Drug Monograph

Drug/Drug Class:	**Sylvant™ (siltuximab) injection/ biologic agent**
Prepared for:	MO HealthNet
Prepared by:	Xerox Heritage, LLC

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Sylvant™ is available in a single-use vial containing either 100 mg or 400 mg of Siltuximab respectively. Janssen Biotech, Inc., Horsham, PA 19044
Summary of Findings:	Sylvant™ produced persistent durable tumor and symptomatic responses of at least 18 weeks' duration in significantly more patients with Multicentric Castleman's Disease (MCD) compared with placebo.
Status Recommendation:	☐ Prior Authorization (PA) Required ☒ Open Access ☐ Clinical Edit ☐ Fiscal Edit
Type of PA Criteria:	☐ Increased Risk of ADE ☒ Preferred Agent ☐ Appropriate Indications ☐ 15 Day First Fill

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payors are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction[2]

Castleman disease is a rare disorder that involves an overgrowth (proliferation) of cells in your body's disease-fighting network (lymphatic system). Also known as giant lymph node hyperplasia and angiofollicular lymph node hyperplasia, Castleman disease can occur in a localized (unicentric) or widespread (multicentric) form.

Dosage Form(s) [1]

Sylvant™ is available in a 100 mg and a 400 mg single-use vial containing 100 mg and 400 mg of Siltuximab respectively.

Manufacturer [1]

Janssen Biotech, Inc., Horsham, PA 19044

Indication(s) [1]

Sylvant™ is for the treatment of MCD in patients who are HIV negative and human herpesvirus-8 (HHV-8) negative.

Clinical Efficacy [1] (mechanism of action/pharmacology, comparative efficacy)

Sylvant™ is a human-mouse chimeric monoclonal antibody that binds soluble and membrane-bound interleukin-6 (IL-6). IL-6 can induce immunoglobulin secretion, and its overproduction is associated with systemic effects in patients with MCD.

Pharmacokinetics

	Sylvant
Volume of distribution	4.5 L
Elimination	0.23 L/day
Half-life	20.6 days

Sylvant ™ demonstrated efficacy in the treatment of MCD in a randomized, double-blind, placebo-controlled, phase 2 clinical trial (n=79). It produced persistent durable tumor and symptomatic responses of at least 18 weeks' duration in significantly more patients when compared with placebo (34% vs 0%) and improved hemoglobin in patients who were anemic.

Multicentric Castleman Disease Study

STUDY DESIGN	Randomized, double-blind, placebo-controlled, multicenter, phase 2 clinical trial (n=79).
INCLUSION CRITERIA	Patients with MCD who were HIV negative and HHV-8 negative.
EXCLUSION CRITERIA	Not specified.
TREATMENT REGIMEN	Patients (median age, 48 years) were randomized to receive best supportive care (BSC) plus Sylvant™ 11 mg/kg IV every 3 weeks (n=53) or BSC plus placebo (n=26) until treatment failure or unacceptable toxicity.
RESULTS	The histologic subtypes of MCD consisted of hyaline vascular (33%), plasmacytic (23%), and mixed (44%). Sylvant™ produced persistent durable tumor and symptomatic responses of at least 18 weeks' duration in significantly more patients when compared with placebo (34% vs 0%). The median time to treatment failure was not yet reached in the Sylvant™ group compared with 134 days in the placebo group. Among the patients who were anemic at study entry (Sylvant™, n=31; placebo, n=11), significantly more patients taking Sylvant™ (61%) achieved at least a 1.5 g/dL increase in hemoglobin at week 13 compared with placebo (0%). None of the patients with hyaline vascular histology responded to Sylvant™.
SAFETY	Not specified.

Contraindications [(1)]

- Severe hypersensitivity to any component

Warnings and Precautions [(1)]

- Gastrointestinal (GI) perforation has been reported; use with caution in high risk patients and promptly evaluate if symptoms suggest GI perforation.
- Infections, concurrent; use not recommended if severe; may mask signs and symptoms of inflammation; monitoring recommended.
- Infusion-related reactions and hypersensitivity (eg, anaphylaxis) may occur; interrupt the infusion for mild to moderate infusion reactions and consider medications; depending on the severity of the reaction, may resume therapy with a reduced infusion rate after resolution of symptoms.
- Live virus vaccines; use not recommended.

Adverse Effects [1]

Most Common, ≥ 10%	Sylvant™ (n=53)	Placebo (n=26)
Rash	28%	12%
Pruritus	28%	8%
Upper respiratory tract infections	26%	15%
Weight increased	19%	0%
Hyperuricemia	11%	0%

Drug Interactions [1]

- CYP450 substrates with narrow therapeutic index: warfarin, cyclosporine, theophylline

Dosage and Administration [1]

- The recommended dose is 11 mg/kg IV over 1 hour every 3 weeks until treatment failure.

Cost

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	COST*/ vial
Siltuximab	Sylvant	Janssen Biotech	100 mg/single-use vial	$833
			400 mg/single-use vial	$3332

*WholesaleAcquisitionCost

Conclusion

Sylvant™ is an IL-6 antagonist monoclonal antibody indicated for the treatment of MCD in patients who are HIV negative and human herpesvirus-8 (HHV-8) negative. It is the first agent approved for the treatment of MCD. Sylvant™ was approved under the US Food and Drug Administration priority review program and was granted orphan product designation. Approval was based on a randomized, double-blind, placebo-controlled, phase 2 clinical trial (n=79) in which Sylvant™ produced persistent durable tumor and symptomatic responses of at least 18 weeks' duration in significantly more patients compared with placebo (34% vs 0%) and improved hemoglobin in patients who were anemic. Sylvant™ has not been studied in patients with MCD who are HIV-positive or HHV-8 positive. The most common adverse effects consist of rash, pruritus, upper respiratory tract infections, weight gain, and hyperuricemia.

Recommendation

MO HealthNet Division recommends Open Access status for this product.

References

1. Product Information: Sylvant™, siltuximab injection. Janssen Biotech, Inc, Horsham, PA, 4/2014.
2. Castleman disease (2014). Retrieved September 5, 2014, from http://www.mayoclinic.org/diseases-conditions/castleman-disease/basics/definition/con20031703

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