

SYLVANT® (siltuximab) for injection

HCP 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 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 that may be associated or

suggestive of GI perforation.

ADVERSE REACTIONS

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

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

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 for additional important safety information.