A Guide to Administering SYLVANT® (siltuximab)

The only FDA-approved therapy for the treatment of patients with multicentric Castleman disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.[1]

INDICATIONS AND USAGE

SYLVANT® (siltuximab) is an interleukin-6 (IL-6) antagonist indicated for the treatment of patients with multicentric Castleman disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.

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.

sylvant® siltuximab

Please see Important Safety Information on page 28 and accompanying full Prescribing Information.

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Coding & Ordering Information

Handy product information, billing and administration codes, and authorized distributor contact information are available at your fingertips.

SYLVANT® (siltuximab) coding information at-a-glance

- Use the correct billing codes to ensure proper reimbursement

Product Information[1]		
SYLVANT 100 mg (3-week formulation)	Lyophilized powder for single-dose intravenous infusion	73090-420-01
SYLVANT 400 mg (3-week formulation)	Lyophilized powder for single-dose intravenous infusion	73090-421-01

Billing Codes	
Diagnostic Code[2]	ICD-10*: D47.Z2
JCODE[3]	J2860

Billing Units	
10 mg[3]	1 billing unit

Drug Administration Codes	
96365[4]	Non-chemo infusion, 1st hour, initial drug
96413[5]	Chemo and complex biologic infusion, 1st hour, initial drug

*ICD-10 code is for Castleman disease.

ICD-10, International Classification of Diseases, Tenth Revision.

Different ways to order SYLVANT

- You can conveniently order SYLVANT directly from any of the 5 distributors below

SYLVANT 100 MG NDC: 73090-420-01[a]	SYLVANT 400 MG NDC: 73090-421-01[a]

Authorized dealer	**ASD Healthcare**
Phone number	800-746-6273
Website	asdhealthcare.com
Item #	10253123
Item #	10253031
Authorized dealer	**Cardinal Health Specialty Distribution**
Phone number	877-453-3972
Website	specialtyonline.cardinalhealth.com
Item #	5694179
Item #	5694187
Authorized dealer	**McKesson Plasma and Biologics**
Phone number	877-625-2566
Website	connect.mckesson.com
Item #	2883965
Item #	2883973
Authorized dealer	**McKesson Specialty Care Distribution**
Phone number	800-482-6700
Website	mscs.mckesson.com
Item #	5016640
Item #	5016641
Authorized dealer	**Oncology Supply**
Phone number	800-633-7555
Website	oncologysupply.com
Item #	10253087
Item #	10253059

[a]SYLVANT® National Drug Code updated as of 2/19/21.

Dosing Recommendations

Administer SYLVANT® (siltuximab) 11 mg/kg over 1 hour as an intravenous infusion every 3 weeks until treatment failure.[1]

Perform hematology laboratory tests prior to each dose of SYLVANT therapy for the first 12 months and every 3 dosing cycles thereafter.[1]

SYLVANT dosing recommendations

Preadministration laboratory tests[1]

- Hematology laboratory tests should be performed prior to each dose of SYLVANT therapy for the first 12 months and every 3 dosing cycles thereafter
- If the treatment criteria in the table below are not met, consider delaying treatment; do not reduce dose

Laboratory parameter	Requirements before first SYLVANT administration	Re-treatment criteria
Absolute neutrophil count	≥1.0 x 10^9/L	≥1.0 x 10^9/L
Platelet count	≥75 x 10^9/L	≥50 x 10^9/L
Hemoglobin[a]	<17 g/dL	<17 g/dL

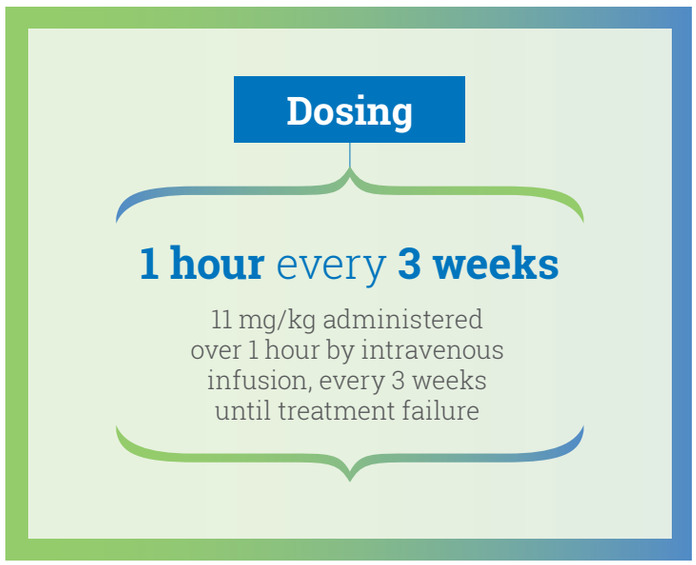
[a] SYLVANT may increase hemoglobin levels in patients with MCD.

Do not administer SYLVANT to patients with severe infections until the infection resolves.

Discontinue SYLVANT in patients with severe infusion-related reactions, anaphylaxis, severe allergic reactions, or cytokine release syndromes. Do not reinstitute treatment.

Dosing[1]

- 11 mg/kg administered over 1 hour by intravenous infusion, every 3 weeks until treatment failure



Preinfusion patient counseling

Advise patients to read the FDA-approved patient labeling (Patient Information)

Inform patients of the following risks[1]:

Infections

Inform patients that SYLVANT may lower their resistance to infections. Advise patients on the importance of contacting their doctor immediately when symptoms suggesting infection appear in order to ensure rapid evaluation and appropriate treatment.

Vaccinations

Inform patients that they should discuss the recommended vaccinations with their doctor prior to treatment with SYLVANT.

Allergic Reactions

Advise patients to seek immediate medical attention if they experience any symptoms of serious allergic reactions during the infusion of SYLVANT. Signs may include difficulty breathing, chest tightness, wheezing, severe dizziness or light-headedness, swelling of the lips, or skin rash.

Pregnancy

Advise patients of childbearing potential to avoid pregnancy, including instructions about the importance of using contraception during treatment and for 3 months after SYLVANT therapy. Advise females with infants exposed to SYLVANT in utero to inform the pediatrician of the exposure.

Lactation

Advise females not to breastfeed during treatment with SYLVANT and for 3 months after the final dose.

FDA, US Food and Drug Administration.

Storage & Handling

SYLVANT® (siltuximab) is supplied in single-dose vials and must be refrigerated and protected from light.[1]

How SYLVANT is supplied and stored

Supplied[1]

SYLVANT is supplied as a **sterile, white, preservative-free, lyophilized powder in single-dose vials**

Each SYLVANT vial is individually packaged in a carton:

One 100-mg vial
or
One 400-mg vial

Storage[1]

Must be refrigerated at 2°C to 8°C (36°F to 46°F)

Protect from light (keep in the original carton)

Do not freeze

Discard beyond the expiration date located on the carton and the vial

Preparation & Administration

SYLVANT® (siltuximab) uses weight-based dosing (11 mg/kg).[1]

Use aseptic technique for reconstitution and preparation of dosing solution.[1]

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.[1]

Instructions for preparation and administration

Use aseptic technique for reconstitution and preparation of dosing solution[1]

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit[1]

Preparation and storage of the dilute solution[1]

- Calculate the dose (mg), total volume (mL) of reconstituted SYLVANT solution required, and the number of vials needed
  - A 21-gauge, 1½-inch needle is recommended for preparation
  - Infusion bags (250 mL) must contain Dextrose 5% in Water and must be made of polyvinyl chloride (PVC), polyolefin (PO), polypropylene (PP), or polyethylene (PE)
  - Alternatively, PE bottles may be used
- Allow the vial(s) of SYLVANT to come to room temperature over approximately 30 minutes. SYLVANT should remain at room temperature for the duration of the preparation
- Aseptically reconstitute each SYLVANT vial as instructed in the adjacent table

Reconstitution of SYLVANT[1]

Strength	100-mg vial	400-mg vial
Amount of Sterile Water for Injection, USP required for reconstitution	5.2 mL	20 mL
Post-reconstitution concentration	20 mg/mL	20 mg/mL

  - Gently swirl the reconstituted vials to aid the dissolution of the lyophilized powder
  - DO NOT SHAKE or SWIRL VIGOROUSLY
  - Do not remove the contents until all of the solids have been completely dissolved
  - The lyophilized powder should dissolve in less than 60 minutes
- Once reconstituted, and prior to further dilution, inspect the vials for particulates and discoloration. Do not use if particles or solution discoloration are present or if visibly opaque. The reconstituted product should be kept for no more than 2 hours prior to addition into the infusion bag
- Dilute the reconstituted SYLVANT solution dose in the infusion bag
  - Withdraw a volume equal to the total calculated volume of reconstituted SYLVANT from the Dextrose 5% in Water, 250 mL bag
  - Slowly add the total calculated volume (mL) of reconstituted SYLVANT solution to the Dextrose 5% in Water infusion bag
  - Gently invert the bag to mix the solution

Administration[1]

- SYLVANT is given over 1 hour by infusion
- Use administration sets lined with PVC, polyurethane (PU), or PE, containing a 0.2-micron inline polyethersulfone (PES) filter
  - The infusion should be completed within 4 hours of reconstitution
- Do not infuse SYLVANT concomitantly in the same intravenous line with other agents
- SYLVANT does not contain preservatives. Do not store any unused portion of the reconstituted product or of the infusion solution. Waste material should be disposed of in accordance with local requirements.

Calculations

Follow the step-by-step instructions to achieve the right patient dose, every time.

SYLVANT® (siltuximab) calculations

- Perform hematology laboratory tests prior to each dose of SYLVANT therapy for the first 12 months and every 3 dosing cycles thereafter. See full PI for treatment criteria[1]

Sample Calculation
85.0 kg / 187.5 lb

Strength	100-mg vial	400-mg vial
Amount of Sterile Water for Injection, USP required for reconstitution[1]	5.2 mL	20 mL
Post-reconstitution concentration[1]	20 mg/mL	20 mg/mL

Interactive dosing calculator

- Enter patient weight in lbs or kg to get recommended SYLVANT dose.

Weight (kg)	0.0
Dose (mg)	0.0
Total volume of reconstituted SYLVANT solution (mL)	0.0
Volume to be removed from Dextrose 5% in water, 250 mL bag (mL)	0.0

Weight (lb)	0.0
Dose (mg)	0.0
Total volume of reconstituted SYLVANT solution (mL)	0.0
Volume to be removed from Dextrose 5% in water, 250 mL bag (mL)	0.0

SYLVANT uses weight-based dosing **(11 mg/kg)[1]**

1 Calculate the weight of the person (kg)

$$187.5\ \cancel{lb} \times \frac{kg}{2.20462\ \cancel{lb}} = 85.0\ kg$$

2 Calculate the dose (mg) of SYLVANT needed

$$85.0\ \cancel{kg} \times \frac{11\ mg}{\cancel{kg}} = 935\ mg$$

3 Calculate the number and strength (100 mg or 400 mg) of SYLVANT vials needed for infusion

935 mg → 2 x 400 mg vials, 2 x 100 mg vials

4 Calculate the total volume (mL) of reconstituted SYLVANT solution required (based on post-reconstitution concentration of 20 mg/mL)

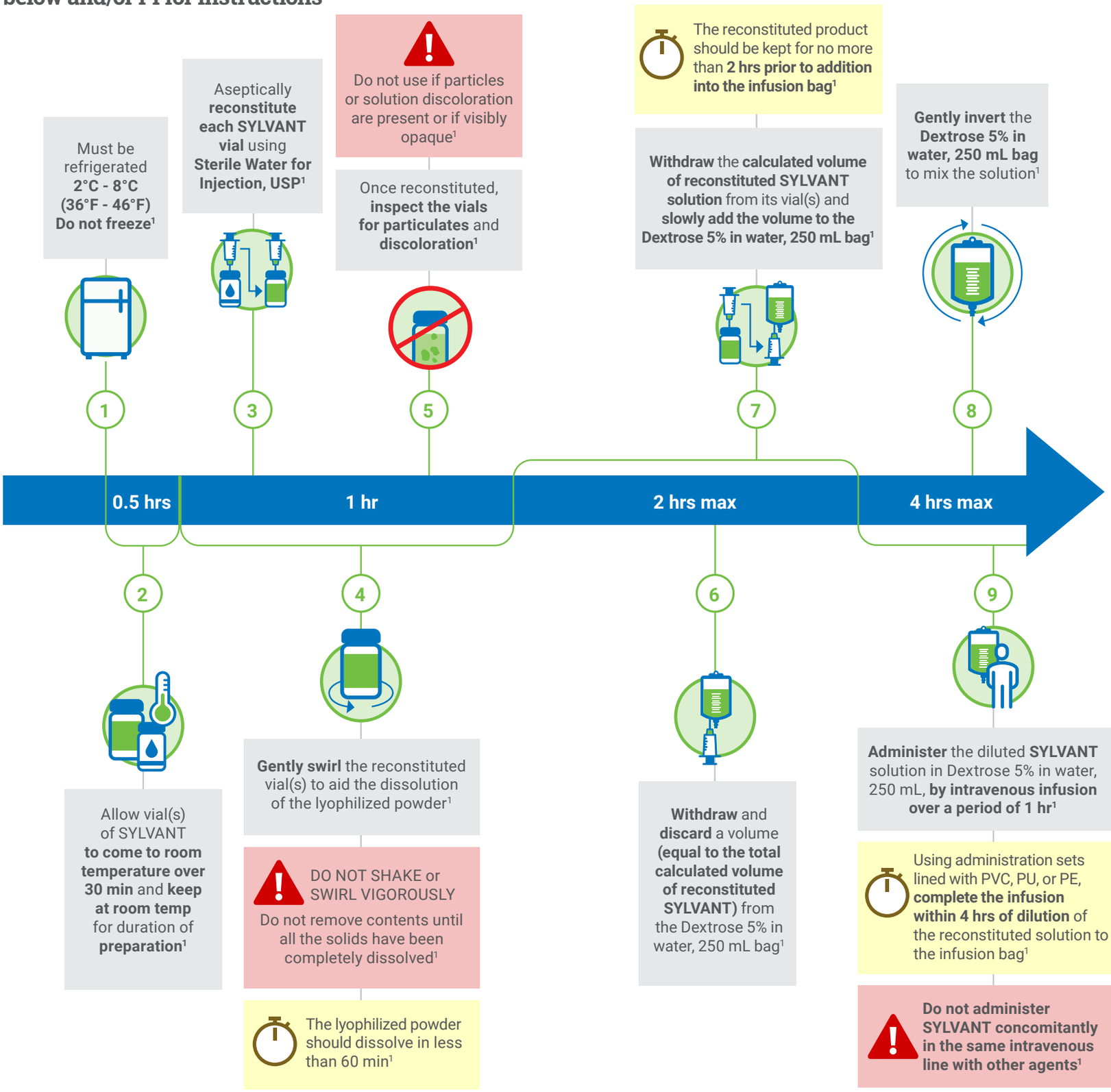
$$935\ \cancel{mg} \times \frac{mL}{20\ \cancel{mg}} = 46.8\ mL$$

Aseptic Technique & Product Reconstitution

Always follow aseptic technique when reconstituting SYLVANT® (siltuximab).[1]

Aseptic technique and product reconstitution

Please see complete diagram below and/or PI for instructions



Important Safety Information

For any additional information, please contact your Recordati representative.

INDICATIONS AND USAGE

SYLVANT® (siltuximab) is an interleukin-6 (IL-6) antagonist indicated for the treatment of patients with multicentric Castleman disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative.

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.

IMPORTANT SAFETY INFORMATION

SYLVANT is contraindicated in patients experiencing a severe hypersensitivity reaction to siltuximab or any of the excipients in SYLVANT. Hypersensitivity reactions, including anaphylactic reaction, hypersensitivity, and drug hypersensitivity have been reported in patients treated with siltuximab.

Concurrent Active Severe Infections: Do not administer SYLVANT to patients with severe infections until the infection resolves. SYLVANT may mask signs and symptoms of acute inflammation including suppression of fever and of acute Phase reactants such as C-reactive protein (CRP). Monitor patients receiving SYLVANT closely for infections. Institute prompt anti-infective therapy and do not administer further SYLVANT until the infection resolves.

Vaccinations: Do not administer live vaccines to patients or infants born to patients receiving SYLVANT because IL-6 inhibition may interfere with the normal immune response to new antigens.

Infusion Related Reactions and Hypersensitivity: SYLVANT may cause infusion-related reactions and anaphylaxis. Stop the infusion of SYLVANT if the patient develops signs of anaphylaxis. Discontinue further therapy with SYLVANT.

Stop the infusion if the patient develops a mild to moderate infusion reaction. If the reaction resolves, the SYLVANT infusion may be restarted at a lower infusion rate. Consider medicating with antihistamines, acetaminophen, and corticosteroids. Discontinue SYLVANT if the patient does not tolerate the infusion following these interventions.

Administer SYLVANT in a setting that provides resuscitation equipment, medication, and personnel trained to provide resuscitation.

Gastrointestinal (GI) Perforation: GI perforation has been reported in clinical trials although not in MCD trials. Use with caution in patients who may be at increased risk for GI perforation. Promptly evaluate patients presenting with symptoms that may be associated or suggestive of GI perforation.

The most common adverse reactions (>10% compared to placebo) during treatment with SYLVANT in the MCD clinical trial were rash, pruritus, upper respiratory tract infection, increased weight, and hyperuricemia.

To report SUSPECTED ADVERSE REACTIONS, contact Recordati Rare Diseases Inc. at 1-888-575-8344, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Drug Interactions with Cytochrome P450 (CYP450) Substrates: Inhibition of IL-6 signaling in patients treated with SYLVANT may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates compared to metabolism prior to treatment with SYLVANT.

Upon initiation or discontinuation of SYLVANT, in patients being treated with CYP450 substrates with a narrow therapeutic index, perform therapeutic monitoring of effect (e.g., warfarin) or drug concentration (e.g., cyclosporine or theophylline) as needed and adjust dose. The effect of SYLVANT on CYP450 enzyme activity can persist for several weeks after stopping therapy. Exercise caution when SYLVANT is co-administered with CYP3A4 substrate drugs where a decrease in effectiveness would be undesirable (e.g., oral contraceptives, lovastatin, atorvastatin).

Pregnancy and Lactation: SYLVANT may cause embryo-fetal harm when administered to pregnant women. Advise female patients of reproductive potential to use effective contraception during treatment with SYLVANT and for 3 months after the last dose. Advise patients not to breastfeed during treatment with SYLVANT and for 3 months after the final dose.

Pediatric Use: The safety and efficacy of SYLVANT have not been established in pediatric patients.

Dosing and Administration: 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 of the Prescribing Information are not met, consider delaying treatment with SYLVANT. Do not reduce dose.

SYLVANT® (siltuximab) for injection, for intravenous use, is available as 100 mg or 400 mg of lyophilized powder in a single-dose vial.

Please see Important Safety Information throughout and accompanying full Prescribing Information, including Patient Information.

References: 1. SYLVANT [package insert]. Hertfordshire, UK: EUSA Pharma UK Ltd; 2019. **2.** 2024 ICD-10-CM Diagnosis Code D47.Z2. ICD10Data.com. Accessed June 14, 2024. https://www.icd10data.com/ICD10CM/Codes/C00-D49/D37-D48/D47-/D47.Z2. **3.** HCPCS Code for Injection, siltuximab, 10 mg. Codify by AAPC. Accessed June 14, 2024. https://www.aapc.com/codes/hcpcs-codes/J2860. **4.** CPT 96365. Under therapeutic, prophylactic, and diagnostic injections and infusions (excludes chemotherapy and other highly complex drug or highly complex biologic agent administration). Codify by AAPC. Accessed June 14, 2024. https://www.aapc.com/codes/cpt-codes/96365. **5.** CPT 96413. Under injection and intravenous infusion chemotherapy and other highly complex drug or highly complex biologic agent administration. Codify by AAPC. Accessed June 14, 2024. https://www.aapc.com/codes/cpt-codes/96413.

Important things to remember while administering SYLVANT® (siltuximab)

Conduct preadministration lab tests[1]

Check whether the treatment criteria are met, and inquire about the patient's previous allergic reactions.

SYLVANT doses must be refrigerated[1]

SYLVANT must be kept at 2°C to 8°C in the original carton and is given every 3 weeks until treatment failure.

Check each vial carefully[1]

Inspect each vial of lyophilized siltuximab powder before use, and reconstitute SYLVANT as described in the packaging information.

Check the preparation guidelines

Follow every step before administering SYLVANT.

Inform patients of risks[1]

Patients should be informed about the risks involved with SYLVANT treatment and advised to read the FDA-approved Patient Information (label).

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sylvant® siltuximab

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