NEW DRUG APPROVAL

Brand Name	Enjaymo™
Generic Name	sutimlimab-jome
Drug Manufacturer	Bioverativ USA Inc

New Drug Approval

FDA approval date: February 4, 2022

Review designation: N/A; Orphan

Type of review: Biologic License Application (BLA): 761164

Dispensing restriction: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Cold agglutinin disease is a rare type of autoimmune hemolytic anemia in which the body's immune system mistakenly attacks and destroys its own red blood cells. When affected people's blood is exposed to cold temperatures (32º to 50º F), certain proteins that normally attack bacteria (IgM antibodies) attach themselves to red blood cells and bind them together into clumps (agglutination). This eventually causes red blood cells to be prematurely destroyed (hemolysis) leading to anemia and other associated signs and symptoms. Cold agglutinin disease can be primary (unknown cause) or secondary, due to an underlying condition such as an infection, another autoimmune disease, or certain cancers. Treatment depends on many factors including the severity of the condition, the signs and symptoms present in each person, and the underlying cause.

CAD most commonly affects people between the ages of 40 and 80. The median age at symptom onset is around 65 years, meaning that half of affected individuals develop symptoms before this age, and the other half after this age. The disease is present in about 16 people per million (prevalence) and develops in one person per million every year (incidence). The disease is almost twice as common in women compared to men. Those living with conditions associated with CAD (see “causes” section above) are more likely to develop the disease. CAD is also potentially more common, or at least more recognized, in colder climates.

Primary CAD is a rare disease. In retrospective reviews from Nordic countries, the incidence has been estimated at approximately 1 to 1.8 per million and the prevalence at approximately 13 to 16 per million. A series that included nearly all affected individuals in Norway and Lombardy (North Italy) found prevalences of approximately 20 per million and 5 per million, respectively, suggesting a four-fold higher prevalence in colder climates (mean temperature in Norway, 7° C colder than North Italy).

Efficacy

The efficacy of Enjaymo™ was assessed in an open-label, single-arm, 6-month trial in 24 patients (CARDINAL, NCT03347396). Following the completion of the 6-month treatment period, patients continued to receive Enjaymo™ in a long-term safety and durability of response extension phase for an additional 24 months.

Patients with a confirmed diagnosis of CAD based on chronic hemolysis, polyspecific direct antiglobulin test (DAT), monospecific DAT specific for C3d, cold agglutinin titer ≥64 at 4°C, and IgG DAT ≤1+ and a recent blood transfusion in the 6 months prior to enrollment were administered 6.5 g or 7.5 g Enjaymo™ (based on body weight) intravenously over approximately 60 minutes on Day 0, Day 7, and every 14 days thereafter through Week 25. Patients with cold agglutinin syndrome secondary to infection, rheumatologic disease, systemic lupus

erythematosus, or overt hematologic malignancy were excluded, whereas patients with a history of or concomitant low-grade lymphoproliferative disease were not excluded.

Efficacy was based on the proportion of patients who met the following criteria: an increase from baseline in Hgb level ≥2 g/dL or a Hgb level ≥12 g/dL at the treatment assessment time point (mean value from Weeks 23, 25, and 26), no blood transfusion from Week 5 through Week 26, and no treatment for CAD beyond what was permitted per protocol from Week 5 through Week 26.

Table: Efficacy Results in Patients with CAD in CARDINAL

Parameter	Statistic	ENJAYMO N=24
Responder*	n (%)	13 (54)
Hemoglobin level ≥12 g/dL or Increase in Hemoglobin level of ≥2 g/dL	n (%)	15 (63)
Hemoglobin level ≥12 g/dL	n (%)	9 (38)
Increase in Hemoglobin level of ≥2 g/dL	n (%)	15 (63)
Patients not receiving RBC transfusion from Week 5 through Week 26 (transfusion avoidance)	n (%)	17 (71)
Patients not receiving protocol-prohibited CAD medications† from Week 5 through Week 26	n (%)	22 (92)

* A responder was defined as a patient with an increase from baseline in Hgb level ≥2 g/dL or a Hgb level ≥12 g/dL at the treatment assessment time point (mean value from Weeks 23, 25, and 26), no blood transfusion from Week 5 through Week 26, and no treatment for CAD beyond what was permitted per protocol from Week 5 through Week 26.

† Prohibited therapies included rituximab alone or in combination with cytotoxic agents.

Among 14 patients with baseline and follow-up bilirubin values, the mean was 3.23 mg/dL (2.7-fold ULN) at baseline and 0.91 mg/dL (0.8-fold ULN) at the treatment assessment time point. The least-squares (LS) mean change was reduction of -2.23 mg/dL (95% CI: -2.49 to -1.98). Among 17 patients with baseline and follow-up LDH values, the mean LDH was 424 U/L (1.7-fold ULN) at baseline and 301 U/L (1.2-fold ULN) at the follow-up time point. The least squared mean change in LDH at the treatment assessment time point was reduction of -126 (95% CI: 218 to -35). In CARDINAL, an increase in mean hemoglobin level of 2.29 g/dL (SE: 0.308) was observed at Week 3 and 3.18 g/dL (SE: 0.476) at treatment assessment time point. The observed model mean change in hemoglobin level from baseline at treatment assessment time point was an improvement of 2.60 g/dL (95% CI: 0.74, 4.46).

Safety

ADVERSE EVENTS

Most common adverse reactions (incidence ≥10%) are respiratory tract infection, viral infection, diarrhea, dyspepsia, cough, arthralgia, arthritis, and peripheral edema.

WARNINGS & PRECAUTIONS

- 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 Enjaymo™ Discontinuation: Monitor patients for signs and symptoms of hemolysis if treatment with Enjaymo™ is interrupted.

CONTRAINDICATIONS

Enjaymo™ is contraindicated in patients with known hypersensitivity to sutimlimab-jome or any of the inactive ingredients.

Clinical Pharmacology

MECHANISMS OF ACTION

Sutimlimab-jome is an immunoglobulin G (IgG), subclass 4 (IgG4) monoclonal antibody (mAb) that inhibits the classical complement pathway (CP) and specifically binds to complement protein component 1, s subcomponent (C1s), a serine protease which cleaves C4. Sutimlimab jome does not inhibit the lectin and alternative pathways. Inhibition of the classical complement pathway at the level of C1s prevents deposition of complement opsonins on the surface of RBCs, resulting in inhibition of hemolysis in patients with CAD.

Dose & Administration

ADULTS

- Vaccinate against encapsulated bacteria at least two weeks prior to treatment.
- Weight-based dosage weekly for two weeks then every two weeks:
  - For patients weighing 39 kg to less than 75 kg: 6,500 mg by intravenous infusion.
  - For patients weighing 75 kg or more: 7,500 mg by intravenous infusion.

PEDIATRICS

Safety and effectiveness in pediatric patients have not been established.

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

No dosage adjustments are needed.

HEPATIC IMPAIRMENT

No dosage adjustments are needed.

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

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