sylvant
siltuximab

STORAGE

Protect from Light
Keep in original carton

Must be refrigerated
2°C - 8°C
(36°F - 46°F)
Do not freeze

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

SUPPLIES

Each SYLVANT® vial is supplied as a sterile, white, preservative-free, lyophilized powder in single-use vials and are individually packaged in a carton as:

one 100mg vial OR one 400mg vial

Use aseptic technique for reconstitution and preparation of dosing solution

A 21-gauge 1.5-inch (38mm) needle is recommended for preparation

Infusion bags must contain **Dextrose 5%** in water and must be made from **PVC, PO, PP or PE.** Alternatively, **PE bottles may be used.** Administration sets lined with PVC or PE containing a 0.2 micron inline PES filter should be used.

Sterile Water for Injection, USP is required for the reconstitution of SYLVANT

PE, polyethylene; PES, Polyethersulfone; PO, polyolefin; PP, polypropylene; PVC, polyvinyl chloride.

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.

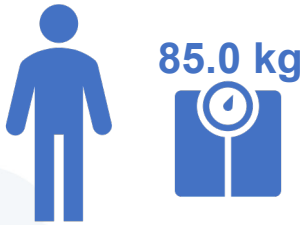
SYLVANT® uses weight-based dosing
(11 mg/kg)

1. Calculate **the weight of the person (kg)**
2. Calculate the **dose (mg) of SYLVANT** needed
3. Calculate the **number and strength (100 mg or 400 mg) of carton(s) containing SYLVANT vials** needed for infusion
4. Calculate the **total volume (mL) of reconstituted SYLVANT solution required** (based on post-reconstitution concentration of 20 mg/mL)

SAMPLE CALCULATION ONLY

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	5.2 mL	20 mL
Post-reconstitution concentration	20 mg/mL	20 mg/mL

SYLVANT® uses weight-based dosing **(11 mg/kg)**

1. Calculate the **weight of the person (kg)**: 187.5 ~~lb~~ X $\frac{\text{kg}}{2.20462\ \text{~~lb~~}}$ = 85.0 kg
2. Calculate the **dose (mg) of SYLVANT** needed: 85.0 ~~kg~~ X $\frac{11\ \text{mg}}{\text{~~kg~~}}$ = 935 mg
3. Calculate the **number and strength (100 mg or 400 mg) of carton(s) containing 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 ~~mg~~ X $\frac{\text{mL}}{20\ \text{~~mg~~}}$ = 46.8 mL

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 siltuximab

ASEPTIC TECHNIQUE

Must be refrigerated **2°C - 8°C (36°F - 46°F) Do not freeze.**

1

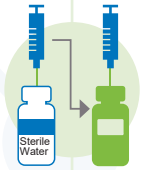
Allow vial(s) of SYLVANT to **come to room temperature over 30 min** and **keep at room temp** for duration of **preparation**

2

0.5 hrs

Aseptically **reconstitute each SYLVANT vial** using **Sterile Water for Injection, USP.**

3



1 hr

Gently swirl the reconstituted vial(s) to aid the dissolution of the lyophilized powder

4

DO NOT SHAKE or SWIRL VIGOROUSLY

Do not remove contents until all the solids have been completely dissolved

Do not use if particles or solution discoloration are present or if visibly opaque

Once reconstituted, **inspect** the **vials for particulates** and **discoloration**

5

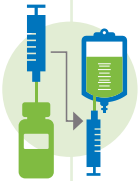
The lyophilized powder should disolve in less than 60 min

The reconstituted product should be kept for no more than **2 hrs prior to addition into the infusion bag**

2 hrs max

Withdraw the **calculted volume of reconstituted Sylvant solution** from its vial(s) and **add the volume to the Dextrose 5% in water, 250 mL bag**

7



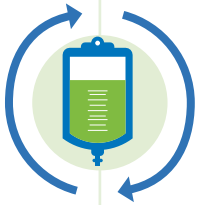
6

Withdraw and **discard** a volume (**equal to the total calculated volume of reconstituted SYLVANT**) from the Dextrose 5% in water, 250 mL bag

4 hrs max

Gently invert the **Dextrose 5% in water, 250 mL bag** to mix the solution

8



9

Administer the diluted **SYLVANT** solution in Dextrose 5% in Water 250 mL **by intravenous infusion over a period of 1 hr**

The **infusion should be completed within 4 hrs of dilution** of the reconstituted solution to the infusion bag

Do not administer SYLVANT concomitantly in the same intravenous line with other agents.

SYLVANT (siltuximab) [prescribing information] Hertfordshire, UK: EUSA Pharma UK Ltd; 2019.

IMPORTANT SAFETY INFORMATION

SYLVANT® (siltuximab) for injection HCP

INDICATIONS AND USAGE

SYLVANT® (siltuximab) is an interleukin-6 (IL-6) antagonist 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.

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.

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 receiving SYLVANT because IL-6 inhibition may interfere with the normal immune response to new antigens.

Infusion Related Reactions and Hypersensitivity: 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: Gastrointestinal (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

IMPORTANT SAFETY INFORMATION

that may be associated or suggestive of GI perforation.

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

Cytochrome P450 Substrates: 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 females not to breastfeed during treatment with SYLVANT and for 3 months after the final dose.

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 the Prescribing Information are not met, consider delaying treatment with SYLVANT. Do not reduce dose.

Directional Statements:

Before prescribing SYLVANT, please read the full Prescribing Information (https://sylvant.com/en-us/assets/docs/sylvant-prescribing-info.pdf)

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