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RESEARCH**

APPLICATION NUMBER:

761164Orig1s000

LABELING

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.

ENJAYMO™ (sutimlimab-jome) injection, for intravenous use
Initial U.S. Approval: 2022

INDICATIONS AND USAGE

ENJAYMO is a classical complement inhibitor indicated to decrease the need for red blood cell (RBC) transfusion due to hemolysis in adults with cold agglutinin disease (CAD). (1)

DOSAGE AND ADMINISTRATION

- Vaccinate against encapsulated bacteria at least two weeks prior to treatment. (2.1)
- 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. (2.2)
 - For patients weighing 75 kg or more: 7,500 mg by intravenous infusion. (2.2)
- See Full Prescribing Information for important preparation and administration instructions. (2.2, 2.3)

DOSAGE FORMS AND STRENGTHS

Injection: 1,100 mg/22 mL (50 mg/mL) in a single-dose vial (3)

CONTRAINDICATIONS

ENJAYMO is contraindicated in patients with known hypersensitivity to sutimlimab-jome or any of the inactive ingredients. (4)

WARNINGS AND PRECAUTIONS

- Serious Infections: Ensure patients are vaccinated against encapsulated bacteria. Monitor patients for early signs and symptoms of infections. (5.1)
- Infusion-Related Reactions: Monitor patients for infusion-related reactions, interrupt if reaction occurs, and institute appropriate medical management as needed. (5.2)
- Risk of Autoimmune Disease: Monitor patients for signs and symptoms and manage medically. (5.3)
- Recurrent Hemolysis After ENJAYMO Discontinuation: Monitor patients for signs and symptoms of hemolysis if treatment with ENJAYMO is interrupted. (5.4)

ADVERSE REACTIONS

Most common adverse reactions (incidence $\geq 10\%$) are respiratory tract infection, viral infection, diarrhea, dyspepsia, cough, arthralgia, arthritis, and peripheral edema. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Bioverativ USA 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.

Revised: 2/2022

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Cold Agglutinin Disease

ENJAYMO (sutimlimab-jome) is indicated to decrease the need for red blood cell (RBC) transfusion due to hemolysis in adults with cold agglutinin disease (CAD).

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Vaccinations

Vaccinate patients against encapsulated bacteria at least 2 weeks prior to initiation of ENJAYMO therapy according to the most current Advisory Committee on Immunization Practices (ACIP) recommendations for patients with persistent complement deficiencies [*see Warnings and Precautions (5.1)*]. If urgent ENJAYMO therapy is indicated in an unvaccinated patient, administer vaccine(s) as soon as possible.

2.2 Recommended Dosage Regimen

The recommended dosage of ENJAYMO for patients with CAD is based on body weight. For patients weighing 39 kg to less than 75 kg, the recommended dose is 6,500 mg and for patients weighing 75 kg or more, the recommended dose is 7,500 mg. Administer ENJAYMO intravenously weekly for the first two weeks, with administration every two weeks thereafter. Administer ENJAYMO at the recommended dosage regimen time points, or within two days of these time points.

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 ENJAYMO weekly for two weeks, with administration every two weeks thereafter.

2.3 Preparation and Administration

ENJAYMO is for intravenous infusion only.

Each vial of ENJAYMO is intended for single dose only.

Use aseptic technique to prepare ENJAYMO as follows:

- 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 1 for infusion rate. Administer the infusion over 1 to 2 hours depending on the patient's body weight. Administer ENJAYMO infusion solution only 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 68°F to 77°F (20°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)phthalate (DEHP) plasticized polyvinyl chloride (PVC), Ethyl Vinyl Acetate (EVA) and polyolefin (PO); administration sets made of DEHP-plasticized PVC, DEHP-free polypropylene (PP) and polyethylene (PE); and vial adapters made of polycarbonate (PC) and acrylonitrile-butadiene-styrene (ABS).

Table 1: Infusion Reference Table

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

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

Slow or stop the infusion in case of infusion reaction during ENJAYMO administration. Monitor the patient for at least two hours following completion of the initial infusion for signs or symptoms of an infusion and/or hypersensitivity reaction. Monitor the patient for one hour following completion of subsequent infusions for signs or symptoms of an infusion reaction.

3 DOSAGE FORMS AND STRENGTHS

Injection: 1,100 mg/22 mL (50 mg/mL) as a clear to slightly opalescent, colorless to slightly yellow solution in a single-dose vial.

4 CONTRAINDICATIONS

ENJAYMO is contraindicated in patients with known hypersensitivity to sutimlimab-jome or any of the inactive ingredients [see *Warnings and Precautions (5.2) and Adverse Reactions (6.1)*].

5 WARNINGS AND PRECAUTIONS

5.1 Serious Infections

ENJAYMO may increase susceptibility to serious infections, including infections caused by encapsulated bacteria such as *Neisseria meningitides* (any serogroup), *Streptococcus pneumoniae*, and *Haemophilus influenzae*.

Serious infections (bacterial and viral) were reported in 17% (4/24) of patients receiving ENJAYMO in a single-arm open-label clinical trial. These infections included sepsis, respiratory, and skin infections [see *Adverse Reactions* (6.1)].

Vaccinate patients for encapsulated bacteria according to the most current ACIP recommendations for patients with persistent complement deficiencies. Revaccinate patients in accordance with ACIP recommendations.

Immunize patients without a history of vaccination against encapsulated bacteria at least two weeks prior to receiving the first dose of ENJAYMO. If urgent ENJAYMO therapy is indicated in an unvaccinated patient, administer vaccine(s) as soon as possible.

Vaccination reduces, but does not eliminate, the risk of encapsulated bacterial infections.

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 sutimlimab-jome or any of the inactive ingredients [see *Contraindications* (4)]. Administration of ENJAYMO may result in infusion-related reactions. In the CARDINAL study, 2 of 24 patients (8%) treated with ENJAYMO experienced infusion-related reactions (shortness of breath, rapid heartbeat, nausea, flushing, and headache) [see *Adverse Reactions* (6.1)].

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. 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)]
- Recurrent Hemolysis After ENJAYMO Discontinuation [see *Warnings and Precautions* (5.4)]

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 and history of blood transfusion in the 6 months prior to study enrollment was evaluated in a six-month, open-label single-arm trial (CARDINAL) (n=24) [see *Clinical Studies* (14)]. The median duration of treatment was 26.1 weeks and 92% completed 26 weeks of therapy.

In CARDINAL, the most common adverse reactions occurring in $\geq 10\%$ of patients were respiratory tract infection, viral infection, diarrhea, dyspepsia, cough, arthralgia, arthritis and peripheral edema. Serious adverse reactions were reported in 13% (3/24) of patients who received ENJAYMO. These serious adverse reactions were streptococcal sepsis and staphylococcal wound infection (n=1), arthralgia (n=1), and respiratory tract infection (n=1). None of the adverse reactions led to discontinuation of ENJAYMO in CARDINAL. Dosage interruptions due to an adverse reaction occurred in 17% (4/24) of patients who received ENJAYMO.

Adverse reactions occurring in $\geq 5\%$ or more patients in CARDINAL are summarized in Table 2.

Table 2: Adverse Reactions ($\geq 5\%$) in Patients Receiving ENJAYMO in CARDINAL

Adverse Reaction	n (%) N=24
Infections	
Respiratory tract infection* ^a	6 (25)

Viral infection* ^b	3 (13)
Urinary tract infection* ^c	2 (8)
Bacterial infection* ^d	2 (8)
Vascular disorders	
Cyanosis	2 (8)
Systemic hypertension ^e	2 (8)
Gastrointestinal disorders	
Diarrhea	3 (13)
Dyspepsia ^f	3 (13)
Gastroenteritis	2 (8)
Abdominal pain	2 (8)
Respiratory, thoracic and mediastinal disorders	
Cough ^g	3 (13)
Musculoskeletal and connective tissue disorders	
Arthralgia, arthritis* ^h	3 (13)
General disorders and administration site conditions	
Peripheral edema	3 (13)
Fatigue* ⁱ	2 (8)
Infusion reaction	2 (8)
Nervous system disorders	
Headache	2 (8)

* Events may be counted in more than one grouped term, e.g., viral upper respiratory tract infection is counted in viral infection and respiratory tract infection.

The following terms were combined:

^a Includes nasopharyngitis, respiratory tract infection, respiratory tract infection viral, upper respiratory tract infection, viral upper respiratory tract infection

^b Includes oral herpes, respiratory tract infection viral, viral infection, viral upper respiratory tract infection

^c Includes cystitis bacterial, urinary tract infection

^d Includes cystitis bacterial, streptococcal sepsis, wound infection staphylococcal

^e Includes hypertension, blood pressure increased

^f Includes dyspepsia, abdominal pain upper

^g Includes cough, productive cough

^h Includes arthralgia, osteoarthritis

ⁱ Includes fatigue and mental fatigue

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibodies) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with incidence of antibodies in other studies may be misleading.

Immunogenicity of sutimlimab-jome was assessed in CAD patients in CARDINAL at baseline, during the treatment period, and at end of treatment (Week 26). None of the 24 patients enrolled in CARDINAL who received at least one dose of sutimlimab-jome developed treatment-emergent antidrug antibodies (ADAs).

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%-20%, 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 doses) 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 34 patients with CAD in clinical studies of ENJAYMO, 79% were 65 years of age and over including 32% 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 clinical 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 polysorbate 80 (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 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.

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 reticulocytes.

After the first treatment with sutimlimab-jome, near normalization of bilirubin associated with a greater than 1 g/dL 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 60 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 ($t_{1/2\beta}$) 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 (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 exposures decreased up to 59% for a patient weighing 98 kg and increased up to 57% for a patient weighing 50.5 kg as

compared with a patient weighing 72 kg. The effect of body weight on pharmacokinetics has been integrated in the recommended dose regimen tiered by body weight.

13 NONCLINICAL TOXICOLOGY

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

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 $\leq 1+$ 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. Major baseline characteristics of the trial population are summarized in Table 3.

Table 3: Baseline Characteristics of Patients Included in CARDINAL

Parameter	Statistic	ENJAYMO N=24
Age	Mean (SD) Range	71.3 (8.2) 55 to 85 years
Sex Female Male	n (%)	15 (63) 9 (38)
Body weight	Mean (SD) Range	67.8 (15.8) 40 to 112 kg
Hemoglobin	Mean (SD), g/dL	8.6 (1.16)
Bilirubin (total)*	Mean (SD), mg/dL	3.1 (1.41) (2.6 × ULN [†])
LDH [†]	Mean (SD), U/L	438 (484.60)
Blood transfusion Within last 6 months Within last 12 months	Median number of transfusions (range)	2.0 (1, 19) 2.0 (1, 23)

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

[†] ULN: Upper limit of normal, LDH: Lactate dehydrogenase.

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.

Efficacy of ENJAYMO in patients with CAD is described in Table 4.

Table 4: 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).

16 HOW SUPPLIED/STORAGE AND HANDLING

ENJAYMO (sutimlimab-jome) injection is a clear to slightly opalescent, colorless to slightly yellow, preservative-free solution supplied as one 1,100 mg/22 mL (50 mg/mL) single-dose vial per carton (NDC 80203-347-01).

Store ENJAYMO vials refrigerated at 36°F to 46°F (2°C to 8°C) in the original carton to protect from light. Do not freeze. Do not shake. Discard unused portion.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Serious Infections

Advise patients of the potential increased risk of infections including infections caused by encapsulated bacteria such as *Neisseria meningitides*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*. 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

Inform 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)].

Manufactured by:

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A SANOFI COMPANY

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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 take ENJAYMO may have an increased risk of getting infections caused by certain kinds of bacteria such as *Neisseria meningitides*, *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
 - severe headache with stiff neck or back
 - pain during urination or urinating more often than usual
 - cough or difficulty breathing
 - flu-like symptoms
 - pain, redness or 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 decrease the need for red blood cell transfusion due to 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.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should 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. See “**What are the possible side effects of ENJAYMO?**”
- **If you have CAD and you stop receiving ENJAYMO, your healthcare provider should monitor you closely for return of your symptoms after you stop ENJAYMO. Stopping ENJAYMO may cause the breakdown of your red blood cells due to CAD to return.** Symptoms or problems that can happen due to red blood cell breakdown include:
 - tiredness
 - shortness of breath
 - rapid heart rate
 - blood in your urine or dark urine
- If you miss an ENJAYMO infusion, call your healthcare provider right away.

What are the possible side effects of ENJAYMO?

ENJAYMO can cause serious side effects, including:

- See "**What is the most important information I should know about ENJAYMO?**"
- **Infusion-related reactions.** Treatment with ENJAYMO may cause infusion-related reactions, including allergic reactions that may be serious or life-threatening. Your healthcare provider may slow down or stop your ENJAYMO infusion if you have an infusion-related reaction, and will treat your symptoms if needed. Tell your healthcare provider right away if you develop symptoms during your ENJAYMO infusion that may mean you are having an infusion-related reaction, including:
 - shortness of breath
 - rapid heartbeat
 - nausea
 - flushing
 - headache
- **Risk of autoimmune disease.** ENJAYMO may increase your risk for developing an autoimmune disease such as SLE. Tell your healthcare provider and get medical help 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:

- | | | |
|-------------------------------|---------------|--|
| • respiratory tract infection | • indigestion | • joint inflammation (arthritis) |
| • viral infection | • cough | • swelling of the lower legs, ankles, and feet |
| • diarrhea | • joint pain | |

These are not all the possible side effects of ENJAYMO.

Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

General information about the safe and effective use of ENJAYMO.

Medicines are sometimes prescribed for purposes other than those listed in a 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.

Manufactured by: Bioverativ USA Inc., Waltham, MA 02451. A SANOFI COMPANY. US License No. 2078

For more information, go to www.ENJAYMO.com or call 1-800-745-4447.

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

Issued: February 2022



Dosage: See prescribing information.

Store refrigerated at 36°F to 46°F (2°C to 8°C). Protect from light. Do not freeze. Do not shake.

Mfd. by: Bioverativ USA Inc.
Waltham, MA 02451
US License No. 0000


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NDC 80203-347-01

Enjaymo™
(sutimlimab-jome)
Injection

1,100 mg/22 mL (50 mg/mL)

For Intravenous Infusion After Dilution

Single-dose vial.
Discard unused portion.

Rx only

Lot:
EXP:

EXP date
format:
YYYY-MM
(MM is in
numerical
format)

Reference ID: 4932699

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/s/

LISA B YANOFF
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