# Clinical Policy: Siltuximab (Sylvant)

Reference Number: ERX.SPA.309
Effective Date: 03.01.19
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

**Description**
Siltuximab (Sylvant®) is an interleukin-6 (IL-6) antagonist

**FDA Approved Indication(s)**
Sylvant is indicated for the treatment of patients with multicentric Castleman's disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.

Limitation(s) 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.

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

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary*.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Sylvant is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Castleman's Disease** (must meet all)**:**

1. Diagnosis of Castleman's disease (CD) (a B-cell lymphoma subtype) confirmed by biopsy of involved tissue (usually a lymph node);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Sylvant is prescribed in one of the following ways (a or b):
   a. As single-agent therapy for MCD;
   b. As single-agent therapy for relapsed or refractory unicentric CD (UCD) (off-label);
5. Documented negative tests for human immunodeficiency virus (HIV) and human herpesvirus-8 (HHV-8);
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 11 mg/kg every 3 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

**Approval duration: 6 months**

**B. Cytokine Release Syndrome (off-label)** (must meet all):
1. Member has a scheduled chimeric antigen receptor (CAR) T cell therapy (e.g., Kymriah™, Yescarta™, Abecma®, Tecartus®, Breyanzi®);
2. Sylvant is prescribed in one of the following ways (a or b):
   a. For the management of grade 4 cytokine release syndrome (CRS) that is refractory to high-dose corticosteroids and anti-IL-6 therapy;
   b. As a replacement for the second dose of Actemra® when supplies are limited or unavailable for CRS or immunotherapy related neurotoxicity;
3. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: Up to 4 doses total**

**C. Other diagnoses/indications**
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

## II. Continued Therapy

**A. Castleman's Disease** (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Sylvant for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 11 mg/kg every 3 weeks;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

**Approval duration: 12 months**

**B. Cytokine Release Syndrome (off-label)** (must meet all):
1. Documentation supports that member is currently receiving Sylvant for CAR T cell-induced CRS and member has not yet received 4 doses total;
2. Member is responding positively to therapy;
3. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: Up to 4 doses total**

**C. Other diagnoses/indications** (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

## III. Diagnoses/Indications for which coverage is NOT authorized:

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

CAR: chimeric antigen receptor
CD: Castleman's disease
CRS: cytokine release syndrome
FDA: Food and Drug Administration
HHV-8: negative and human hperesvirus-8
HIV: human immunodeficiency virus
MCD: multicentric Castleman's disease
UCD: unicentric Castleman's disease

*Appendix B: Therapeutic Alternatives*
Not applicable

*Appendix C: Contraindications/Boxed Warnings*
- Contraindication(s): severe hypersensitivity reaction to siltuximab or any of the excipients in Sylvant
- Boxed warning(s): none reported

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| CD | 11 mg/kg over 1 hour IV every 3 weeks | 11 mg/kg |

## VI. Product Availability
Lyophilized powder in a single-use vial: 100 mg, 400 mg

## VII. References

1. Sylvant Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; December 2019. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/125496s018lbl.pdf. Accessed September 29, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed September 29, 2021.
3. B-Cell Lymphomas Version 5.2021. National Comprehensive Cancer Network Guidelines. Available at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed September 29, 2021.
4. Management of Immunotherapy-Related Toxicities Version 4.2021. National Comprehensive Cancer Network Guidelines. Available at https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf. Accessed September 29, 2021.


| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created | 11.20.18 | 02.19 |
| 1Q 2020 annual review: no significant changes; references reviewed and updated. | 11.08.19 | 02.20 |
| 1Q 2021 annual review: lab parameters removed from criteria sets given they do not represent a treatment contraindication; references reviewed and updated. | 10.13.20 | 02.21 |
| 1Q 2022 annual review: added criteria set for NCCN compendium supported use for CRS associated with CAR or autologous T cell therapy; references reviewed and updated. | 09.29.21 | 02.22 |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.