintenance

ii. 75 kg or more: 7,500 mg every 2 weeks maintenance

Approval duration: 6 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- For treatment of hemolysis in adults with cold agglutinin disease (CAD):
  - Weight-based dosage weekly for two weeks, then every two weeks thereafter
    - 39 kg to less than 75 kg: 6,500 mg by IV infusion
    - 75 kg or more: 7,500 mg by IV infusion
  - If a dose is missed, administer as soon as possible; thereafter, resume dosing every two weeks. If the duration after the last dose exceeds 17 days, administer weekly for two weeks, then every two weeks thereafter

Dose Adjustments

- The effects of severe renal impairment or severe hepatic impairment are unknown

Drug Availability

- 1,100 mg/22 mL (50 mg/mL) in a single dose vial

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Patients with known hypersensitivity to sutimlimab-jome or any of the inactive ingredients

Precautions/Warnings

- Serious Infections: ensure patients are vaccinated against encapsulated bacteria. Monitor patients for early signs and symptoms of infections
- Infusion-related reactions: Monitor patients for infusion-related reactions, interrupt if reaction occurs, and institute appropriate medical management as needed
- Risk of Autoimmune Disease: Monitor patients for signs and symptoms and manage medically
- Recurrent Hemolysis After discontinuation: Monitor patients for signs and symptoms of hemolysis if treatment is interrupted.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J1302	Injection, sutimlimab-jome, 10 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

D59.12	Cold autoimmune hemolytic anemia

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 2024 Aug 30]. Available from: http://www.clinicalpharmacology.com/.
2. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2024 Aug 30].
3. Enjaymo (sutimlimab-jome) injection [package insert]. Bioverativ USA Inc. Waltham, MA. Feb 2023.
4. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 2024 Aug 30]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 09/11/24.

GUIDELINE UPDATE INFORMATION:

06/15/22	New Medical Coverage Guideline.
07/01/22	Revision: Added HCPCS code C9094.
10/01/22	Revision: Added HCPCS code J1302 and deleted codes C9094 and J3590.
03/15/23	Review and revision to guideline; consisting of removing transfusion requirement and updating the FDA-approved indication.
10/15/24	Review and revision to guideline; consisting of updating documentation requirement and references.