**INDICATIONS AND USAGE**

ENJAYMO® (sutimlimab-jome) is a classical complement inhibitor indicated for the treatment of hemolysis in adults with cold agglutinin disease (CAD).

**DOSAGE AND ADMINISTRATION**

- **Recommended Vaccinations**
- **Recommended Dosage Regimen**
- **Preparation and Administration**

**DOSE FORMS AND STRENGTHS**

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

**CONTRAINDICATIONS**

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

**WARNINGS AND 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 of hemolysis if treatment with ENJAYMO is interrupted.

**ADVERSE REACTIONS**

Most common adverse reactions in the CADENZA study (Part A) are rhinitis, headache, hypertension, acrocyanosis, and Raynaud’s phenomenon. The most common adverse reactions in the CARDINAL study (incidence ≥25%) are urinary tract infection, respiratory tract infection, bacterial infection, dizziness, fatigue, peripheral edema, arthralgia, cough, hypertension, and nausea.

To report SUSPECTED ADVERSE REACTIONS, contact Bioverativ Therapeutics Inc. (A SANOFI COMPANY) at 1-800-745-4447 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

**RECENT MAJOR CHANGES**

- Indications and Usage (1)
- Dosage and Administration (2.3)
- Warnings and Precautions (5.1, 5.2)

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use ENJAYMO safely and effectively. See full prescribing information for ENJAYMO.

**FULL PRESCRIBING INFORMATION: CONTENTS**

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2.1 Recommended Vaccinations
2.2 Recommended Dosage Regimen
2.3 Preparation and Administration
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5 WARNINGS AND PRECAUTIONS
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**FULL PRESCRIBING INFORMATION**

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**CONTRAINdications**

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

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Revised: 03/2023
Use aseptic technique to prepare ENJAYMO as follows:

- Remove ENJAYMO from the refrigerator. To minimize foaming, do not shake ENJAYMO.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
- ENJAYMO solution is a clear to slightly opalescent and colorless to slightly yellow solution. Do not administer if discolored or if foreign particulate matter is present.
- Withdraw the calculated volume of ENJAYMO from the appropriate number of vials based on the recommended dosage (see Table 1). Dilute the calculated volume with 0.9% Sodium Chloride Injection, USP to a total volume of 500 mL.
- Refer to Table 2 for infusion rate. Administer the infusion over 1 to 2 hours depending on the patient’s body weight. Administer ENJAYMO infusion solution through a 0.2 micron in-line filter with a polyethersulfone (PES) membrane.
- Prime the infusion tubing with the dosing solution immediately before infusion and flush immediately following completion of the infusion with a sufficient quantity (approximately 20 mL) of 0.9% Sodium Chloride Injection, USP.
- If the ENJAYMO infusion solution is not used immediately, store refrigerated at 36°F to 46°F (2°C to 8°C).
- Once removed from refrigeration, allow the ENJAYMO infusion solution to adjust to room temperature 59°F to 77°F (15°C to 25°C) and administer within 8 hours. Total time from the time of preparation, including refrigeration, adjustment to room temperature and the expected infusion time should not exceed 36 hours. In-line infusion warmers may be used; do not exceed a temperature of 104°F (40°C).
- No incompatibilities have been observed between ENJAYMO infusion solution and infusion bags made of Di(2-ethylhexyl) sebacate (DEH) plasticized polyvinyl chloride (PVC), Ethyl Vinyl Acetate (EVA) and polyolefin (PO); administration sets made of DEH-plasticized PVC, DEH-free polypropylene (PP) and polyethylene (PE); and vial adapters made of polycarbonate (PC) and acrylonitrile-butadiene-styrene (ABS).

### Table 2: Infusion Reference Table for ENJAYMO (diluted in 0.9% Sodium Chloride Injection, USP)

<table>
<thead>
<tr>
<th>Body Weight Range</th>
<th>Dose</th>
<th>Number of ENJAYMO Vials Needed</th>
<th>ENJAYMO Volume</th>
<th>NaCl Diluent</th>
<th>Total Volume</th>
<th>Maximum Infusion Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>39 kg to less than 70 kg</td>
<td>6,500 mg</td>
<td>6</td>
<td>130 mL</td>
<td>370 mL</td>
<td>500 mL</td>
<td>250 mL/hour</td>
</tr>
<tr>
<td>70 kg to less than 75 kg</td>
<td>6,500 mg</td>
<td>6</td>
<td>130 mL</td>
<td>370 mL</td>
<td>500 mL</td>
<td>500 mL/hour</td>
</tr>
<tr>
<td>75 kg or greater</td>
<td>7,500 mg</td>
<td>7</td>
<td>150 mL</td>
<td>350 mL</td>
<td>500 mL</td>
<td>500 mL/hour</td>
</tr>
</tbody>
</table>

*Patients with cardiopulmonary disease may receive the infusion over 120 minutes.

If ENJAYMO treatment is administered to patients with active systemic infections, monitor closely for signs and symptoms of worsening infection. Some infections may become rapidly life-threatening or fatal if not recognized and treated promptly. Inform patients of these signs and symptoms and steps to be taken to seek immediate medical care. Consider interruption of ENJAYMO treatment in patients who are undergoing treatment for serious infection. ENJAYMO has not been studied in patients with chronic systemic infections such as hepatitis B, hepatitis C, or HIV. Consider patients’ immune status when initiating treatment with ENJAYMO.

### 5.2 Infusion-Related Reactions

ENJAYMO is contraindicated in patients with known hypersensitivity to sulfmethimazole or any of the inactive ingredients (see Contraindications [4.1]). Administration of ENJAYMO may result in infusion-related reactions. In the two phase 3 studies, 19 of 66 (29%) patients treated with ENJAYMO experienced infusion-related reactions (e.g., shortness of breath, rapid heartbeat, nausea, flushing, headache, hypotension, chest discomfort, pruritus, rash, injection site reaction, and dizziness) were reported in patients from the two clinical studies. One patient permanently discontinued ENJAYMO due to an infusion-related reaction. Monitor patients for infusion-related reactions and interrupt if a reaction occurs. Discontinue ENJAYMO infusion and institute appropriate supportive measures if signs of hypersensitivity reactions, such as cardiovascular instability or respiratory compromise, occur.

### 5.3 Risk of Autoimmune Disease

Based on its mechanism of action, ENJAYMO may potentially increase the risk for developing autoimmune diseases such as systemic lupus erythematosus (SLE). Development of systemic lupus erythematosus (SLE) has been associated with inherited classical complement deficiency. Patients with SLE or autoimmune disease with positive anti-nuclear antibody were excluded from clinical trials with ENJAYMO. In clinical trials, 3/66 (4.5%) patients developed a relapse or worsening of preexisting autoimmune disease. Monitor patients being treated with ENJAYMO for signs and symptoms and manage medically.

### 5.4 Recurrent Hemolysis After ENJAYMO Discontinuation

If treatment with ENJAYMO is interrupted, closely monitor patients for signs and symptoms of recurrent hemolysis, e.g., elevated levels of total bilirubin or lactate dehydrogenase (LDH) accompanied by a decrease in hemoglobin, or reappearance of symptoms such as fatigue, dyspnea, palpitations, or hemoglobinuria. Consider restarting ENJAYMO if signs and symptoms of hemolysis occur after discontinuation.

### 6. ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed in greater detail in other sections of the labeling:

- Serious infections (see Warnings and Precautions [5.1])
- Infusion-Related Reactions (see Warnings and Precautions [5.2])
- Risk of Autoimmune Disease (see Warnings and Precautions [5.3])

#### 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of ENJAYMO in patients with a confirmed diagnosis of CAD was evaluated in a placebo-controlled study (CADERNA) in Part A (n=42) followed by an open-label single-arm study in Part B (n=39) and an open-label single-arm study (CARDINAL) in Part C (n=44). The median duration of treatment exposure to ENJAYMO was 104 weeks (patients randomized to ENJAYMO in CADERNA Part A) and 93 weeks (patients randomized to placebo in CADERNA Part A) and 143 weeks for CARDINAL. In CADERNA (Part A), there were no clinically significant differences in the safety profile of ENJAYMO compared to placebo. One patient permanently discontinued ENJAYMO due to Raynaud’s phenomenon (n=1). No clinically significant differences in the safety profile of ENJAYMO compared to placebo were observed in the CARDINAL study.

#### 6.2 Laboratory Tests

In clinical trials, no clinically significant differences in laboratory test results were observed between patients treated with ENJAYMO and placebo.

<p>| Table 3: Adverse Reactions (≥10%) in Patients Who Received ENJAYMO with a Difference Between Arms of ≥5% Compared to Placebo in the CADERNA Study (Part A) |</p>
<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>ENJAYMO (N=22)</th>
<th>Placebo (N=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>5 (23%)</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5 (23%)</td>
<td>0</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>4 (18%)</td>
<td>0</td>
</tr>
<tr>
<td>Acrocyanosis</td>
<td>4 (18%)</td>
<td>0</td>
</tr>
<tr>
<td>Raynaud’s phenomenon</td>
<td>4 (18%)</td>
<td>0</td>
</tr>
</tbody>
</table>

**CARDINAL**

Serious adverse reactions occurred in 10/24 (42%) patients who received ENJAYMO. The most common adverse reaction (≥5%) was acrocyanosis (n=2). A fatal adverse reaction of pneumonia klebsiella occurred in one patient who received ENJAYMO. Permanent discontinuation of ENJAYMO due to an adverse reaction occurred in 2/24 (8%) patients. Adverse reactions which resulted in permanent discontinuation of ENJAYMO included pneumonia klebsiella (n=1) and infection related reactions (n=1). Dosage interruptions of ENJAYMO due to an adverse reaction occurred in 7/24 (30%) patients. Adverse reactions which required dosage interruption included pneumonia, 2019-2020 coronavirus pneumonia, abdominal pain, upper urinary tract infection, bacterial, urosepsis, acrocyanosis, viral infection, blood creatinine increase and infusion-related reaction.

The most common adverse reaction (≥25%) reported in the CADERNA study were urinary tract infection, respiratory tract infection, bacterial infection, dizziness, fatigue, peripheral edema, arthralgia, cough, hypertension, and nausea.

#### 7.2 Precautions

**SLE or autoimmune disease with positive anti-nuclear antibody were excluded from clinical trials with ENJAYMO.**
Table 4: Adverse Reactions (≥15%) in Patients Receiving ENJAYMO in the CARDINAL Study

<table>
<thead>
<tr>
<th>Adverse Reaction/Body System</th>
<th>n (%)</th>
<th>[N=24]</th>
</tr>
</thead>
<tbody>
<tr>
<td>INFECTIONS AND INFESTATIONS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary tract infection&lt;sup&gt;a&lt;/sup&gt;</td>
<td>9 (38%)</td>
<td></td>
</tr>
<tr>
<td>Respiratory tract infection&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6 (25%)</td>
<td></td>
</tr>
<tr>
<td>Bacterial infection&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6 (25%)</td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>5 (21%)</td>
<td></td>
</tr>
<tr>
<td>Viral infection&lt;sup&gt;c&lt;/sup&gt;</td>
<td>5 (21%)</td>
<td></td>
</tr>
<tr>
<td>NEUROLOGICAL SYSTEM DISORDERS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness&lt;sup&gt;d&lt;/sup&gt;</td>
<td>7 (29%)</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>5 (21%)</td>
<td></td>
</tr>
<tr>
<td>GENERAL DISORDERS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue&lt;sup&gt;e&lt;/sup&gt;</td>
<td>8 (33%)</td>
<td></td>
</tr>
<tr>
<td>Peripheral edema&lt;sup&gt;f&lt;/sup&gt;</td>
<td>6 (25%)</td>
<td></td>
</tr>
<tr>
<td>Pyrexia</td>
<td>5 (21%)</td>
<td></td>
</tr>
<tr>
<td>MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>6 (25%)</td>
<td></td>
</tr>
<tr>
<td>VASCULAR DISORDERS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension&lt;sup&gt;g&lt;/sup&gt;</td>
<td>6 (25%)</td>
<td></td>
</tr>
<tr>
<td>Acrocyanosis</td>
<td>5 (21%)</td>
<td></td>
</tr>
<tr>
<td>GASTROINTESTINAL DISORDERS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>6 (25%)</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain&lt;sup&gt;h&lt;/sup&gt;</td>
<td>5 (21%)</td>
<td></td>
</tr>
<tr>
<td>RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough&lt;sup&gt;i&lt;/sup&gt;</td>
<td>6 (25%)</td>
<td></td>
</tr>
<tr>
<td>INJURY, POISONING AND PROCEDURAL COMPLICATIONS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infusion-related reaction&lt;sup&gt;j&lt;/sup&gt;</td>
<td>4 (17%)</td>
<td></td>
</tr>
</tbody>
</table>

Please note: if a subject has multiple events in a grouped term the subject is only counted once. The following terms were combined for the analysis:

- Urinary Tract Infection includes cystitis, urethrosis
- Respiratory tract infection includes upper respiratory tract infection, bronchitis, lower respiratory tract infection.
- COVID-19 pneumonia
- Bacterial infection includes Escherichia urinary tract infection, urinary tract infection bacteria, cystitis bacterial, Escherichia sepsis, pneumococcal sepsis, pneumonia klebsiella, streptococcal sepsis, wound infection staphylococcal
- Viral infection includes oral herpes, herpes zoster, respiratory tract infection viral, viral upper respiratory tract infection, Herpes simplex viremia
- Dizziness includes dizziness postural and vortigo
- Fatigue includes asthenia, malaise, mental fatigue
- Peripheral edema includes peripheral swelling
- Hypertension includes, blood pressure increased, essential hypertension
- Abdominal pain includes abdominal pain upper, abdominal tenderness
- Cough includes productive cough
- Infusion-related reaction includes stress cardiomyopathy, feeling cold (All occurred within 24 hours of start of ENJAYMO infusion)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on ENJAYMO use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Human immunoglobulin G (IgG) antibodies are known to cross the placental barrier; therefore, sutimlimab-jome may be transmitted from the mother to the developing fetus. In animal reproduction studies, intravenous administration of sutimlimab-jome to pregnant monkeys during organogenesis at doses 2 to 3 times the maximum recommended human doses did not result in adverse effects on pregnancy or offspring development (see Data). The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2%-4% and 15%-25%, respectively.

Data

Animal data

Pregnant monkeys were administered sutimlimab-jome at doses of 60 and 180 mg/kg/dose via 30-minute intravenous infusion once-weekly from gestation Day 20 to parturition (approximately 21 days) resulting in exposures 2 to 3 times the human exposures at the maximum recommended doses based on area under the curve (AUC). Sutimlimab-jome was detectable in infants born to pregnant females exposed to 180 mg/kg/week. No effects on reproductive and developmental parameters were observed in maternal animals and offspring, respectively.

8.2 Lactation

Risk Summary

There are no data on the presence of sutimlimab-jome in human milk, effects on the breastfed child, or the effects on milk production. Maternal IgG is known to be present in human milk. The effects of local gastrointestinal exposure and limited systemic exposure in the breastfed child to sutimlimab-jome are unknown. No conclusions can be drawn regarding whether or not ENJAYMO is safe for use during breastfeeding. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for ENJAYMO and any potential adverse effects on the breastfed child from ENJAYMO or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Of the 66 patients with CAD in clinical studies of ENJAYMO, 65% were 65 years of age and over, including 27% who were 75 years of age and over. No overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

11 DESCRIPTION

Sutimlimab-jome, a classical complement inhibitor, is a humanized monoclonal antibody expressed by recombinant in Chinese hamster ovary (CHO) cells and produced in vitro using standard mammalian cell culture methods. Sutimlimab-jome is composed of two heterodimers. Each heterodimer is composed of a heavy and a light polypeptide chain. Each heavy chain (H-chain) is composed of 445 amino acids and each light chain (L-chain) contains 216 amino acids. Sutimlimab-jome has a molecular weight of approximately 147 kDa.

ENJAYMO (sutimlimab-jome) injection is a sterile, clear to slightly opalescent, colorless to slightly yellow, preservative-free solution for intravenous use. Each single-dose vial contains 1,100 mg sutimlimab-jome at a concentration of 50 mg/mL with a pH of 6.1. Each mL contains 50 mg of sutimlimab-jome and also contains polysorbat 60 (0.2 mg), sodium chloride (8.18 mg), sodium phosphate dibasic heptahydrate (0.48 mg), sodium phosphate monobasic monohydrate (1.13 mg), and Water for Injection, USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism 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 C1q, a serine protease which cleaves C1r/C1s, a, q (C1r/C1s, a, q) serine protease which cleaves C1r/C1s, a, q. This cleavage leads to the formation of C1r and C1s, which are essential for complement activation. Sutimlimab-jome selectively binds to C1q, the first component of the classical pathway, and inhibits the formation of C1r/C1s, thereby preventing further activation of the classical pathway.

12.2 Pharmacodynamics

Greater than 90% inhibition of CP was observed following a single sutimlimab-jome infusion and sustained in patients with CAD when sutimlimab-jome concentrations were greater than or equal to 100 mcg/mL. C4 levels returned to normal levels (0.2 g/L) in patients with CAD within one week following the first dose of sutimlimab-jome. Complete CP inhibition following initiation of sutimlimab-jome treatment led to inhibition of hemolysis as evidenced by normalization of bilirubin, decrease in LDH, increase in haptoglobin, and decrease in reticuloocytes.

After the first treatment with sutimlimab-jome, near normalization of bilirubin associated with a greater than 1 g/L increase in hemoglobin was observed, demonstrating the effect of CP inhibition. The extent and duration of the pharmacodynamic response in patients with CAD were exposure dependent for sutimlimab-jome.

12.3 Pharmacokinetics

Following administration of the approved weight-based recommended dosages, the exposure of sutimlimab-jome increases proportionally over a dosage range of 50 mg/kg to 100 mg/kg by intravenous infusion (0.3 to 1.5 times the maximum approved recommended dosage based on 75 kg body weight). Steady state was achieved by Week 7 after starting sutimlimab-jome treatment, with an accumulation ratio of less than 2.

Distribution

Sutimlimab-jome binds to C1s in the serum. The volume of distribution at steady state was approximately 5.8 L in patients with CAD.

Elimination

The terminal elimination half-life and clearance varies at different doses due to target-mediated drug disposition at lower sutimlimab-jome concentrations. The terminal elimination half-life (t1/2) of sutimlimab-jome is 21 days with a clearance (CL) of approximately 0.14 L/day at the approved recommended dosage.

Metabolism

Sutimlimab-jome is a protein. It is generally recognized that antibodies are metabolized by degradation into small peptides and individual amino acids.

Specific Populations

No clinically significant differences in the pharmacokinetics of sutimlimab-jome were observed based on sex, age (19 to 88 years of age), ethnicity (Japanese, non-Japanese), and mild to moderate renal impairment (GFR 30 to 89 mL/min/1.73 m² measured by estimated glomerular filtration rate (eGFR)). The effects of severe renal impairment and hepatic impairment on the pharmacokinetics of sutimlimab-jome are unknown.

Body weight

Population pharmacokinetic analysis shows that sutimlimab-jome AUC at steady-state decreased up to 40% for a patient weighing 110 kg following the 7.5 g dose and increased up to 170% for a patient weighing 40 kg following the 6.5 g dose. The effect of body weight on pharmacokinetics has been integrated in the recommended dose regimen tiered by body weight.

12.5 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of sutimlimab-jome or of other sutimlimab products. During the treatment period in CARDINAL and CADAENA, 8/68 (12%) ENJAYMO-treated patients developed anti-sutimlimab-jome antibodies (duration of exposure up to 177 weeks). There was no identified clinically significant effect of anti-drug antibodies on pharmacokinetics, pharmacodynamics, safety, or effectiveness of ENJAYMO over the treatment duration [see Clinical Studies (14)].
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity and mutagenicity studies have not been conducted with sutimlimab-jome. Effects of sutimlimab-jome on male and female fertility have not been studied in animals. In repeat-dose studies in cynomolgus monkeys with sutimlimab-jome administered once-weekly at exposures 3 to 4 times the human exposures at the maximum recommended human doses of sutimlimab-jome, no effects on male or female reproductive tissues were observed.

14 CLINICAL STUDIES

14.1 CADENZA

The efficacy of ENJAYMO was assessed in a placebo-controlled 6-month trial in 42 patients (CADENZA, NCT 02375454). Following the completion of the 6-month treatment period (Part A) in which 22 patients received ENJAYMO and 20 patients received placebo, 39 patients (19 patients on ENJAYMO and 20 patients on placebo) continued to receive ENJAYMO in a long-term safety and durability of response extension phase (Part B) for an additional 12 months following last patient out from Part A. The trial included a 9 week safety follow-up after the last dose of ENJAYMO. 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, an IgG DAT ≥1+ and no history of transfusion within 6 months, or more than one blood transfusion in the 12 months prior to enrollment in the trial were administered 6.5 g or 7.5 g ENJAYMO (based on body weight) intravenously 16 times the human exposures at the maximum recommended human doses of sutimlimab-jome, no effects on male or female reproductive tissues were observed.

Major baseline characteristics of the trial population are summarized in Table 5.

Table 5: Baseline Characteristics of Patients Included in CADENZA

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo N=20</th>
<th>ENJAYMO N=22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>68.2</td>
<td>65.3</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td>4 (20.0)</td>
<td>5 (22.7)</td>
</tr>
<tr>
<td></td>
<td>48 (90.0)</td>
<td>45 (77.3)</td>
</tr>
<tr>
<td>Body weight</td>
<td>Mean, Kg</td>
<td>64.9</td>
</tr>
<tr>
<td></td>
<td>Min, Max</td>
<td>48, 95</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>Mean, g/dL</td>
<td>9.33</td>
</tr>
<tr>
<td>Bilirubin (total)†</td>
<td>µmol/L</td>
<td>35.77</td>
</tr>
<tr>
<td></td>
<td>(1.75 x ULN)</td>
<td>(2 x ULN)</td>
</tr>
<tr>
<td>LDH</td>
<td>U/L</td>
<td>380.8</td>
</tr>
<tr>
<td>History of transfusion</td>
<td>Mean number of transfusions (range)</td>
<td>0</td>
</tr>
<tr>
<td>Within last 6 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within last 12 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACIT-Fatigue scale</td>
<td>Mean</td>
<td>32.99</td>
</tr>
</tbody>
</table>

†The Mantel-Haenszel stratum-weighted estimator of the rate difference with 95% CI was calculated using the Sato variance estimator. The stratifaction factors are baseline hemoglobin (< median vs ≥ median) and geographic region (Asia/Other, North America, and Europe) ±LS: Least Square, FACIT-Fatigue: Functional Assessment of Chronic Illness Therapy-Fatigue Scale N=22

The data from this study demonstrated a statistically significant treatment effect of ENJAYMO over placebo in terms of the rate of patients who met the efficacy criteria (responder) as well as improving symptoms and impacts of fatigue (FACIT-Fatigue). The responder rate difference between ENJAYMO and placebo was 58.7% (95% CI: 34.8% to 82.9%) with a p-value of 0.0004. At the treatment assessment timepoint (TAT), 16 of 22 patients on ENJAYMO (72.7%; 95% CI: 49.8% to 89.3%) and 3 of 20 patients on placebo (15.0%; 95% CI: 3.2% to 37.9%) met primary criteria. Efficacy of ENJAYMO in the inhibition of hemolysis in patients with CAD was demonstrated across multiple end points as described in the table below (see Table 6).

Table 6: Efficacy Results in Patients with CAD in the CADENZA Part A Study

<table>
<thead>
<tr>
<th>Responder†</th>
<th>Placebo N=20</th>
<th>ENJAYMO N=22</th>
<th>Treatment Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>3 (15)</td>
<td>16 (72.7)</td>
<td>58.78 [34.6, 82.96]†</td>
</tr>
<tr>
<td>p-value:</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The data from this study demonstrated a statistically significant treatment effect of ENJAYMO over placebo in terms of the rate of patients who met the efficacy criteria (responder) as well as improving symptoms and impacts of fatigue (FACIT-Fatigue). The responder rate difference between ENJAYMO and placebo was 58.7% (95% CI: 34.8% to 82.9%) with a p-value of 0.0004. At the treatment assessment timepoint (TAT), 16 of 22 patients on ENJAYMO (72.7%; 95% CI: 49.8% to 89.3%) and 3 of 20 patients on placebo (15.0%; 95% CI: 3.2% to 37.9%) met primary criteria. Efficacy of ENJAYMO in the inhibition of hemolysis in patients with CAD was demonstrated across multiple end points as described in the table below (see Table 6).

Table 6: Efficacy Results in Patients with CAD in the CADENZA Part A Study (continued)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo N=20</th>
<th>ENJAYMO N=22</th>
<th>Treatment Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>Mean change from baseline (LS Mean), g/dL</td>
<td>0.09</td>
<td>2.66</td>
</tr>
<tr>
<td>95% CI of LS Mean</td>
<td>(1.75, 3.38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value:</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The data from this study demonstrated a statistically significant treatment effect of ENJAYMO over placebo in terms of the rate of patients who met the efficacy criteria (responder) as well as improving symptoms and impacts of fatigue (FACIT-Fatigue). The responder rate difference between ENJAYMO and placebo was 58.7% (95% CI: 34.8% to 82.9%) with a p-value of 0.0004. At the treatment assessment timepoint (TAT), 16 of 22 patients on ENJAYMO (72.7%; 95% CI: 49.8% to 89.3%) and 3 of 20 patients on placebo (15.0%; 95% CI: 3.2% to 37.9%) met primary criteria. Efficacy of ENJAYMO in the inhibition of hemolysis in patients with CAD was demonstrated across multiple end points as described in the table below (see Table 6).

Table 7: Baseline Characteristics of Patients Included in CARDINAL

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo N=24</th>
<th>ENJAYMO N=22</th>
<th>Treatment Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean (SD)</td>
<td>71.3 (8.2)</td>
<td>55 to 85 years</td>
</tr>
</tbody>
</table>
Serious Infections These infections may be serious or life-threatening. Inform patients that they are required to receive vaccinations against these bacteria according to current medical guidelines prior to initiation of and during treatment with ENJAYMO. Educate patients on the symptoms of infections and advise them to seek immediate medical attention if any new symptoms of infection occur [see Warnings and Precautions (5.1)].

Infusion-Related Reactions

Advise patients that administration of ENJAYMO may result in infusion-related reactions including hypersensitivity reactions. Hypersensitivity reactions may be serious or life-threatening (e.g., anaphylaxis). Educate patients on the symptoms of infusion-related reactions and advise them to seek medical attention if any new symptoms of infusion-related reactions occur [see Contraindications (4) and Warnings and Precautions (5.2)].

Risk of Autoimmune Disease

Educate patients that there may be an increased risk of developing an autoimmune disease such as SLE during ENJAYMO therapy. Advise patients on signs and symptoms of SLE and to report any new symptoms of SLE and seek medical attention [see Warnings and Precautions (5.3)].

Discontinuation

Informs patients with CAD that they may develop hemolysis due to CAD when ENJAYMO is discontinued and that they should be monitored by their healthcare provider following ENJAYMO discontinuation [see Warnings and Precautions (5.4)].

This product’s labeling may have been updated. For the most recent prescribing information, please visit www.enjaymo.com.

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For patent information: https://www.sano.fi/en/products-and-resources/patents

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**Table 7: Baseline Characteristics of Patients Included in CARDINAL (continued)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Statistic</th>
<th>ENJAYMO N=24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>n (%)</td>
<td>15 (63)</td>
</tr>
<tr>
<td>Female</td>
<td>n (%)</td>
<td>13 (54)</td>
</tr>
<tr>
<td>Male</td>
<td>n (%)</td>
<td>9 (38)</td>
</tr>
<tr>
<td>Body weight</td>
<td>Mean (SD)</td>
<td>67.8 (15.8)</td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td>40 to 112 kg</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>Mean (SD), g/dL</td>
<td>8.6 (1.16)</td>
</tr>
<tr>
<td>Blirubin (total)</td>
<td>Mean (SD), mg/dL</td>
<td>3.1 (1.41)</td>
</tr>
<tr>
<td>(2.6 x ULN)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDH^1</td>
<td>Mean (SD), U/L</td>
<td>438 (484.60)</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>Median number of transfusions (range)</td>
<td>2.0 (1, 19)</td>
</tr>
<tr>
<td>Within last 6 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within last 12 months</td>
<td></td>
<td>2.0 (1, 23)</td>
</tr>
</tbody>
</table>

*N=21 for bilirubin data excluding patients with Gilbert’s syndrome.

^ULN: Upper limit of normal, LDH: Lactate dehydrogenase.

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**Table 8: Efficacy Results in Patients with CAD in CARDINAL Part A Study**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Statistic</th>
<th>ENJAYMO N=24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responder^1</td>
<td>n (%)</td>
<td>13 (54)</td>
</tr>
<tr>
<td>Hemoglobin level ≥12 g/dL or Increase in Hemoglobin level of ≥2 g/dL</td>
<td>n (%)</td>
<td>15 (63)</td>
</tr>
<tr>
<td>Hemoglobin level ≥12 g/dL</td>
<td>n (%)</td>
<td>9 (38)</td>
</tr>
<tr>
<td>Increase in Hemoglobin level of ≥2 g/dL</td>
<td>n (%)</td>
<td>15 (63)</td>
</tr>
<tr>
<td>Patients not receiving RBC transfusion from Week 5 through Week 26 (transfusion avoidance)</td>
<td>n (%)</td>
<td>17 (71)</td>
</tr>
<tr>
<td>Patients not receiving protocol-prohibited CAD medications^1 from Week 5 through Week 26</td>
<td>n (%)</td>
<td>22 (82)</td>
</tr>
</tbody>
</table>

*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.

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**MEDICATION GUIDE**

ENJAYMO® (en-jaye-moe) (sutimlimab-jome) injection, for intravenous use

What is the most important information I should know about ENJAYMO?

ENJAYMO can cause serious side effects, including:

Serious infections. ENJAYMO is a prescription medicine that affects your immune system. ENJAYMO can lower the ability of your immune system to fight infections. People who are treated with ENJAYMO may have an increased risk of getting infections caused by certain kinds of bacteria such as Neisseria meningitidis, Streptococcus pneumoniae, and Haemophilus influenzae. These infections may be serious or life-threatening. Some infections may quickly become life-threatening or cause death if not recognized and treated early.

- You need to receive vaccinations against infections caused by certain kinds of bacteria at least 2 weeks before your first dose of ENJAYMO. You may need to have additional vaccinations during treatment with ENJAYMO. If your healthcare provider decides that urgent treatment with ENJAYMO is needed, you should receive vaccinations as soon as possible.
- Vaccinations may reduce the risk of these infections, but do not prevent all infections. Call your healthcare provider or get medical help right away if you get any new signs and symptoms of an infection, including:
  - fever
  - cough or difficulty breathing
  - severe headache with stiff neck or back
  - flu-like symptoms
  - pain during urination or urinating more often than usual
  - swelling of the skin

See “What are the possible side effects of ENJAYMO?” for more information about side effects.
What is ENJAYMO?
ENJAYMO is a prescription medicine used to treat the breakdown of red blood cells (hemolysis) in adults with cold agglutinin disease (CAD). It is not known if ENJAYMO is safe and effective in children.

Who should not receive ENJAYMO?
Do not receive ENJAYMO if you are allergic to sutimlimab-jome or any of the ingredients in ENJAYMO. See the end of this Medication Guide for a complete list of ingredients in ENJAYMO.

Before receiving ENJAYMO, tell your healthcare provider about all of your medical conditions, including if you:
- have a fever or infection, including a history of human immunodeficiency virus (HIV), hepatitis B, or hepatitis C.
- have an autoimmune disease such as systemic lupus erythematosus (SLE), also known as lupus.
- are pregnant or plan to become pregnant. It is not known if ENJAYMO will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if ENJAYMO passes into your breast milk. You should talk to your healthcare provider about the best way to feed your baby during treatment with ENJAYMO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive ENJAYMO?
- ENJAYMO is given through a vein by intravenous (I.V.) infusion, usually over 1 to 2 hours.
- You will usually receive a starting dose of ENJAYMO, followed by a second dose of ENJAYMO 1 week later. Then 2 weeks after your second dose, you will start to receive an ENJAYMO infusion every 2 weeks.
- After your first infusion, you should be monitored for infusion and allergic reactions for at least 2 hours. For all future infusions, you should be monitored for infusion reactions for 1 hour.

What are the possible side effects of ENJAYMO?
- Injection site reaction
- Rash
- Fever
- Headache
- Nausea
- Rash on the cheeks and nose
- Unexplained fever

Risk of autoimmune disease. ENJAYMO may increase your risk for developing an autoimmune disease such as SLE. Tell your healthcare provider if you develop any symptoms of SLE, including:
- Joint pain or swelling
- Rash on the cheeks and nose
- Unexplained fever

The most common side effects of ENJAYMO include:
- Increase in blood pressure
- Urinary tract infection
- Respiratory tract infection
- Bacterial infection
- Swelling in lower legs or hands
- Joint pain
- Headache
- Chest discomfort
- Rash
- Dizziness
- Feeling tired or weak
- Cough
- Changes in color or sensation in the fingers and toes (Raynaud's phenomenon)

These are not all the possible side effects of ENJAYMO.

General information about the safe and effective use of ENJAYMO.

Medicines are sometimes prescribed for purposes other than those listed in this Medication Guide. You can ask your pharmacist or healthcare provider for information about ENJAYMO that is written for health professionals.

What are the ingredients in ENJAYMO?
Active ingredient: sutimlimab-jome

Inactive ingredients: polysorbate 80, sodium chloride, sodium phosphate dibasic heptahydrate, sodium phosphate monobasic monohydrate, and Water for Injection, USP.

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This Medication Guide has been approved by the U.S. Food and Drug Administration.

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ENJ-FPLR-SL-MAR23 Rx Only