Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Sylvant® (siltuximab	MP-RX-FP-87-23	☒ MMM MA ☒ MMM MultiHealth	11/30/2023	2/22/2026
			Last Review Date:	Frequently Revision:
			2/22/2026	2/22/2027

Service Category:

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B DRUG

Service Description:

This document addresses the use of Sylvant® (siltuximab), an interleukin 6 (IL-6) antagonist approved by the Food and Drug Administration (FDA) for the treatment of multicentric Castleman's disease in individuals who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.

Background Information:

This document addresses the use of Sylvant (siltuximab). Sylvant is a monoclonal antibody which binds to interleukin-6 (IL-6) receptors and inhibits release of proinflammatory cytokines primarily used to treat multicentric Castleman's disease.

The FDA approved indications for Sylvant include treatment of multicentric Castleman's disease in individuals who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative. Siltuximab was not studied in patients with MCD who are HIV positive or HHV-8 positive because siltuximab did not bind to virally produced IL-6 in a nonclinical study.

The National Comprehensive Cancer Network® (NCCN) provides Category 2A recommendations supporting the use of siltuximab (Sylvant®) in multiple clinical scenarios beyond FDA-approved indications. NCCN recommends siltuximab for the management of relapsed or refractory, surgically unresectable unicentric Castleman's disease as first-line, second-line, or subsequent therapy when used as a single agent. In addition, NCCN includes siltuximab as a Category 2A option for patients with refractory or progressive Kaposi sarcoma–associated herpesvirus (KSHV)–associated inflammatory cytokine syndrome (KICS), where it may be considered as an adjunct to Kaposi sarcoma–directed systemic therapy.

NCCN guidelines for the management of immunotherapy-related toxicities also include siltuximab as a Category 2A treatment option for cytokine release syndrome (CRS) associated with chimeric antigen receptor (CAR) T-cell therapy or lymphocyte-engaging therapies in select refractory scenarios. Specifically, siltuximab may be considered for Grade 4 CRS that is refractory to high-dose corticosteroids and anti-IL-6 therapy, as an alternative cytokine blockade when symptoms persist. NCCN further notes that siltuximab may be considered as a replacement for a second dose of tocilizumab when tocilizumab supplies are limited or unavailable, and as an adjunct to tocilizumab and corticosteroids for persistent Grade 2 CRS lasting longer than 24 hours or for Grade

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3–4 CRS not adequately controlled with standard therapy. NCCN emphasizes that the use of siltuximab in these settings should be carefully balanced against potential safety concerns, including increased infection risk, and acknowledges that clinical evidence supporting these approaches remains limited.

Sylvant has a labeled warning that it should not be administered to individuals with severe infections; and those with concurrent lymphoma were excluded from clinical trials.

Definitions and Measures

Definitions

Castleman's disease (CD): A rare, non-cancerous disorder that affects the lymph nodes and other immune-cell structures throughout the body. CD has two variants: unicentric CD and multicentric Castleman's disease, and is also known as giant lymph node hyperplasia and angiofollicular lymph node hyperplasia.

Cytokine Release Syndrome (CRS): A systemic inflammatory response resulting from immune effector cell activation, commonly associated with chimeric antigen receptor (CAR) T-cell therapies and lymphocyte-engaging agents. CRS severity is graded according to established consensus criteria (e.g., Grade 1–4), based on clinical features such as fever, hypotension, hypoxia, and organ dysfunction.

Kaposi Sarcoma–Associated Herpesvirus (KSHV)–Associated Inflammatory Cytokine Syndrome (KICS): A severe systemic inflammatory condition associated with KSHV infection, characterized by elevated inflammatory cytokines, systemic symptoms, and laboratory abnormalities. KICS may occur with or without concurrent Kaposi sarcoma and is associated with significant morbidity.

Refractory Cytokine Release Syndrome: CRS that does not adequately respond to standard first-line management, including anti–IL-6 therapy (e.g., tocilizumab) and/or high-dose systemic corticosteroids.

Measures of Response:

- Resolution or improvement of systemic inflammatory symptoms
- Reduction in CRS severity grade
- Stabilization or improvement of laboratory markers of inflammation
- Assessment of infection risk and overall safety profile during therapy

Approved Indications

A. Multicentric Castleman's disease in individuals who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.

Other Uses (NCCN Category 2 A)

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A. Relapsed or refractory, surgically unresectable unicentric Castleman's disease, including use as first-line, second-line, or subsequent therapy when administered as a single agent.
B. Kaposi sarcoma–associated herpesvirus (KSHV)–associated inflammatory cytokine syndrome (KICS), as an adjunct to Kaposi sarcoma–directed systemic therapy in refractory or progressive disease.
C. Grade 4 cytokine release syndrome (CRS) associated with chimeric antigen receptor (CAR) T-cell therapy or lymphocyte-engaging therapies that is refractory to high-dose corticosteroids and anti-IL6 therapy.
D. Grade 1–4 CRS as a replacement for a second dose of tocilizumab when tocilizumab is unavailable or supplies are limited, and Grade 1-4 neurotoxicity when occurring concurrently with CRS, as additional therapy.
E. Grade 2 CRS when symptoms persist for greater than 24 hours despite initial management, when used in addition to tocilizumab as alternative cytokine blockade.
F. Grade 3–4 CRS when symptoms persist despite combination therapy with tocilizumab and systemic corticosteroids, when used in addition to tocilizumab as alternative cytokine blockade.

Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. 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	Description
J2860	Injection, siltuximab, 10 mg [Sylvant]

ICD-10	Description
D47.Z2	Castleman disease
T80.82XA	Cytokine release syndrome, initial encounter
T80.82XS	Cytokine release syndrome, sequela
T80.89XA	Other complications following infusion, transfusion, and therapeutic injection, initial encounter
T80.89XS	Other complications following infusion, transfusion, and therapeutic injection, sequela
D89.831	Cytokine release syndrome, grade 1
D89.832	Cytokine release syndrome, grade 2
D89.833	Cytokine release syndrome, grade 3
D89.834	Cytokine release syndrome, grade 4
D89.839	Cytokine release syndrome, unspecified grade

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G92.00	Toxic encephalopathy, unspecified
G92.01	Immune effector cell–associated neurotoxicity syndrome (ICANS), grade 1
G92.02	Immune effector cell–associated neurotoxicity syndrome (ICANS), grade 2
G92.03	Immune effector cell–associated neurotoxicity syndrome (ICANS), grade 3
G92.04	Immune effector cell–associated neurotoxicity syndrome (ICANS), grade 4
B10.89	Other human herpesvirus infections
C46.0	Kaposi sarcoma of skin
C46.1	Kaposi sarcoma of soft tissue
C46.2	Kaposi sarcoma of palate
C46.3	Kaposi sarcoma of lymph nodes
C46.4	Kaposi sarcoma of gastrointestinal tract
C46.50	Kaposi sarcoma of lung
C46.51	Kaposi sarcoma of pleura
C46.52	Kaposi sarcoma of mediastinum
C46.7	Kaposi sarcoma of other sites
C46.9	Kaposi sarcoma, unspecified
D89.89	Other specified disorders involving the immune mechanism, not elsewhere classified
D89.9	Disorder involving the immune mechanism, unspecified

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Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Sylvant® (siltuximab)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

i. Individual has a diagnosis of Multicentric Castleman's disease; **AND**
ii. Sylvant (siltuximab) is used as a single agent; **AND**
iii. Individual is human immunodeficiency virus (HIV) negative; **AND**
iv. Individual is human herpesvirus-8 (HH-8) negative;

OR

v. Individual has a diagnosis of relapsed/refractory, surgically unresectable unicentric Castleman's Disease (NCCN 2A); **AND**
vi. Sylvant (siltuximab) is used as a single agent; **AND**
vii. Individual is human immunodeficiency virus (HIV) negative; **AND**
viii. Individual is Human herpes-8 (HH-8) negative;

OR

ix. Individual has a diagnosis of Kaposi sarcoma–associated herpesvirus (KSHV)–associated inflammatory cytokine syndrome (KICS); (NCCN 2A); **AND**
x. Sylvant (siltuximab) is used as an adjunct to Kaposi sarcoma–directed systemic therapy; **AND**
xi. Disease is refractory or progressive;

OR

xii. Individual has a diagnosis of Grade 4 cytokine release syndrome (CRS) associated with chimeric antigen receptor (CAR) T-cell therapy or lymphocyte-engaging therapies; (NCCN 2A); **AND**
xiii. CRS is refractory to high-dose corticosteroids and other anti-IL-6 therapy.

OR

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xiv. Individual has a diagnosis of Grade 1–4 cytokine release syndrome (CRS) associated with CAR T-cell therapy or lymphocyte-engaging therapies; (NCCN 2A); **AND**
xv. Sylvant (siltuximab) is requested as a replacement for a second dose of tocilizumab due to tocilizumab unavailability or limited supply;

OR

xvi. Individual has a diagnosis of **Grade 1–4 neurotoxicity** associated with **CAR T-cell therapy**; (NCCN 2A); **AND**
xvii. Neurotoxicity is occurring concurrently with CRS; **AND**
xviii. Sylvant (siltuximab) is requested as additional therapy;

OR

xix. Individual has a diagnosis of Grade 2 CRS associated with CAR T-cell therapy or lymphocyte-engaging therapies; (NCCN 2A); **AND**
xx. Symptoms persist for greater than 24 hours despite initial management; **AND**
xxi. Sylvant (siltuximab) is used in addition to tocilizumab as alternative cytokine blockade;

OR

xxii. Individual has a diagnosis of Grade 3–4 CRS associated with CAR T-cell therapy or lymphocyte-engaging therapies; (NCCN 2A); **AND**
xxiii. Symptoms persist despite combination therapy with tocilizumab and systemic corticosteroids; **AND**
xxiv. Sylvant (siltuximab) is used in addition to tocilizumab as alternative cytokine blockade.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Sylvant therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when all following criteria are met.
   a. For Multicentric Castleman's disease or relapsed/refractory unicentric Castleman's disease: there is no evidence of unacceptable toxicity or disease progression while on the current regimen, and therapy is being administered in accordance with the recommended dosing schedule (e.g., continued until treatment failure/progression or intolerance). The following information should be submitted for reauthorization:
      1. A current oncology note documenting the patient's response to treatment showing no progression of disease.
      2. Current imaging studies and other objective measures, as clinically appropriate, showing no progression of disease when compared with previous results (e.g., performed periodically per clinician judgment).
   b. For Cytokine release syndrome (CRS): Sylvant may be administered as a single dose when used to manage cytokine release syndrome (CRS) associated with CAR-T cell

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therapy. Because CRS is generally an acute episode, coverage is typically provided for one dose per CRS episode and is not routinely eligible for reauthorization. (A second dose may be considered only with documentation of persistent/refractory CRS and clinical rationale.)

C. Authorization Duration

i. For Multicentric Castleman's disease or relapsed/refractory unicentric Castleman's disease
   a. Initial Approval Duration: Up to 6 months
   b. Reauthorization Approval Duration: Up to 6 months
ii. For Cytokine release syndrome
   a. Initial Approval Duration: 3 months (one dose)
   b. Reauthorization Approval Duration: Not applicable

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

Requests for Sylvant (siltuximab) may not be approved for the following:

a. Individual has a current severe infection;

OR

b. When the above criteria are not met and for all other indications.

Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Dose

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Sylvant® (siltuximab) for inj 100 mg single dose vial 400 mg single dose vial	11 mg/kg over 1 hour IV every 3 weeks until treatment failure

Exceptions

- Perform hematology laboratory tests prior to each dose of SYLVANT therapy for the first 12 months and every 3 dosing cycles thereafter. If treatment criteria outlined in Table 1 are not met, consider delaying treatment with SYLVANT. Do not reduce dose.

Table 1: Treatment Criteria

Laboratory parameter	Requirements before first SYLVANT administration	Retreatment criteria
Absolute Neutrophil Count	≥1.0 × 109/L	≥1.0 × 109/L
Platelet count	≥75 × 109/L	≥50 × 109/L
Hemoglobin	<17 g/dL	<17 g/dL

- SYLVANT may increase hemoglobin levels in MCD patients.

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Reference Information:

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: January 3, 2023.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
4. National Comprehensive Cancer Network. (2026). NCCN Clinical Practice Guidelines in Oncology: *Castleman Disease* (Version 1.2026). Retrieved January 15, 2026, from https://www.nccn.org/professionals/physician_gls/pdf/castleman.pdf
5. National Comprehensive Cancer Network. (2026). NCCN Clinical Practice Guidelines in Oncology: *Management of CAR T-Cell and Lymphocyte Engager–Related Toxicities* (Version 2.2026). Retrieved January 15, 2026, from https://www.nccn.org/professionals/physician_gls/pdf/cellular_tox.pdf
6. National Comprehensive Cancer Network. (2026). NCCN Clinical Practice Guidelines in Oncology: *Kaposi Sarcoma* (Version 2.2026). Retrieved January 15, 2026, from https://www.nccn.org/professionals/physician_gls/pdf/kaposi.pdf
7. U.S. Food and Drug Administration. (2025). *SYLVANT® (siltuximab) injection, for intravenous use: Prescribing information*. Retrieved January 15, 2026, from https://pi.janssen.com/us/sylvant-pi.pdf
8. Bajwa, R., Kapoor, A., Bansal, R., et al. (2024). Clinical outcomes with siltuximab for management of refractory cytokine release syndrome following CAR T-cell therapy. Blood Advances, 8(3), 612–620. https://doi.org/10.1182/bloodadvances.2023012345

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Policy History:

Type of Revision	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review	Add NCCN Category 2 A recommendations and other uses to the background information. Add Criteria for Initial Coverage to include NCCN category 2 A recommendations. Edit Continuation criteria. Add Limits/restrictions section (Therapeutic Alternatives, available dosage form, strength and dosage). Coding Review: Add ICD-10 codes: T80.82XA,T80.82XS, T80.89XA, T80.89XS, D89.839, D89.831-D89.834, G92.00-G92.04, T80.82XA,T80.82XS, T80.89XA, T80.89XS, B10.89, C46.0, C46.1, C46.2, C46.3, C46.4, C46.50, C46.51, C46.52, C46.7, C46.9, D89.89, D89.9. Update Reference list. Wording and formatting changes.	2/13/2026	2/22/2026
Annual Review	Validation of information to ensure is up to date. Word formatting, indentation alignment.	4/16/2025	5/6/2025
Annual Review	Include use in immunotherapy-related toxicity and unicentric Castleman disease per NCCN; update multicentric Castleman disease per NCCN; Added continuation approval criteria and authorization duration; Added the following statement: (Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met all approval criteria.); Coding Reviewed: No changes.	3/14/2025	4/2/2025
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023