Important Safety Information

Indications and Usage

SYLVANT® (siltuximab) 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.

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.

Contraindications

Severe hypersensitivity reaction to siltuximab or any of the excipients in SYLVANT.

Warnings and Precautions

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 Reaction and Hypersensitivity

If treatment criteria outlined in Table 1 of the Dosage & Administration section of the Prescribing Information are not met, consider delaying treatment with SYLVANT. Do not reduce dose.

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 that may be associated with or suggestive of GI perforation.

Adverse Reactions

Most common adverse reactions (>10% of patients) included rash, pruritus, upper respiratory tract infection, increased weight, and hyperuricemia.

Drug Interactions

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).

Dosage and Administration

Administer SYLVANT 11 mg/kg over 1 hour as an intravenous infusion every 3 weeks until failure.

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.

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.

Please see Full Prescribing Information in pocket.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas V.1.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed [February 2020]. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **2.** van Rhee F, Voorhees P, Dispenzieri A, et al. International, evidence-based consensus treatment guidelines for idiopathic multicentric Castleman disease. *Blood*. 2018;132(20):2115-2124. **3.** SYLVANT [package insert]. Hertfordshire, UK: EUSA Pharma UK Ltd; 2019.

US-SIL-2000014 2/20 Printed in USA

An iMCD Treatment That's NOW PREFERRED

Siltuximab (SYLVANT®) is now recommended by the National Comprehensive Cancer Network® (NCCN®) as a preferred treatment option for idiopathic multicentric Castleman disease (iMCD) for plasmacytic/mixed histology.[1]

Siltuximab continues to be the first-line therapy recommended by the Castleman Disease Collaborative Network (CDCN) guidelines with Category 1 evidence, regardless of histopathologic subtype.[2]

- Siltuximab (SYLVANT) is recommended as a preferred primary treatment option for the treatment of patients with iMCD (plasmacytic or mixed histology) within NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[1]
- The NCCN Guidelines® also state to continue treatment with siltuximab (SYLVANT) until disease progression occurs in patients with disease responding to primary treatment[1]
- The NCCN Guidelines® also include the consensus diagnostic criteria for iMCD created by the CDCN[1]
- The CDCN recommends siltuximab as first-line therapy for both severe and non-severe iMCD with category 1 evidence, regardless of histopathologic subtype[2]

The only FDA-approved therapy for the treatment of patients with multicentric Castleman disease (MCD) who are negative for human immunodeficiency virus (HIV) and human herpesvirus 8 (HHV-8).[3]

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.[3]

Access the updated NCCN Guidelines

(while supplies last)

Please see Important Safety Information on back and accompanying Full Prescribing Information in pocket.

Abbreviations: FDA, US Food and Drug Administration; IL-6, interleukin 6.

EUSAPharma™ | sylvant® siltuximab