POLICY: Oncology (Injectable) – Sylvant Utilization Management Medical Policy
- Sylvant® (siltuximab intravenous infusion – EUSA)

EFFECTIVE DATE: 1/1/2021
LAST REVISION DATE: 02/18/2026

COVERAGE CRITERIA FOR: All Aspirus Medicare Plans

OVERVIEW
Sylvant, an interleukin-6 (IL-6) antagonist, is indicated for treatment of **multicentric Castleman disease** (MCD) in patients who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.[1]

Limitations of Use: Sylvant was not studied in patients with MCD who are HIV positive or HHV-8 positive because Sylvant did not bind to virally produced IL-6 in a nonclinical study.[1]

Safety and efficacy have not been established in patients < 18 years of age.[1]

Dosing Information
Sylvant is administered in a dose of 11 mg/kg as an intravenous infusion every 3 weeks until treatment failure, defined as disease progression based on increased symptoms, radiologic progression, or deterioration in performance status.[1] Laboratory monitoring is recommended during treatment. If parameters for absolute neutrophil count, platelet count, and/or hemoglobin are not met, consider delaying treatment. Do not reduce the dose of Sylvant.

Guidelines
The National Comprehensive Cancer Network (NCCN) recommends Sylvant for treatment or supportive care for the following uses (all recommendations listed are Category 2A):
- **Castleman Disease**: Guidelines (version 1.2026 – November 24, 2025) list Sylvant as first line therapy option for patients with MCD who are HIV negative and HHV-8 negative and also as a treatment option for certain patients with surgically unresectable, incompletely resected, relapsed/refractory or progressive unicentric Castleman disease who are HIV negative and HHV-8 negative.[2]
- **Chimeric Antigen Receptor T-Cell and Lymphocyte Engager Related Toxicities Management**: Guidelines (version 2.2026 – November 11, 2025) provide recommendations for use of Sylvant as a treatment option in the management chimeric antigen receptor T-cell-related toxicities, including immune effector cell-associated neurotoxicity syndrome (ICANS) and cytokine release syndrome (CRS) in certain patients.[8].
- **Kaposi Sarcoma**: Guidelines (version 2.2026 – September 16, 2025) advise to consider adding Sylvant to current therapy for refractory/progressive Kaposi Sarcoma-Associated Herpesvirus (KSHV)-Associated Inflammatory Cytokine Syndrome (KICS).[9] Of note, KSHV is also known as HHV-8.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Sylvant. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Sylvant, as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Sylvant to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

*Indications and/or approval conditions noted with **[EviCore]** apply to Sylvant and are managed by EviCore healthcare for those clients who use EviCore for oncology and/or oncology-related reviews. For these conditions, a prior authorization review should be directed to EviCore at www.EviCore.com.*

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Sylvant is recommended in those who meet one of the following criteria:

FDA-Approved Indication

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1. **Castleman Disease.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient is negative for the human immunodeficiency virus (HIV); AND
     - **iii.** Patient is negative for the human herpesvirus-8 virus (HHV-8); AND
     - **iv.** Patient meets ONE of the following (a or b):
       - **a)** Patient has multicentric disease; OR
       - **b)** Patient has unicentric disease that is unresectable, incompletely resected, relapsed/ refractory or progressive; AND
     - **v.** The medication is prescribed by or in consultation with an oncologist or hematologist; OR
   - **B)** Patient is Currently Receiving Sylvant. Approve for 1 year if the patient meets BOTH of the following (i and ii):
     - **i.** Patient has been established on therapy for at least 6 months; AND
       Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).
     - **ii.** Patient meets at least ONE of the following (a or b):
       - **a)** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
         Note: Examples of objective measures include clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate, fibrinogen, albumin, and/or hemoglobin), increased body mass index, and/or reduction in lymphadenopathy.

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom.
Note: Examples of symptoms include constitutional symptoms such as fatigue, physical function.

Dosing. Approve up to 11 mg/kg as an intravenous infusion administered not more frequently than once every 3 weeks.

Other Uses with Supportive Evidence

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2. **Immunotherapy-Related Toxicities Associated with Chimeric Antigen Receptor (CAR) T-Cell Therapy.** Approve for 1 month if the patient has been or will be treated with a CAR T-cell therapy.
Note: Examples of immunotherapy-related toxicities associated with CAR T-cell therapy include Cytokine Release Syndrome (CRS), Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), and other toxicities.

   Dosing. Approve up to 11 mg/kg as an intravenous infusion administered not more frequently than once every 3 weeks.

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3. **Kaposi Sarcoma.** ***[EviCore]*** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has Kaposi sarcoma-associated herpesvirus (KSHV)-associated inflammatory cytokine syndrome; AND
     Note: KSHV-associated inflammatory cytokine syndrome is also known as Kaposi sarcoma inflammatory cytokine syndrome (KICS).
   - **C)** Patient has refractory/progressive disease; AND
   - **D)** The medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 11 mg/kg as an intravenous infusion administered not more frequently than once every 3 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Sylvant is not recommended in the following situations:

1. **Multiple Myeloma**. Efficacy is not established. In a Phase II study (n = 286) evaluating patients with relapsed or refractory multiple myeloma, median progression-free survival was similar in patients treated with Velcade (bortezomib injection) + Sylvant (8.0 months) vs. in those treated with Velcade + placebo (7.6 months).[3] Following 24.5 months of follow-up, there was not a significant difference between the groups in median overall survival (30.8 months in the group that received Velcade + Sylvant vs. 36.8 months in the Velcade + placebo group). There was not a significant difference in overall response rate or other secondary endpoints. Another Phase II study evaluated Sylvant in patients (n = 106) with previously untreated symptomatic multiple myeloma who were transplant-ineligible.[4] There was not a significant difference in complete response rate or overall response rate

in patients treated with Velcade/melphalan/prednisone (VMP) vs. those treated with VMP + Sylvant. Progression-free survival and overall survival were the same in the two treatment groups. Another Phase II study in adults with relapsed or refractory multiple myeloma did not show any response with Sylvant monotherapy compared with 8% response rate in those who received Sylvant + dexamethasone.[5]

2. **Myelodysplastic Syndrome (MDS).** Efficacy is not established. A double-blind, placebo-controlled, Phase II study assigned adults with MDS (n = 76) to treatment with best supportive care in combination with Sylvant or placebo.[6] There was not a significant difference in the proportion of patients with reduced transfusions to treat anemia (primary endpoint). The study was terminated early due to lack of efficacy.

3. **Prostate Cancer.** Efficacy is not established. An open-label Phase II study did not demonstrate added efficacy with Sylvant added on to mitoxantrone/prednisone vs. mitoxantrone/prednisone.[7] Although the treatment groups were not balanced, progression-free survival was 97 days in the group that received Sylvant/mitoxantrone/prednisone vs. 228 days with mitoxantrone/prednisone. The study was stopped early.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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2. The NCCN Castleman Disease Clinical Practice Guidelines in Oncology (version 1.2026 – November 24, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 9, 2026.
3. Orlowski RZ, Gercheva L, Williams C, et al. A phase 2, randomized, double-blind, placebo-controlled study of siltuximab (anti-IL-6 mAb) and bortezomib versus bortezomib alone in patients with relapsed or refractory multiple myeloma. *Am J Hematol*. 2015;90(1):42-49.
4. San-Miguel J, Bladé J, Shpilberg O, et al. Phase 2 randomized study of bortezomib-melphalan-prednisone with or without siltuximab (anti-IL-6) in multiple myeloma. *Blood*. 2014;123(26):4136-4142.
5. Voorhees PM, Manges RF, Sonneveld P, et al. A phase 2 multicentre study of siltuximab, an anti-interleukin-6 monoclonal antibody, in patients with relapsed or refractory multiple myeloma. *Br J Haematol*. 2013;161(3):357-366.
6. Garcia-Manero G, Gartenberg G, Steensma DP, et al. A phase 2, randomized, double-blind, multicenter study comparing siltuximab plus best supportive care (BSC) with placebo plus BSC in anemic patients with International Prognostic Scoring System low- or intermediate-1-risk myelodysplastic syndrome. *Am J Hematol*. 2014;89(9):E156-62.
7. Fizazi K, De Bono JS, Flechon A, et al. Randomised phase II study of siltuximab (CNTO 328), an anti-IL-6 monoclonal antibody, in combination with mitoxantrone/prednisone versus mitoxantrone/prednisone alone in metastatic castration-resistant prostate cancer. *Eur J Cancer*. 2012;48(1):85-93.
8. The NCCN Management of CAR T-Cell and Lymphocyte Engager-Related Toxicities Clinical Practice Guidelines in Oncology (version 2.2026 – November 11, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 9, 2026.
9. The NCCN Kaposi Sarcoma Clinical Practice Guidelines in Oncology (version 2.2026 – September 16, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 9, 2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	01/18/2023
Annual Revision	No criteria changes.	02/14/2024
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/16/2024

Annual Revision	**Castleman's Disease - Patient is Currently Receiving Sylvant**: The following verbiage "such as improvement or resolution of constitutional symptoms (e.g., fatigue, physical function)" was moved into a clarifying Note.	02/26/2025
Selected Revision	**Policy Statement**: Removed "All reviews for COVID-19 and/or cytokine release syndrome associated with COVID-19 will be forwarded to the Medical Director." **COVID-19 (Coronavirus Disease 2019)**: Diagnosis removed from Conditions Not Recommended for Approval.	04/23/2025
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/15/2025
Annual Revision	**Castleman Disease:** The requirement that the patient is negative for both the human immunodeficiency virus and human herpesvirus-8 virus were separated. For unicentric disease, approval conditions were added for a patient who has unresectable, incompletely resected, or progressive disease. The dosing limitation verbiage was updated to allow coverage for "up to" 11 mg/kg and "not more frequently than" every 3 weeks. **Immunotherapy-Related Toxicities Associated with Chimeric Antigen Receptor T-Cell Therapy:** This new condition of approval and dosing was added under Other Uses with Supportive Evidence. **Kaposi Sarcoma**: This new condition of approval and dosing was added under Other Uses with Supportive Evidence.	02/18/2026
Update	**Kaposi Sarcoma:** Routing to EviCore was added for this diagnosis.	02/26/2026