Enjaymo™ (Sutimlimab-Jome)

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Instructions for Use

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Coverage Rationale

See Benefit Considerations

Enjaymo has been added to the Review at Launch program. Some members may not be eligible for coverage of this medication at this time.

Enjaymo is proven for the treatment of cold agglutinin disease (CAD). Enjaymo is medically necessary for the treatment of CAD in patients who meet all of the following criteria:

- For initial therapy, all of the following:
  - Diagnosis of CAD by, or in consultation with, a hematologist with expertise in the diagnosis of CAD; and
  - Confirmation of the CAD diagnosis based on all of the following:
    - Evidence of chronic hemolysis (e.g., elevated lactated dehydrogenase [LDH], decreased haptoglobin, increased indirect bilirubin, increased reticulocyte count); and
    - Positive polyspecific direct antiglobin test (DAT); and
    - Positive monospecific DAT specific for C3d; and
    - Immunoglubulin G (IgG) DAT ≤ 1+; and
    - Cold agglutinin titer ≥ 64 at 4°C

    and
  - Cold agglutinin syndrome secondary to other factors has been ruled out (e.g. infection, rheumatologic disease, systemic lupus erythematosus, overt hematologic malignancy, other autoimmune disorders); and
  - Patient has a baseline hemoglobin level ≤ 10 g/dL; and
  - Enjaymo is prescribed by a hematologist; and
  - Enjaymo dosing is in accordance with the United States Food and Drug Administration approved labeling; and
  - Patient is not receiving Enjaymo in combination with a complement inhibitor [e.g., Soliris (eculizumab), Ultomiris (ravilizumab-cwzb), Empaveli (pegcetacoplan)]; and
  - Initial authorization will be for no more than 6 months.

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- For continuation of therapy, all of the following:
  - Documentation of positive clinical response to therapy (e.g., increase in hemoglobin, decreased transfusion requirements, decreased markers of hemolysis, improvement in anemia-related symptoms); and
  - Enjaymo is prescribed by, or in consultation with, a hematologist; and
  - Enjaymo dosing is in accordance with the United States Food and Drug Administration approved labeling; and
  - Patient is not receiving Enjaymo in combination with a complement inhibitor [e.g., Soliris (eculizumab), Ultomiris (ravilizumab-cwzb), Empaveli (pegcetacoplan)]; and
  - Reauthorization will be for no more than 12 months.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
C9399	Unclassified drugs or biologicals
J3590	Unclassified biologics

Diagnosis Code	Description
D59.12	Cold autoimmune hemolytic anemia

Background

Cold agglutinin disease (CAD) is a form of autoimmune hemolytic anemia (AIHA) in which cold agglutinins can cause clinical symptoms related to agglutination of red blood cells in cooler parts of the body and hemolytic anemia. Primary chronic cold (hem)agglutinin disease accounts for about 15-25% of AIHAs. CAD is defined as an AIHA mediated by cold agglutinins (CAs), without any obvious underlying disease such as aggressive lymphoma, other overt malignancies, or specific infections. CAs are autoantibodies that are able to agglutinate red blood cells (RBCs) at an optimum temperature of 3-4°C, but can also react at higher temperatures, depending on the thermal amplitude.

Hemolysis in CAD is primarily extravascular and mediated by complement. The IgM cold agglutinin binds to an antigen on the surface of RBCs in sites of the body where the temperature is low enough to be in the thermal range of the antibody. The bound IgM recruits components of the classical pathway of complement, such as C1, C4, and C2. C1-esterase activates C4 and C2, leading to production of the C3 convertase, which cleaves C3 to C3a and C3b. Lastly, C3b-coated RBCs undergo extravascular hemolysis due to phagocytosis by macrophages in the liver.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

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Clinical Evidence

An International Consensus Group published recommendations in 2019 on the diagnostic and therapeutic approach for autoimmune hemolytic anemias, including cold agglutinin disease (CAD). Diagnostic recommendations for CAD include markers of chronic hemolysis accompanied by a direct antiglobin test (DAT, direct "Coombs test") for C3d, with a cold agglutinin (CA) titer of 64 or greater at 4°C. Treatment recommendations included watchful waiting in patients with hemoglobin levels > 10 g/dL unless comorbid ischemic cardiac disease or chronic obstructive pulmonary disease was present with blood transfusions recommended when indicated. Recommended treatment goals included improvement in hemoglobin levels and improvement in symptoms. Rituximab monotherapy was a recommended first-line therapy for those requiring chronic treatment as response rates of 50% have been reported in uncontrolled trials. Alternative first and second-line recommendations include rituximab combined with bendamustine or fludarabine. A 71% response rate has been reported with rituximab plus bendamustine combination therapy, with 40% achieving complete response (CR) and 31% partial response (PR). Hemoglobin levels increased by a median of 4.4 g/dL in the complete responders and 3.9 g/dL in those who had a PR. Median time to response was 1.9 months, and less than 10% of the responders had relapsed at 32 months. A 76% response rate has been reported with rituximab plus fludarabine combination therapy, with 21% achieving CR and 55% achieving PR. Median increase in Hb level was 3.1 g/dL in the responders and 4.0 g/dL among those who achieved CR. Median time to response was 4.0 months, and estimated median response duration was more than 66 months.

Sutimlimab was studied in a 26-week open-label, single-arm, multicenter phase 3 CARDINAL study (Part A) with a 2-year extension phase (Part B). Patients with a confirmed diagnosis of CAD based on chronic hemolysis, polyspecific DAT, monospecific DAT specific for C3d, cold agglutinin titer ≥ 64 at 4°C, and IgG DAT ≤ 1+ were enrolled. Eligibility criteria included baseline hemoglobin (Hb) ≤ 10 g/dL, total bilirubin level above normal, and ≥ 1 blood transfusion in the prior 6 months. Sutimlimab was administered intravenously on Days 0 and 7, followed by biweekly infusions. Patients weighing < 75 kg or ≥ 75 kg received a 6.5 g or 7.5 g dose, respectively. The primary efficacy endpoint was response rate based on a composite of Hb increase ≥ 2 g/dL or Hb ≥ 12 g/dL at treatment assessment and transfusion avoidance from Weeks 5 to 26. Secondary efficacy endpoints included change from baseline in hemolytic markers (e.g., bilirubin) and quality of life (QOL) measured by the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F) Scale.

Twenty-four patients enrolled and received ≥ 1 dose of sutimlimab. The mean (standard deviation) age was 71.3 (8.2) years with 62.5% females. Mean (range) baseline Hb was 8.6 (4.9-11.1) g/dL. The median (range) number of transfusions within 6 months prior to enrollment was 2 (1-19) and 62.5% of patients had failed prior therapies. Out of 24 patients, 22 completed Part A; 2 patients were withdrawn early for reasons unrelated to the study drug. The prespecified primary endpoint was met in 13 (54.2%) patients. The estimated mean Hb increase at treatment assessment time point was 3.2 g/dL. Hb improved rapidly after the first dose of sutimlimab with 1.2 g/dL and 2.3 g/dL increases by Weeks 1 and 3, respectively. Mean overall Hb was maintained above 11 g/dL after Week 3. Twenty (83.3%) patients had a Hb increase ≥ 1 g/dL. Fifteen (63%) patients had a Hb increase ≥ 2 g/dL. Nine (38%) of patients had a Hb level of ≥ 12 g/dL. Mean total bilirubin was normalized by Week 3. Seventeen (70.8%) patients remained free of transfusions from Weeks 5 to 26. FACIT-F scores improved within 1 week, peaking by Week 5, and remained stable through Week 26.

Interim results of the Part B extension phase have been reported at 1-year follow-up. The primary objectives of the interim Part B analysis are to evaluate long-term safety and tolerability of sutimlimab for ≥ 53 weeks; secondary objectives are to investigate the durability of response over time. Efficacy endpoints included change from baseline in hemolytic markers and the patient-reported outcome: Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Scale. All patients who completed Part A entered Part B. Hb improved rapidly after first sutimlimab dose and mean Hb was > 11 g/dL from Week 5 to Week 53. Mean total bilirubin was normalized by Week 3 and remained < 20 µmol/L to Week 53. Normalization of mean absolute reticulocyte count was observed alongside normalized haptoglobin levels and reductions in lactate dehydrogenase. Seventeen (70.8%) and 19 (86.4%) patients remained transfusion-free from Week 5 to Week 26 and Week 26 to Week 53, respectively. From baseline to Week 53, all 24 patients experienced ≥ 1 treatment-emergent adverse event (TEAE); 12 (50.0%) patients experienced a serious TEAE. One serious TEAE (viral infection) was associated with sutimlimab. Serious (including bacterial) infections were reported, but no meningococcal infections were identified. There was 1 TEAE of device-related thrombosis (assessed as unrelated to study drug) in Part B; there were no other vascular thromboembolic TEAEs. One patient died due to a progressive carcinoma (unrelated to study drug).

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U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

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).

References

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Policy History/Revision Information

Date	Summary of Changes
05/01/2022	• New Medical Benefit Drug Policy

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

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This Medical Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

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Nondiscrimination & Language Access Policy

Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, sex, sexual orientation, or gender identity. *We* do not exclude people or treat them differently because of race, color, national origin, age, disability, sex, sexual orientation, or gender identity.

We will:
Provide free aids and services to people with disabilities to communicate effectively with us, such as:
- Qualified sign language interpreters
- Written information in other formats (large print, audio, accessible electronic formats, other formats)

Provide free language services to people whose primary language is not English, such as:
- Qualified interpreters
- Information written in other languages

If *you* need these services, contact *us* at the phone number shown on the inside cover of this *contract*, *your* id card, or aspirushealthplan.com.

If *you* believe that *we* have failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, sex, sexual orientation, or gender identity, *you* can file a grievance with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1062
Minneapolis, MN 55440
Phone: 1.866.631.5404 (TTY: 711)
Fax: 763.847.4010
Email: customerservice@aspirushealthplan.com

You can file a grievance in person or by mail, fax, or email. If *you* need help filing a grievance, the Nondiscrimination Grievance Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1.866.631.5404 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً . اتصل بن اعلى رقم الهاتف 1.866.631.5404(رقم هاتف الصم والبك : 711)

French: ATTENTION : Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelezle 1.866.631.5404 (ATS : 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1.866.631.5404 (TTY: 711).

Hindi: _यान द_: य_द आप ि◌हंदी बोलते ह_ तो आपके ि◌लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_। 1.866.631.5404 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1.866.631.5404 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 1.866.631.5404 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer 1.866.631.5404 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода.Звоните 1.866.631.5404 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1.866.631.5404 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1.866.631.5404 (TTY: 711)

Traditional Chinese: 注意：如果您使用繁體中文，您可以免費獲得語言援助服務。請 致電 1.866.631.5404 (TTY:711).

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1.866.631.5404 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1.866.631.5404 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັ້ງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1.866.631.5404 (TTY:711).

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