09-J2000-16

Original Effective Date: 09/15/14

Reviewed: 06/12/19

Revised: 07/15/19

Subject: Siltuximab (Sylvant™) Injection

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DESCRIPTION:

Castleman's disease is an uncommon lymphoproliferative disorder characterized by enlarged hyperplastic lymph node(s); two different clinical presentations can be distinguished. Unicentric Castleman's disease is an indolent condition that is often treated with local approaches. In contrast, those with multicentric Castleman's disease (MCD) have a more aggressive form of the disease, a less favorable prognosis, and require systemic treatment.

Siltuximab (Sylvant), a chimeric monoclonal antibody that binds human interleukin-6, was approved by the U.S. Food and Drug Administration (FDA) in April 2014 for the treatment of MCD in those who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative. Prior to FDA approval, siltuximab received orphan drug status for the treatment of MCD.

The safety and efficacy of siltuximab were evaluated in subjects (n=53) with MCD who were HIV and HHV-8 negative in a randomized, double-blind, placebo controlled study. Patients received either best supportive care (BSC) and siltuximab 11 mg/kg every 3 weeks or BSC and placebo. The primary endpoint was durable tumor and symptomatic response, defined as tumor response. A durable response was defined as tumor and symptomatic response that persisted for a minimum of 18 weeks without treatment failure.

The durable tumor and symptomatic response in the siltuximab arm was 34% compared to 0% in the placebo arm (95% CI: 11.1, 54.8; p=0.0012). At the time of the analysis, overall survival data were not mature. One year survival rate was 100% in the siltuximab arm and 92% in the placebo arm. The most common adverse reactions (>10% compared to placebo) during treatment with siltuximab were pruritus, increased weight, rash, hyperuricemia, and upper respiratory tract infection.

National Comprehensive Cancer Network (NCCN) Guidelines for Non-Hodgkin's Lymphomas recommend siltuximab as primary treatment for MCD and second-line therapy for relapsed or refractory unicentric Castleman's disease.

POSITION STATEMENT:

Initiation of siltuximab (Sylvant) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

A. Castleman's disease
    1. Member is diagnosed with one of the following:
        a. Multicentric Castleman's disease
        b. Relapsed or refractory unicentric Castleman's disease
    2. Member is human immunodeficiency virus (HIV) negative – laboratory documentation must be provided
    3. Member is human herpes virus 8 (HHV-8) negative – laboratory documentation must be provided
    4. Member has an absolute neutrophil count greater than or equal to 1.0×10^9/L – laboratory documentation must be provided
    5. Member has a platelet count greater than or equal to 75×10^9/L – laboratory documentation must be provided
    6. Member has a hemoglobin less than 17 g/dL – laboratory documentation must be provided
    7. Siltuximab will be used as a single agent
    8. The dose does not exceed 11 mg/kg every 3 weeks
B. Other FDA-approved or NCCN supported diagnosis (not previously listed above)
    1. **ONE** of the following is met:
        a. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)
        b. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation
    2. Dose does not exceed the maximum FDA-approved dose

Duration of approval: 6 months

Continuation of siltuximab (Sylvant) **meets the definition of medical necessity** for the treatment of Castleman's disease or other FDA approved of NCCN supported diagnosis when **ALL** of the following criteria are met:

1. The member has been previously approved by Florida Blue or another healthplan in the past 2 years, OR the member has previously met all indication-specific criteria for coverage
2. Member's disease has not progressed during treatment with siltuximab

3. Member has an absolute neutrophil count greater than or equal to 1.0 x 10^9/L – laboratory documentation must be provided
4. Member has a platelet count greater than or equal to 50 x 10^9/L – laboratory documentation must be provided
5. Member has a hemoglobin less than 17 g/dL – laboratory documentation must be provided
6. Siltuximab will be used as a single agent
7. The dose does not exceed 11 mg/kg every 3 weeks

Duration of approval: 6 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- 11 mg/kg dose given over 1 hour by intravenous infusion every 3 weeks
- Hematology laboratory testing is required prior to each dose for the first 12 months and every 3 dosing cycles thereafter
- Consider delaying treatment if the treatment criteria are not met (Table 1)

Table 1

Treatment Criteria		
Laboratory parameter	**Requirements before first siltuximab administration**	**Retreatment criteria**
Absolute Neutrophil Count	≥1.0 × 10^9/L	≥1.0 × 10^9/L
Platelet count	≥75 × 10^9/L	≥50 × 10^9/L
Hemoglobin	<17 g/dL	<17 g/dL

Drug Availability

100 mg powder, single-dose vial; 400 mg powder, single-dose vial

PRECAUTIONS:

Boxed Warning

None

Contraindications

- Severe hypersensitivity reaction to siltuximab or any of the excipients

Precautions/Warnings

- **Current active severe infections:** Do not administer to patients with severe infections until infection resolves. Monitor patients closely for infections.

- **Vaccinations**: Do not administer live vaccines because IL-6 inhibition may interfere with the normal immune response to new antigens.
- **Infusion Related Reactions:** Administer in a setting that provides resuscitation equipment, medication, and personnel trained to provide resuscitation.
- **Gastrointestinal perforation**: Use with caution with those who may be at increased risk. Promptly evaluate patients presenting with symptoms that may be associated or suggestive of GI perforation.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J2860	Injection, siltuximab, 10 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

D36.0	Benign neoplasm of lymph nodes
D47.Z2	Castleman Disease
R59.0	Localized enlarged lymph nodes
R59.1	Generalized enlarged lymph nodes
R59.9	Enlarged lymph nodes, unspecified

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

DEFINITIONS:

No guideline specific definitions apply.

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. AHFS Drug Information. Bethesda (MD): American Society of Health-System Pharmacists, Inc; 2017 [cited 2017 Apr 20]. In: STAT!Ref Online Electronic Medical Library [Internet]. Available from: http://online.statref.com/.
2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2019 [cited 2019 May 27]. Available from: http://www.clinicalpharmacology.com/.
3. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 2015 Apr 16]. Available from: http://clinicaltrials.gov/.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2019 May 27]. Available from: http://www.thomsonhc.com/.
5. Janssen. Sylvant (siltuximab) injection. 2019 [cited 2019 May 30]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=451f535b-8b6b-4ecf-9f19-d921b72eea39/.
6. National Comprehensive Cancer Network®. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). B-cell Lymphomas, v. 3.2019 [cited 2019 May 30]. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
7. NCCN Drugs & Biologics Compendium [Internet]. Fort Washington (PA): National Comprehensive Cancer Network; 2019 [cited 2019 May 27]. Available from: http://www.nccn.org/professionals/drug_compendium/content/contents.asp/.
8. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2019 [cited 2019 May 27]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 06/12/19.

GUIDELINE UPDATE INFORMATION:

09/15/14	New Medical Coverage Guideline.
06/15/15	Review and revision to guideline; consisting of updating description, position statement, coding, and references.
07/01/15	Revision to guideline; consisting of coding update.
10/01/15	Revision to guideline; consisting of coding update.
11/01/15	Revision: ICD-9 Codes deleted.
01/01/16	Annual HCPCS coding update: added code J2860 and deleted codes C9445 and J3590.
06/15/16	Review and revision to guideline consisting of updating position statement, warnings and references.
10/01/16	Update to ICD-10 codes.
06/15/17	Review and revision to guideline consisting of updating references.
05/15/18	Review and revision to guideline consisting of updating references.
07/15/19	Review and revision to guideline consisting of updating position statement and references.