Effective Date: 11/01/2018

Sylvant® (siltuximab)

FDA approval: April 23, 2014
HCPCS: J3590
Benefit: Medical

Policy/Criteria:

Note: Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the below criteria are met:
   a. Adults with multicentric Castleman’s disease (MCD) who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limit: Quantity Supply = Day Supply
   b. Initial Authorization Period: 3 months
   c. Renewal Criteria:
      i. Lab values are consistent with those listed in Table 1 (and FDA label) for retreatment

C. Sylvant is considered investigational when used for all other conditions, including but not limited to:
   a. Multiple myeloma
   b. Castleman’s disease who are HIV and/or HHV-8 positive

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Therapeutic considerations:

A. FDA approved indication / Diagnosis
   a. 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
      i. Limitation 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 non-clinical study.
*Please refer to most recent prescribing information.

B. Background Information
a. Sylvant (siltuximab) is a new molecular entity human-mouse chimeric monoclonal antibody that binds human interleukin-6 (IL-6) produced by Chinese hamster ovary cells.
b. First-ever drug to be approved by the US Food and Drug Administration (FDA) for the treatment of multicentric Castleman's disease (MCD), a rare blood disorder similar to lymphoma.
c. Current treatment options include tocilizumab (Actemra), an IL-6 receptor antagonist, and rituximab (Rituxan), a CD-20 antibody, have been used off-label for MCD.
d. Castleman’s disease, also known as angiofollicular lymph node hyperplasia, is a rare lymphoproliferative disease. There are two subtypes, unicentric (UCD) and multicentric (MCD) which are recognized as two distinct diseases. MCD is strongly associated with immunosuppression (e.g. HIV infection) and HHV-8 infections and may progress to B-cell plasmablastic lymphoma. HIV/HHV-8 negative MCD is less common.
e. Symptoms of MCD include fever, weight loss, anemia, fatigue, peripheral lymphadenopathy, hepatomegaly, and cough or dyspnea. Most patients die of fulminant infection, progressive disease, or related malignancies.
f. Existing treatment alternatives for HIV/HHV-8 negative MCD include tocilizumab (Actemra), rituximab (Rituxan), chlorambucil (with or without corticosteroids), single-agent (e.g. vinblastine, etoposide) or combination chemotherapy (e.g. CHOP- cyclophosphamide, doxorubicin, vincristine, prednisone, or CVAD-cyclophosphamide, vincristine, doxorubicin, and dexamethasone).
g. Anti-IL-6 therapies such as siltuximab (Sylvant) and tocilizumab (Actemra) are generally ineffective in patients co-infected with either HIV or HHV-8.
h. US 10 year prevalence estimated to be 2.4 per million. Incidence estimated at 0.15 cases per million person years with at least 45 new cases annually.

C. Efficacy
*Please refer to most recent prescribing information.

D. Medication Safety Considerations

Black Box Warning: No

*Please refer to most recent prescribing information.

E. Dosing and administration
a. For intravenous (IV) infusion only.
b. Administer as an 11 mg/kg dose given over 1 hour by intravenous infusion every 3 weeks.
c. Special handling:
   i. Aseptic technique required, should not be kept for more than 2 hours prior to adding to the infusion bag once reconstituted, infusion should be completed within 4 hours of the dilution of the reconstituted solution to the infusion bag

d. Dosing in renal impairment:
   i. No initial dosage adjustment is necessary for patients with CrCl ≥15 mL/min.
   ii. Potential effect in CrCl < 15 mL/min (ESRD) cannot be determined
e. Dosing in hepatic impairment:
   i. No initial dosage adjustment is necessary for patients with mild to moderate hepatic impairment (Child-
Pugh Class A and B).
ii. Severe liver impairment (Child-Pugh Class C) was excluded from study

*Please refer to most recent prescribing information.

F. How supplied
a. 100mg and 400 mg vials

References:

5. 2014 Express Scripts Holding Company – Drug Evaluations
6. © 2014 OmedaRx™ PreviewRx™ - Preliminary Medication Assessments

Policy History

<table>
<thead>
<tr>
<th>#</th>
<th>Date</th>
<th>Change Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>Effective Date: 8/14/2014</td>
<td>New Policy</td>
</tr>
<tr>
<td>1.1</td>
<td>Effective Date: 11/10/2016</td>
<td>Annual Review of Policy</td>
</tr>
<tr>
<td>1.2</td>
<td>Effective Date: 11/09/2017</td>
<td>Annual Review of Medical Policy</td>
</tr>
<tr>
<td>1.3</td>
<td>Effective Date: 11/01/2018</td>
<td>Updated criteria per oncology vendor</td>
</tr>
</tbody>
</table>

* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.