Sylvant® (siltuximab)
(Intravenous)

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I. Length of Authorization [2,6]

Coverage will be provided for 6 months and may be renewed (unless otherwise specified).

- Management of CAR T-Cell-Related Toxicities: Coverage will be provided for 1 dose only and may NOT be renewed

II. Dosing Limits

Quantity Limit (max daily dose) [NDC Unit]:

- Sylvant 100 mg single-dose vial: 3 vials per 21-day supply
- Sylvant 400 mg single-dose vial: 3 vials per 21-day supply

Max Units (per dose and over time) [HCPCS Unit]:

Diagnosis	Billable Units	Interval (days)
MCD, UCD	130	21
Management of Immunotherapy-Related Toxicities	130	1 course of therapy only

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Patient is human immunodeficiency virus (HIV) negative; **AND**
- Patient is human herpesvirus-8 (HHV-8) negative; **AND**
- Patient is currently free of all clinically significant active infections; **AND**
- Patient will NOT receive any live vaccines during treatment with siltuximab; **AND**
- Must be used as a single agent; **AND**

Multicentric Castleman's Disease (MCD) † Φ [1-4]

Unicentric Castleman's Disease (UCD) ‡ [2]

- Used as second-line therapy for relapsed or refractory disease

Management of CAR T-Cell-Related Toxicities ‡ [2,6]

- Patient has received or will be receiving chimeric antigen receptor (CAR)-T cell therapy (e.g., axicabtagene ciloleucel, brexucabtagene autoleucel, idecabtagene vicleucel, lisocabtagene maraleucel, tisagenlecleucel, etc.); **AND**
    - Used for the management of Grade 4 cytokine release syndrome (CRS); **AND**
        - Patient is refractory to high-dose corticosteroids and anti-interleukin-6 therapy (e.g., tocilizumab); **OR**
    - Used as a replacement for the second dose of tocilizumab when supplies are limited or unavailable; **AND**
        - Used for Grade 1-4 CRS; **OR**
        - Used for Grade 1-4 neurotoxicity as additional therapy if the patient has concurrent CRS

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,2,6]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: gastrointestinal perforation, severe infusion related reactions and hypersensitivity, etc.

Management of CAR T-Cell-Related Toxicities

- May not be renewed

V. Dosage/Administration [1,3,4,6]

Indication	Dose
MCD, UCD	Administer 11 mg/kg intravenously every 21 days until treatment failure
Management of CAR T-Cell-Related Toxicities	Administer 11 mg/kg intravenously one time only

VI. Billing Code/Availability Information

HCPCS code:

- J2860 - Injection, siltuximab, 10 mg; 10 mg = 1 billable unit

NDC:

- Sylvant 100 mg lyophilized powder in a single-dose vial: 73090-0420-xx
- Sylvant 400 mg lyophilized powder in a single-dose vial: 73090-0421-xx

VII. References

1. Sylvant [package insert]. Hemel Hempstead, Hertfordshire, U.K.; EUSA Pharma (UK), Ltd; December 2019. Accessed December 2022.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for siltuximab. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed December 2022.
3. van Rhee F, Wong RS, Munshi N, et al. Siltuximab for multicentric Castleman's disease: a randomised, double-blind, placebo-controlled trial. Lancet Oncol. 2014 Aug;15(9):966-74. Doi: 10.1016/S1470-2045(14)70319-5. Epub 2014 Jul 17.
4. Kurzrock R, Voorhees PM, Casper C, et al. A phase I, open-label study of siltuximab, an anti-IL-6 monoclonal antibody, in patients with B-cell non-Hodgkin lymphoma, multiple myeloma, or Castleman disease. Clin Cancer Res. 2013 Jul 1;19(13):3659-70. Doi: 10.1158/1078-0432.CCR-12-3349. Epub 2013 May 9.
5. Chen F, Teachey DT, Pequignot E, et al. Measuring IL-6 and sIL-6R in serum from patients treated with tocilizumab and/or siltuximab following CAR T cell therapy. J Immunol Methods. 2016 Jul;434:1-8. doi: 10.1016/j.jim.2016.03.005.
6. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Management of Immunotherapy-Related Toxicities Version 1.2022. National Comprehensive Cancer Network, 2022. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed December 2022.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D47.Z2	Castleman disease
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

ICD-10	ICD-10 Description
D89.839	Cytokine release syndrome, grade unspecified
G92.00	Immune effector cell-associated neurotoxicity syndrome, grade unspecified
G92.01	Immune effector cell-associated neurotoxicity syndrome, grade 1
G92.02	Immune effector cell-associated neurotoxicity syndrome, grade 2
G92.03	Immune effector cell-associated neurotoxicity syndrome, grade 3
G92.04	Immune effector cell-associated neurotoxicity syndrome, grade 4
T80.82XA	Complication of immune effector cellular therapy, initial encounter
T80.82XS	Complication of immune effector cellular therapy, sequela
T80.89XA	Other complications following infusion, transfusion and therapeutic injection, initial encounter
T80.89XS	Other complications following infusion, transfusion and therapeutic injection, sequela

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC